Neuromodulation of Spatial Associations

Evidence from Choice Reaction Tasks During Transcranial Direct Current Stimulation

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To Julia

ZUSAMMENFASSUNG

Wesentliche Anteile des menschlichen Denkens und Verhaltens werden durch implizite Prozesse beeinflusst, die der bewussten Handlungssteuerung wenig zugänglich sind. Obwohl entsprechende Verhaltenseffekte aufgrund automatisch ablaufender impliziter Prozesse gut belegt sind, ist der Ursprung impliziter Handlungsverzerrungen im Gehirn nicht geklärt und wird möglicherweise durch präfrontale Aktivierungen unterstützt. Die vorliegende Arbeit untersucht daher den funktionalen Beitrag des linken präfrontalen Kortex bei impliziten Prozessen, die durch implizite räumlich-numerische Assoziationen (SNARC Effekt) sowie den Impliziten Assoziationstest (IAT) Effekt modelliert werden.

Mittels transkranieller Gleichstromstimulation (tDCS) können kortikale Aktivierungsmuster des präfrontalen Kortex experimentell und niederschwellig manipuliert werden. Hierdurch erlaubt es die tDCS, neurokognitive Hypothesen zur Aktivierung impliziter Prozesse zu testen. Allerdings sind die Effekte der tDCS nicht einzig durch den applizierten Gleichstrom bestimmt, sondern auch durch die aufgabeninduzierte kortikale Aktivität. In der vorliegenden Arbeit erprobe ich eine aufgabenspezifische Zielbestimmung der tDCS durch die systematische Variation und Kopplung der Stimulation mit verschiedenen Aufgaben, Stimuli, und Instruktionen in den erprobten Verhaltensparadigmen.

Hierzu werden implizite kognitive Effekte parallel zur links-hemisphärischen präfrontalen tDCS gemessen, um eine Theorie auf Grundlage des verbalen Arbeitsgedächtnisses zu überprüfen und weiterzuentwickeln. Psychologische Experimente zeigen in einfachen Entscheidungs-Reaktionszeitaufgaben die impliziten SNARC Effekte anhand schnellerer Antworten der linken vs. rechten Hand bei kleineren vs. größeren Zahlen. Eine Reduktion präfrontaler Aktivität durch die kathodale Gleichstromstimulation verringert die impliziten SNARC Effekte bei Zahlen, allerdings zeigt sich keine Modulation von Kompatibilitätseffekten bei der expliziten visuell-räumlichen Präsentation von neutralen Zielreizen.

In weiteren Experimenten zeigen verschiedene Kombinationen der tDCS mit numerischen und nicht-numerischen, ordinalen Zielwörtern weiterhin auch domänenspezifische Einflüsse. Entgegen einer postulierten gemeinsamen Grundlage impliziter räumlicher Assoziationen zeigt die Neuromodulation mit exzitabilitätssteigernder, anodaler tDCS dissoziative Effekte zwischen kardinalen Zahlen und den getesteten ordinalen Sequenzen (Wochentage, Monate). Auf dieser Grundlage entwickle ich ein verteiltes und erweitertes verbales Arbeitsgedächtnismodell impliziter Assoziationen. Dabei wird auch die Möglichkeit von Effekten der psycholinguistischen Markiertheit neben multiplen konkurrierenden verdeckten Kodierungsmechanismen etabliert. Die Generalisierbarkeit dieser Rationale zeigt sich auch in der Reduktion von IAT Effekten durch die kathodale Stimulation.

Ich entwickle hierauf aufbauend eine Hypothese psychologischer Markiertheit, die eine Gemeinsamkeit der impliziten Assoziationsprozesse im flüssigen Zugang zu unmarkierten und salienten Standards postuliert. Stimulationsspezifisch zeigen die Ergebnisse eine polaritätsbezogene Asymmetrie der tDCS Effekte sowie eine Abhängigkeit aufgabeninduzierter Aktivität bei der Neuromodulation, die sich durch die Variation der Aufgabeninstruktionen operationalisieren lässt. Weiterhin ergibt sich, dass die identische Elektrodenkonfiguration abhängig von Eigenschaften der kognitiven Aufgabe zu entscheidend unterschiedlichen Modulationen beobachtbaren Verhaltens führt. Die aufgaben- und domänenspezifische Zielbestimmung der tDCS kann hierdurch optimiert werden.

SUMMARY

Various portions of human behavior and cognition are influenced by covert implicit processes without being necessarily available to intentional planning. Implicit cognitive biases can be measured in behavioral tasks yielding SNARC effects for spatial associations of numerical and non-numerical sequences, or yielding the implicit association test effect for associations between insect-flower and negative-positive categories. By using concurrent neuromodulation with transcranial direct current stimulation (tDCS), subthreshold activity patterns in prefrontal cortical regions can be experimentally manipulated to reduce implicit processing. Thus, the application of tDCS can test neurocognitive hypotheses on a unique neurocognitive origin of implicit cognitive biases in different spatial-numerical and non-numerical domains. However, the effects of tDCS are not only determined by superimposed electric fields, but also by task characteristics. To outline the possibilities of task-specific targeting of tDCS, task characteristics and instructions can be varied systematically when combined with neuromodulation.

In the present thesis, implicit cognitive processes are assessed in different paradigms concurrent to left-hemispheric prefrontal tDCS to investigate a verbal processing hypothesis for implicit associations in general. In psychological experiments, simple choice reaction tasks measure implicit SNARC and SNARC-like effects as relative left-hand vs. right-hand latency advantages for responding to smaller number or ordinal sequence targets. However, different combinations of polarity-dependent tDCS with stimuli and task procedures also reveal domain-specific involvements and dissociations.

Discounting previous unified theories on the SNARC effect, polarity-specific neuromodulation effects dissociate numbers and weekday or month ordinal sequences. By considering also previous results and patient studies, I present a hybrid and augmented working memory account and elaborate the linguistic markedness correspondence principle as one critical verbal mechanism among competing covert coding mechanisms. Finally, a general stimulation rationale based on verbal working memory is tested in separate experiments extending also to non-spatial implicit association test effects. Regarding cognitive tDCS effects, the present studies show polarity asymmetry and task-induced activity dependence of state-dependent neuromodulation. At large, distinct combinations of the identical tDCS electrode configuration with different tasks influences behavioral outcomes tremendously, which will allow for improved task- and domain-specific targeting.

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I would like to thank 214 volunteers who participated in the empirical parts of my thesis (Chapters II-VI). The presented studies and their theoretical implications are based on empirical observations of healthy participants' behaviors in experimental studies. These anonymized participants committed their time and effort to solving simple choice reaction tasks, with or without concurrent stimulation for transient neuromodulation of their brain activity. I wish to appreciate their interest and consent in the studies of psychology, because observations in experimental designs are the critical foundation of any scientific theory as elaborated in the thesis at hand. In this vein, I also take the opportunity to express my gratitude to Prof. Dr. Andreas J. Fallgatter, the director of the Psychiatry Hospital in Tübingen, who generously supported my doctorate studies.

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TABLE OF CONTENTS

ABBREVIATIONS

ANS = Autonomic Nervous System
BOLD = Blood-Oxygen-Level Dependent
CNS = Central Nervous System
dlPFC = dorsolateral Prefrontal Cortex
fMRI = functional Magnetic Resonance Imaging
IAT = Implicit Association Task
IPS = Intraparietal Sulcus
M1 = Primary Motor Cortex
mA = milli Ampere
MARC = Markedness Association of Response Codes
MEP = Motor Evoked Potential
mPFC = medial Prefrontal Cortex
ms = milliseconds
NIRS = Near-Infrared Spectroscopy
PE = Percentage of Errors
PFC = Prefrontal Cortex
RT = Response Times
SNARC = Spatial-Numerical Association of Response Codes
SO = (contralateral) Supra-Orbital Region
tES = transcranial Electric Stimulation
  tACS = transcranial Alternating Current Stimulation
  tDCS = transcranial Direct Current Stimulation
  tRNS = transcranial Random Noise Stimulation
TMS = Transcranial Magnetic Stimulation
V1 = Primary Visual Cortex
WM = Working Memory
Xc = extracephalic tDCS return placement (~ contralateral upper arm)

LIST OF PUBLICATIONS

A) Accepted Papers

Schroeder, P.A., Dresler, T., Artemenko, C., Bahnmueller, J., Cohen-Kadosh, R., Nuerk, H.-C. (2017). Cognitive enhancement of numerical and arithmetic capabilities: A mini-review of available transcranial electric stimulation studies. *Journal of Cognitive Enhancement*, 1(1):39-48. doi:10.1007/s41465-016-0006-z

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Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2017). Space in Numerical and Ordinal Information: A common construct? *Journal of Numerical Cognition*, *3*(2):164-181. doi:10.5964/jnc.v3i2.40

Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2017). Prefrontal neuromodulation reverses spatial associations of non-numerical sequences, but not numbers. *Biological Psychology, 128:*39-49. doi:10.1016/j.biopsycho.2017.07.008

Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2017). Switching Between Multiple Codes of SNARC-like Associations: Two Conceptual Replication Attempts with Anodal tDCS in Sham-Controlled Cross-Over Design. *Frontiers in Neuroscience, 11*:654. doi:10.3389/fnins.2017.00654

Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2018). Reduction of Implicit Cognitive Bias with Cathodal tDCS to the Left Prefrontal Cortex. *Cognitive, Affective, & Behavioral Neuroscience,* 18(2), 263-272. doi:10.3758/s13415-018-0567-7

B) Submitted Manuscripts

– No Further Manuscripts –

C) Ready for Submission Manuscripts

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PERSONAL CONTRIBUTIONS

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> *PAS and CP designed the study. PAS collected empirical data. All authors contributed to data analyses and interpretation. PAS, RP, and CP wrote the first draft, all authors contributed to the revised manuscript. All authors approved the final version for publication.*

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> *All authors designed the study together. PAS ran participants and wrote the first draft. All authors contributed to the analyses, interpretation, revision of the manuscript, and approved the final version for publication.*

Chapter IV: Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2017). Prefrontal neuromodulation reverses spatial associations of non-numerical sequences, but not numbers. *Biological Psychology, 128*:39-49. doi:10.1016/j.biopsycho.2017.07.008

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Chapter V: Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2017). Switching Between Multiple Codes of SNARC-like Associations: Two Conceptual Replication Attempts with Anodal tDCS in Sham-Controlled Cross-Over Design. *Frontiers in Neuroscience, 11*:654. doi:10.3389/fnins.2017.00654

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GENERAL INTRODUCTION

Essential portions of cognitive processing happen implicitly and automatic, much like habitual responses to internally perceived stimuli and without being necessarily consciously intended. Such mechanisms of implicit cognitive processing can offload restricted capacities when operating on a task and still govern human thinking and acting in a goal-relevant direction, but the unintended processes may influence decisions also in less adaptive ways or even thwart more abstract deliberate goals. Intuitively, by drawing on implicit biases, the heavily filtered neurocognitive systems can consider increased amounts of information than available to deliberate decision making, which was already established in early psychological research on heuristic decisions and anchoring biases (Tversky & Kahneman, 1974) and is still reflected in recent views on heuristics (Gigerenzer & Gaissmaier, 2011). In the first seminal studies, the initial presentation of an arbitrary numerical value would bias subsequent judgments of quantity estimation or intuitive multiplication (adjustment from an anchor; Tversky & Kahneman, 1974). In fact, to date, many more cognitive biases in various overt and also in subtler behaviors were discovered. Implicit biases are not always available to an agent’s deliberate awareness, e.g., as assessed in self-report measurements (Gawronski & De Houwer, 2014) or as compared with explicit tasks (Priftis, Zorzi, Meneghello, Marenzi, & Umiltà, 2006). However, the neurocognitive mechanisms that maintain, activate, or even produce such implicit biases are poorly understood and a majority of research in psychology, psychiatry, and cognitive neuroscience is focused on the mechanisms that inhibit cognitive biases, rather than on the neurocognitive sources that characterize them.

Of course, domain-specific processes that pertain to the exact stimulus domains are involved in different implicit biases. For example, implicit spatial-numerical association in the SNARC effect would also recruit bilateral parietal regions based on their involvements in spatial and numerical cognition, as well as multisensory integration. Beyond that, paradoxically, the human prefrontal cortex (PFC) can be hypothesized to be a highly influential brain region that would contribute to both the inhibition of cognitive biases, but also their active maintenances. Importantly, already the influential integrative theory of PFC function by Miller & Cohen (2001) proposed that unique prefrontal characteristics allow for the selected maintenance of information regardless of sensory input along rich association networks (Miller & Cohen, 2001, p. 180, p. 175). While this theory was not specifically designed to account for implicit associations, its characteristics appear well suited to allow for activations thereof.

At first, this claim does not fit well to the notion that implicit biases are generated and maintained relatively automatically and without deliberate effort, given that the PFC is not a critical structure for simple and habitual behaviors such as orienting or bottom-up reactions to external stimuli. However, PFC is indeed characterized by a comprehensive connectivity throughout much of the remaining cortex. Moreover, as implicit biases must necessarily build on some kind of internal processing, the PFC's relevance in active maintenance of information (Miller & Cohen, 2001) may be well suited to perform this behavior. In fact, computational modeling confirms that PFC serves to recurrent connectivity and active maintenance of information (Botvinick & Cohen, 2014). However, the causal involvement of PFC in implicit biases had not been established experimentally in neuromodulation studies, eg., by transient controlled changes in brain excitability from tDCS (transcranial direct current stimulation), which is essential for understanding behaviorally relevant brain activity patterns. Therefore, the present thesis investigates effects of prefrontal tDCS on implicit associations as modelled by the SNARC effect, while considering both domain- and stimulus-specific processing in numerical cognition, but also domain-general effects on the activation of implicit associations.

A modulation of implicit processes in general also holds a certain therapeutic potential for psychiatric conditions that include biased information processing. Beyond that, implicit cognitive simulations of very basic sensorimotor patterns may even set the grounds for an understanding of abstract verbal concepts without direct physical manifestation, such as *love*, *loss*, or *good* and *bad* (Barsalou, 2008; Casasanto, 2009). Considering also domain-specific activations and frontoparietal numerical cognition networks (e.g., Klein et al., 2016), numbers and their associated *numerical magnitude* provide highly insightful effects that allow researchers to also investigate this embodied cognition proposal (Fischer, 2012): In order to grasp the meaning of *four*, it may be instructive to draw on visual experiences with groups of four objects, movements with four fingers, and so on. In the external world, physical magnitudes coincide with visual dimensions: More apples cover more area of visual space, fill a basket to the brim, and extend to the left or right when aligned in a row. The magnitude concept itself can be flexibly utilized by neurocognitive mechanisms when applied to groups of real and virtual objects (such as a currency). It thus appears intuitive for human agents to include visual, visuo-spatial, and motor simulations to achieve a precise internal representation of verbal thoughts such as *four* or *Thursday*. Currently, however, multiple theories are discussed in numerical cognition research and there is no agreement on the precise cognitive mechanisms beyond spatial-numerical associations. Furthermore, it is not clear whether seemingly related implicit associations in different stimuli (e.g., numbers or weekdays) or even entirely different domains (e.g., implicit spatial associations or implicit insect-flower negative-positive evaluations; Greenwald et al., 1998; Proctor & Cho, 2006) draw on (a) generalizable cognitive mechanism(s).

Much previous research indeed approves that a confrontation with single stimuli (e.g., single-digit number symbols) can activate another spatial tendency that effectively facilitates or interferes with spatial decisions that are required by a task. In respective psychological experiments, participants are repeatedly asked to classify stimuli by means of a button press with their left or right index finger. The recordings of their response latencies (and errors) can be differentiated across different conditions and allow for proxy evaluation of the involved cognitive processes. With numerical stimuli, it is consistently observed that left-hand decisions are faster for small digits (e.g., *4*), and right-hand decisions are faster for large digits (e.g., *8*). Interestingly, this behavioral signature – termed the SNARC effect – is even apparent when decision criteria do not necessarily require the activation of the magnitude concept. Routinely, in SNARC research, stimulus judgments are made upon the parity status of a number (Dehaene, Bossini, & Giraux, 1993; Wood, Nuerk, & Willmes, 2006b). Moreover, numerical stimuli can bias the execution of overt movements such as walking decisions (Shaki & Fischer, 2014). But also the other way round, when asked to name random digits, participants' choices can be influenced by head rotation directions (Loetscher, Schwarz, Schubiger, & Brugger, 2008). Considering these vast consequences of implicitly activated spatial-numerical associations, automatically acting upon them may occur detrimental in certain situations. For instance, when asked to distribute playing cards in a fair way to two opposing players, student volunteers displayed a small, but consistent bias favoring the player seated on the right-side, who steadily received more cards and cards of higher value (Schroeder & Pfister, 2015).

Although the phenomenon of SNARC is one of the key findings in numerical cognition research, with more than 2,100 citations of Dehaene et al.'s original research report from 1993 and hundreds of replications in different experimental approaches, its theoretical interpretation is still not agreed upon and multiple elaborate conceptions controversially discuss its underlying cognitive foundation(s). Recent theories pointed to a critical involvement of verbal working memory, which is typically associated with left-hemipsheric prefrontal activation patterns in imaging studies (Smith & Jonides, 1997; D'Esposito et al., 1998; Baddeley, 2003), as was also confirmed by recent tDCS results (Ruf, Fallgatter, & Plewnia, 2017). Moreover, previous tDCS studies in different verbal working memory tasks showed effectivity of a left-hemispheric electrode configuration with extracephalic return electrode placement (Zaehle et al., 2011; Wolkenstein et al., 2014).

The aim of the present thesis is to examine effects of this PFC neuromodulation on SNARC effects and to juxtapose predictions from different theoretical accounts. Moreover, using the SNARC effect as a model for implicit associations (Chapters II – V) and later extending upon another behavioral signature in the Implicit Association Test effect (IAT effect; Chapter VI), I will provide an initial demonstration showing how, with which stimuli, and under which circumstances a neuromodulation with tDCS can alleviate the internal activation of biased cognitive processing. Stimulation of brain areas with tDCS offers an innovative and cost-efficient, yet relatively controversial approach to investigate the causal involvement of cortical areas in different behaviors. However, neuromodulation with tDCS provides interesting options for training and remediation in psychiatric and neurologic conditions. For these reasons, it is important to also outline the basic principles of tDCS for neuromodulation of implicit cognition. In the present thesis, I vary the stimulus and instruction parameters for cognitive tasks that were performed concurrent to stimulation with the same electrode configuration across studies, which demonstrates systematically different behavioral outcomes due to task-specific targeting. Likewise, the manipulation of a prefrontal brain network with tDCS is used as experimental manipulation to advance the theoretical and neurocognitive basis of implicit spatial associations in the SNARC effect.

Theories on the SNARC Effect

The neuromodulation studies presented in this thesis will utilize the SNARC effect as a well-studied behavioral index of implicit associations. Based on previous accounts, theoretical predictions can be tested with tDCS in a systematic framework according to the taxonomy of spatial-numerical associations. To understand differential effects from prefrontal tDCS, domain-specific aspects have to be considered, which will be introduced in the next section along with a brief presentation of the most relevant theoretical accounts.

The Mental Number Line Account

The Spatial-Numerical Association of Response Codes (SNARC) effect describes the behavioral performance of healthy human participants in spatially distributed bimanual classifications of numerical symbols. The original finding of the SNARC effect reflects the relative latency (and accuracy) advantage of responding with the right hand to large numbers and with the left hand to small numbers, when the number parity status (odd vs. even) is evaluated (Dehaene et al., 1993; Wood, Willmes, Nuerk, & Fischer, 2008). Similar response patterns are obtained in magnitude classification tasks (large vs. small decision). When symbolic numerals precede a target stimulus situated towards the left or towards the right of a visual display, spatial-numerical associations could facilitate the detection of the non-numeric visual target in respective locations for a specific time window between number and target onset (Fischer, Castel, Dodd, & Pratt, 2003; but see Zanolie & Pecher, 2014 for 5/6 published failed replications and the upcoming registered replication report by Holcombe et al., in preparation). Moreover, SNARC effects were also observed in free-choice tasks (e.g., without a predefined decision rule) and participants were more likely to respond with the left (right) hand to small (large) numbers (Ruiz Fernández, Rahona, Hervás, Vázquez, & Ulrich, 2011; Schroeder & Pfister, 2015). When asked to randomly produce number sequences, head turn and gaze directions predicted the generation of relatively small or large numbers (Loetscher, Bockisch, Nicholls, & Brugger, 2010; Loetscher et al., 2008). In all of these tasks, a spatial response dimension is superimposed on responding, but a purely conceptual link between numerical magnitude and spatial direction (operationalized in leftwards- and rightwards-facing object displays) was also observed when a single (non-spatial) response in a Go-Nogo Implicit Association Test was required (Fischer & Shaki, 2016, 2017). However, with classification features not necessarily connected to number semantics such as font color, SNARC effects are not always observed (at least they are reduced in size; Fias, Lauwereyns, & Lammertyn, 2001;

see also Chapter III).[1] Nevertheless, the firm link between numbers and spatial direction under various circumstances is corroborated by a long tradition of research in manifold paradigms. However, its theoretical underpinning is currently not fully understood.

The *Mental Number Line* account of the SNARC effect proposes that spatial codes are an intrinsic part of the representation of numerical information in long-term memory. Proponents of the mental number line hypothesis argue that a left-to-right visuospatial representation of numerical magnitude is based on shared processing pathways for spatial and numerical information in parietal regions of the brain (Hubbard, Piazza, Pinel, & Dehaene, 2005). The fixed and predefined nature of a hypothesized mental number line was further corroborated by highly controversial evidence from non-human animals and preverbal, neonate humans: Using specialized tasks, it was shown that newly fetched chicks (Rugani, Vallortigara, Priftis, & Regolin, 2015), chimpanzees (Adachi, 2014), gorillas and orangutans (Gazes et al., 2017), but also neonate children’s behaviors can reveal directional spatial-numerical associations akin to the SNARC effect (Rugani & de Hevia, 2017). The mental number line hypothesis holds that spatial associations of number concepts present an inborn architecture which can be readily incorporated for later numerical learning and mathematics (Dehaene, 2011; Rugani et al., 2015). Yet, of course, more recent theories on human behavior can better account for results from psychological studies in adults. Moreover, it is mandatory to note severe limitations to the transfer of controversial results from different paradigms in animal studies to theories of human cognition, and fundamental criticeria for number-to-space mappings that were overlooked in some animal studies (Patro & Nuerk, 2016; Núñez & Fias, 2017). For example, at closer inspection, a left-to-right spatial-numerical bias was not consistently observed in all gorillas and orangutans (Gazes et al., 2017), contradictorily to the steady patterns observed in newly hatched chicks (Rugani et al., 2015).

Nevertheless, a shared neural circuitry for space and number in parietal brain regions is generally accepted given a vast amount of neuroimaging, patient and also animal studies (Arsalidou & Taylor, 2011; Bueti & Walsh, 2009; Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Hubbard et al., 2005). The mental number line view was also bolstered by

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[1] As a side note, results from the Garner and Stroop paradigms demonstrated that numerical magnitude can be processed also without automatic intrusion of irrelevant size information, if all factors of context were matched to the same degree of salience and discriminability (Pansky & Algom, 1999).

recordings of seemingly topographic numerosity maps in parietal regions, most prominently in the intraparietal sulcus (Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004), and more recently also distributed across other brain areas in the form of multiple topographic numerosity maps (Harvey & Dumoulin, 2017). Specialized number-selective neurons were observed in primate prefrontal and parietal cortex areas (Nieder, 2016; Tudusciuc & Nieder, 2009). Evidence from right brain-damaged patients with hemispatial neglect indicated resembling errors for numerical and physical bisection (i.e., patients had to indicate the midpoint of a numerical interval or of a physical line). This finding was taken to indicate that mental number lines and physical lines share a common neurocognitive metric (Umiltà, Priftis, & Zorzi, 2009; Zorzi, Priftis, & Umiltà, 2002). Furthermore, neglect patients showed deficits also for vertical mappings of numerals in the lower middle range, pointing to more general spatial mapping mechanisms (Mihulowicz, Klein, Nuerk, Willmes, & Karnath, 2015). However, there were also dissociations between physical spatial and mental number bisection tasks in patients with prefrontal damage, which was not compatible with the proposal that visuospatial operations and number processing would recruit the same brain networks (Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005).

Developmental Theories: Between Innate and Encultured Spatial-Numerical Associations

In recent years, primarily behavioral studies in experimental psychology have accumulated other findings as well, which are not entirely compatible with a purely fixed association between numbers and space. The most radically opposed theoretical view holds that spatial-numerical associations are shaped by continuous sensorimotor experience with the environment (Patro, Nuerk, & Cress, 2016). In fact, very bodily number experiences such as finger counting habits appear to be predictive of the spatial orientation of numbers in several empirical studies (Fischer, 2008; Fischer & Shaki, 2017). This embodied cognition account will not be introduced or discussed in depth here due to a lack of immediate relevance to the current investigations, but its general significance may be briefly highlighted.

Moreover, a recurrent debate on developmental theories regards whether numerical capacities are innate or encultured (e.g., see discussions by Nieder, 2017 & Núñez, 2017). Interestingly, this debate also includes the presence of implicit spatial-numerical associations in neonate children (Rugani & de Hevia, 2017) and non-human animals (e.g., Gazes et al., 2017). Empirical evidence is available for both accounts: For instance, next to capabilities for non-numerical magnitude processing even in wild animals (Benson-Amram, Heinen, Dryer, & Holekamp, 2011) or fish (Agrillo, Miletto Petrazzini, Bisazza, 2017), spatial-numerical abilities are available in chicken and non-human primates as well (Rugani et al., 2015; Gazes et al., 2017; but see Patro & Nuerk, 2016). However, the latter study also documented large individual variability in the tested orang-utans and gorillas, which somewhats contradicts a purely hardwired and biological source of spatial-numerical associations in these animals. At least in humans, enculturation was put forward as a highly influential factor in numerical cognition (Ansari, 2008) and a potential cause for differenes in spatial-numerical directionality based on reading habits (Shaki, Fischer, & Petrusic, 2009), but also as reflected by the effects of finger counting habits (M. H. Fischer, 2008). Moreover, in preschool children, brief directional spatial-numerical experiences could trigger directed SNARC effects (Patro, Nuerk, & Cress, 2015), but preliterate children showed different response tendencies dependent on the exact task, e.g., object counting, numerical, or finger counting (Patro & Haman, 2018).

In brief, while this debate cannot be concluded exhaustively here, it is also relevant to the current thesis, because results from animal studies and developmental psychology also encompass theoretical restrictions, e.g., purely verbal origins are hardly the source of implicit spatial-numerical associations in these species. As I will argue throughout this work, the existence of spatial-numerical associations in non-verbally communicating animals and the importance of markedness processing are not mutually exclusive if considering multiple coding strategies and a psychological interpretation of default (unmarked and marked) features which emerge through fluent action, which is consistent with an enculturation account.

Situated Influences

Most importantly, the malleability of SNARC effects by different task context instructions (also discussed as situatedness; Cipora et al., in press) appears to involve a more flexible cognitive processing in humans than a literal mental number line. For example, when participants read texts that included small and large numbers either printed on the left-side or the right-side of a visual display, respectively, and vice versa, the SNARC effect was flexibly modulated in its direction (Fischer, Mills, & Shaki, 2010). But also at a more rapid pace, it was observed that SNARC effects can vary in their effect size as a function of responding on a previous trial in the so-called congruency sequence effect (Pfister, Schroeder, & Kunde, 2013). Even earlier, it was suggested that the SNARC effect would not display a fixed component of the long-term representation of numbers, but rather a dynamic allocation to different representation reference frames (Fias & Fischer, 2005). To date, situatedness and flexibility of SNARC effects in humans (but also in apes, Gazes et al., 2017) are established findings, which already contradicts the position of a fixed mental number line. These and other results led to alternative nuanced theoretical accounts of the SNARC effect that will be introduced and explicated next.

The Verbal Working Memory Account

Already in the earliest seminal article on the SNARC effect, Dehaene et al. (1993, Exp. 4) explored the idea that mental associations in spatial dimensions are driven by the general sequential structure of stimuli, and not (exclusively) by the concept of numerical magnitude in terms of cardinal quantity (i.e., set size). Since numbers can ambiguously reflect both the order of a sequence or precisely convey quantity information, Dehaene et al. (1993) also studied spatial associations of alphabetical letters in two different tasks. Importantly, letters are taken to indicate clear sequential information, but not numerical quantity information. For instance, alphabetically, it can be generally said that *B* follows *A*, but *B* is not accepted to indicate double the amount of *A* (e.g., in contrast to the number symbols *1* and *2*). In Dehaene's study, the first letter task was isomorphic to a parity judgment task with arbitrary letter groups assigned to left-hand and right-hand buttons (ACE vs. BDF). The second task was a consonant-vowel classification with letter stimuli distributed across the whole alphabet (A, C, E, G, I, L, O, R, U, and X). However, neither task induced a significant SNARC-like effect in terms of a correspondence between letter sequence position with spatial left-hand over right-hand responding. Thus, the origin of SNARC was first assumed to be exclusively numerical.

This interpretation was challenged by later data that documented SNARC-like effects with non-numerical, but (exclusively) sequential stimuli in classification tasks actively incorporating the ordinal information. In the order-relevant letter tasks, specifically, participants were to indicate whether a letter (E, G, I, L, R, U, W, and Y) came before or after the reference letter O. In a separate order-irrelevant task, participants performed a consonant-vowel classification of the same letter stimuli. With more participants than in experiment 4 from Dehaene et al. (1993), and bolstered by additional linear regression analyses earlier introduced for the study of SNARC effects (Fias, Brysbaert, Geypens, & D'Ydewalle, 1996), scientists documented significant spatial associations elicited by letters and month names (Gevers, Reynvoet, & Fias, 2003), and also by weekdays (Gevers, Reynvoet, & Fias, 2004).

In the *working memory account of the SNARC effect* (van Dijck & Fias, 2011), the neurocognitive process for linking order with space is elaborated upon and a single mechanism is proposed based on the results of a delayed working memory (WM) procedure. Empirically, a novel paradigm was introduced to dissociate numerical magnitude from ordinal information in number symbols: By keeping in memory a series of random digits during a delay period, the task can flexibly assign a new and unique ordinal information to numerical digits (van Dijck & Fias, 2011; see also: Lindemann, Abolafia, Pratt, & Bekkering, 2008). SNARC-like signatures emerged for the new item order when participants were then asked for parity decisions on the maintained digits in a delay phase (and they also had to reject digits outside of the maintained item set to activate the order information; Ginsburg, van Dijck, Previtali, Fias, & Gevers, 2014). Importantly, these SNARC-like effects appeared to flexibly adjust to the order of the WM sequence, but not the semantic digit magnitude. In Posner tasks, the stored sequential items could facilitate the visual detection of a corresponding cue, thus actively directing attention (van Dijck, Abrahamse, Acar, Ketels, & Fias, 2014), as was also assumed for the SNARC effect with number symbols (Fischer et al., 2003; but see Holcombe et al., in preparation).

Amid these observations, the previous studies were still not fully convincing as to whether the sequence-position WM account could fully explain the SNARC effect obtained in single-task settings. For instance, different manipulations already demonstrated that the SNARC effect was modulated by contextual manipulations (Fischer et al., 2010; Pfister et al., 2013), including additional WM load (Herrera, Macizo, & Semenza, 2008; van Dijck, Gevers, & Fias, 2009), as it is also clearly imposed upon participants by asking them to maintain random digit or other object sequences. Moreover, using the delayed WM paradigm, Huber et al. (2016) documented co-existing spatial associations which were driven by both numerical magnitude and sequential order. In the most recent theoretical complementation of the WM account of the SNARC effect, this fact was acknowledged and the according mechanism was adjusted (Abrahamse, van Dijck, & Fias, 2016). In brief, this proposal highlighted the functional coordination of sequential stimuli along spatial dimensions elicited by specific tasks at the level of WM. It was hypothesized that in such cases a spatial template is flexibly fitted to effectively represent the sequential set, allowing for further computation by the exact task requirements (previously referred to as the mental whiteboard hypothesis; Abrahamse, van Dijck, Majerus, & Fias, 2014). The systematic and frequent use of spatial associations for ordered item sets would also lead to long-term memory representations. Triggered by number items in a left-to-right orientation due to experience, spatial codes would then be generated due to referential coding of items in the WM sequence. Multiple item sets could be active in WM, accounting for parallel spatial-numerical and -positional associations (Abrahamse et al., 2016).

Verbal-Spatial Categorical and Linguistic Accounts

So far, I discussed spatial associations as unitary and visuospatial concept, possibly characterized by the ordinal meaning of target stimuli in case of the WM account of the SNARC effect. In contrast to this, multiple modality-specific coding mechanisms could be involved in the generation and maintenance of the internal information. In Paivio's outstanding work on mental representations in general, for example, dual-coding theory proposes at least two internal codes to be involved in a cognitive representation of abstract words in the form of pictorial Imagens and verbal Logens (Paivio, 1986). This approach is largely compatible with the influential separation of WM into verbal, visuospatial, and central-executive components of working memory (Baddeley, 1992, 2000), possibly also including serial-order (Hurlstone, Hitch, & Baddeley, 2014). Importantly, coined for abstract number representations and somewhat paralleling the view that multiple coding strategies are available for mental representations, Dehaene suggested the Arabic, verbal, and analogical magnitude codes to subserve number representations in his influential triple-code model (Dehaene, 1992). With number symbols, the unresolved matter pertains to the question as to whether spatial-numerical associations specifically or even numbers in general are encoded in a single symbolic and modality-independent representation (Cohen Kadosh & Walsh, 2009; Nuerk, Wood, & Willmes, 2005). Finally, verbal and modality-specific influences can be also garnered to better specifiy the *processes* rather than the *representations* that link number with space.

Interestingly, effects of verbal processes were already considered in the original publication of the SNARC effect (Dehaene et al., 1993; experiments 8 & 9). In their experiments, it was observed that the SNARC effect was reduced for verbal number words and also for mirror-image verbal words as compared to Arabic symbols. This result led to the interpretation that different notation-specific representations can be used for mental operations, because SNARC effects should be identical if they were converted from the presented notation to a common format. In a later study, the critical role of verbal processing was picked up and highlighted experimentally in magnitude comparison tasks by means of visual-verbal spatial labels next to the response keys (Gevers et al., 2010). In one of their conditions, the response labels were exactly opposed to the physical (and bodily) response dimension, that is: the left-hand key was labeled as “RECHTS” (right) and the right-hand key was labeled as “LINKS” (left). In this condition, intriguingly, spatial-numerical associations emerged for label positions, thus the SNARC effect appeared to be reversed from a physical spatial viewpoint, being factually aligned from right-to-left (Gevers et al., 2010; Imbo, Brauwer, Fias, & Gevers, 2012).

Furthermore, SNARC effects were also studied with crossed hands, but results were overall inconsistent. Verbal labels could address these inconsistencies because fixed “left”- “right” response key labels were available when significant SNARC effects emerged in parallel design (Dehaene et al., 1993). In contrast to this, SNARC effects were diminished in the crossed-hands condition of another study in cross-over design (Wood, Nuerk, & Willmes, 2006a).

Having touched upon the role of verbal processing in the SNARC effect, it can now be also illustrated *how* verbal mechanisms may exert their influence. I will introduce two similar theoretical accounts: the polarity correspondence account and the linguistic markedness of response codes (MARC) effect.

Polarity Correspondence

The polarity correspondence account suggests that a structural similarity between two concept characteristics (such as small / large numerical magnitude and spatial left / right responding) is sufficient to obtain stimulus-response compatibility effects like the SNARC effect and other implicit biases (Proctor & Cho, 2006), including the renown Implicit Association Test (IAT) effect.[2] Importantly, this view can explain the compatibility effects in SNARC and other tasks without requiring a perceptual or conceptual overlap of the two crossed dimensions. Instead, it is determined that any task-related dimension can be coded into a “+” polarity and a “-” polarity, possibly along a continuum (see also: Lakens, 2012). The core assumption states that a correspondence between polarity codes facilitates response selection and thus produces faster latencies, which also explicitly accounts for a series of reported effects including SNARC and IAT effects (Proctor & Xiong, 2015).

As a generalized model, the polarity correspondence principle was criticized to not account for some empirical research findings. For example, the SNARC effect remained unchanged when polarity in the response dimension was modulated experimentally by changing the physical position of response keys (i.e., a keyboard was moved to the left/ right of participants); in turn, the perceptual correspondence of response keys with visually displayed spatial information in another spatial conflict effect (Simon effect; see also: Chapter II) was reversed (Santiago &

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[2] The Implicit Association Test (IAT) actually describes a certain procedure and it is a prominent paradigm in social and clinical psychological research (Greenwald et al., 1998; Roefs et al., 2011). The test is used to detect implicit associations between different target and attribute concepts, including stereotypes and biased processing in psychiatric conditions. Please refer to Chapter VI for a more elaborate description of the IAT.

Lakens, 2015). Further questioning the generalizability of polarity correspondence, congruency effects between even-odd judgments of Arabic single-digits using left-right and good-bad vocal classifications revealed selective interactions between space and number (e.g., SNARC) only for left-right classifications, but not for good-bad classifications. In contrast, associations between number parity and space were obtained for good-bad classifications only (Leth-Steensen & Citta, 2016).

Linguistic Markedness

Another verbal account was proposed based on observed associations between number parity and spatial responding in the markedness association of response codes (MARC) effect (Nuerk, Iversen, & Willmes, 2004; Berch, Foley, Hill, & McDonough Ryan, 1999). Here, the authors documented a compatibility effect with faster latencies for right-hand responding to *even* numbers and left-hand responding to *odd* numbers. In contrast to the polarity correspondence account, the MARC effect proposed shared assignment of a linguistic mark (as opposed to polarity) for the difficult classifications of *odd* and *left*. However, this parity-space association could be replaced by asking for multiples-of-three (3, 6, 9; the *6* was excluded in their actual test to juxtapose judgments on odd vs. multiple-of-three status), which would lead to compatibility between *yes-even* and *no-odd* pairs (Cho & Proctor, 2007). Although this result effectively also showed a reversal of the original parity-space association, it is actually consistent with both linguistic markedness (i.e., *no* and *odd* are considered marked) and polarity correspondence, given that the task-relevant linguistic structure was a yes-no classification. Notably, individual and group differences in MARC effects were documented early on, somewhat limiting the universal validity of fixed linguistic structures and suggesting additionally involved psychological processes (Iversen et al., 2004, 2006; Huber et al., 2016).

Linguistic markedness is a rather extensive linguistic concept that describes how and why verbal structures are derived from their original form. Marked members of apparently binary pairs can be recognized by the presence of pre- or suffixes, a more specific meaning (e.g., dog vs. bitch), or a relatively lower distributional frequency, rendering the marked members more complex, difficult, or abnormal. Thus, already the surface structure of the respective word members displays a certain asymmetry (Jakobson, 1932). Psychologically, one of the two members is usually perceived as more convenient, which was captured by learning-related, generative accounts of markedness (Battistella, 1995; Chomsky, 1965). Marked feature members are acquired later in development and lead to worse performance in cognitive tasks.

In judgments of numerical symbols, for example, the *odd*-effect describes longer response times to odd number symbols than to even ones (Hines, 1990). As explicated above, classification dimensions that share marked or unmarked codes are faster to process, which is somewhat conceptualized in both the markedness correspondence and polarity correspondence principles.

Both presented accounts thus provide alternative explanations for the apparent associations between concepts such as space and number, or space and order, as reflected in the SNARC effects. The accounts essentially capture a categorical polarity-based coding, but operate at different levels of description: Whereas the polarity correspondence account was presented as general principle, the linguistic markedness account offers a higher degree of resolution and precise predictions. Earlier, the MARC effect was even perceived to describe the association between parity and space exclusively, but also the *small*/ *large* classifications in magnitude comparison tasks[3] could actually constitute verbal markedness correspondence (Schroeder & Pfister, 2015; see also Chapter IV: SNARC becomes MARC).

The Taxonomy of Spatial-Numerical Associations

Complementary to the efforts of previous theories to unify spatial associations and to expose a potential single underlying cognitive mechanism, it may prove equally important to address and theoretically envelop the diversity of spatial associations within, but also across stimulus domains. This becomes especially important when considering that spatial associations had been documented also in arithmetic operations, for multi-digit place-value integration, but also for non-symbolic number presentations. As originally evidenced for spatial-numerical associations in children, the taxonomy of spatial-numerical associations discriminates spatial extension vs. spatial direction and ordinality vs. cardinality (Patro, Nuerk, Cress, & Haman, 2014). To also consider results from adult studies, an extended version of the taxonomy was introduced which also considered the directional associations in arithmetic operations (e.g., operational momentum; McCrink, Dehaene, & Dehaene-Lambertz, 2007). Moreover, the important distinction between implicit and explicit activation of directional spatial associations was introduced to the taxonomy (Cipora, Patro, & Nuerk, 2015). This distinction between explicit and implicit processes highlights that directional spatial information can be generated

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[3] In the laterality effect, it was established that number symbols are automatically classified as being small or large, at least for the 1-9 number range crossing “5” (Cohen Kadosh, 2008; Tzelgov, Meyer, & Henik, 1992).

intentionally in different tasks such as counting (explicit), but there are also numerous reports of interference with directional spatial information that was generated without direct instruction, such as in the SNARC effect (implicit). As it is long accepted in the literature on IAT effects, implicit and explicit associations of the same dimensions were driven by convergent and discriminatory mechanisms (e.g., Nosek, Greenwald, & Banaji, 2007). Eventually, the neuromodulation studies presented in this thesis will utilize the taxonomy of spatial associations to provide a systematic framework for domain-specific influences on the implicit spatial directional coding of numbers and to test according theoretical predictions. A simplified model of the most recent taxonomy from Cipora et al. (in press) is presented below (Figure 0.1).

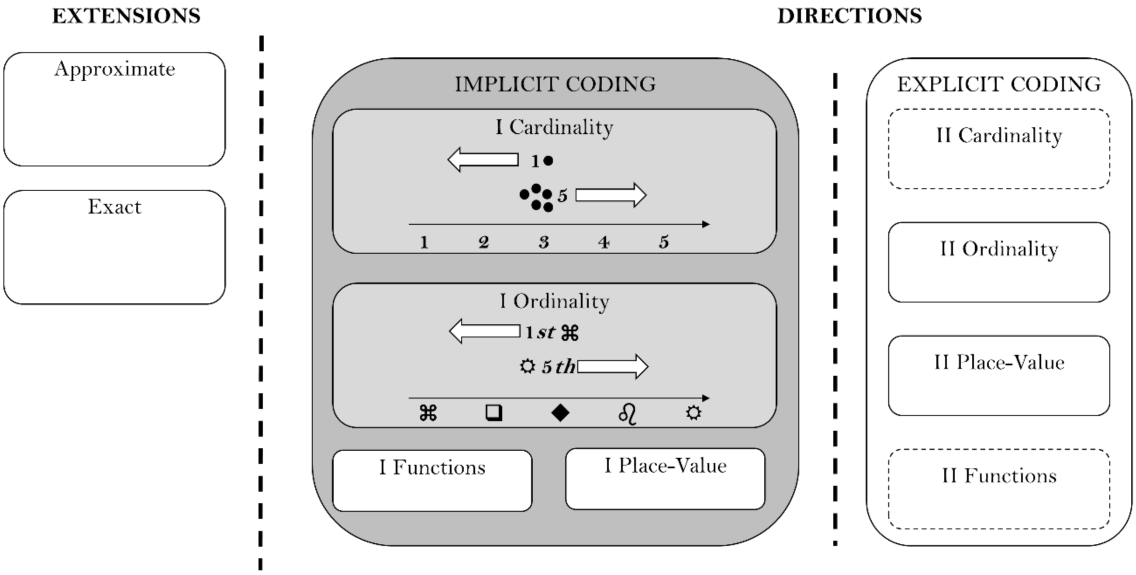

Figure 0.1. *Overview of taxonomy of spatial-numerical associations from Cipora et al. (in press; 2015; reprinted in modified form with permission from John Wiley and Sons, Inc). Dashed boxes indicate postulated spatial associations. The present thesis research investigates directional spatial associations with implicit coding for cardinality and/ or ordinality (highlighted section).*

It can be seen that spatial associations are evident on different levels of observation and with different kinds of tasks and stimuli. In the present research, I was particularly interested in the implicit coding of directional spatial associations as it is measured by the SNARC effect. Before departing in more detail on the proposed distinction of these implicit effects, however, I would like to highlight that also the explicit and implicit associations of extension and magnitude with space are far from being resolved. Selected controversies in the current literature include the indistinguishable correlations between continuous physical and numerical measures (Leibovich, Katzin, Harel, & Henik, 2016), numerical abilities in non-human animals such as monkeys (Cantlon & Brannon, 2006) or wild songbirds (Hunt, Low, & Burns, 2008), and the utility of number line estimation tasks for arithmetic learning and performance (Sella, Tressoldi, Lucangeli, & Zorzi, 2016). Particularly for trainings with the number line estimation task, neuromodulation techniques can present a major advancement, for example, in the remediation of impaired performance (e.g., Looi et al., 2016). On the other spectrum of the continuum of spatial associations, the explicit coding of space-number linkages in the domains of cardinality and functions are not yet empirically assessed. Finger counting and search direction are prime examples for explicit spatial associations of ordinality (Opfer, Thompson, & Furlong, 2010).

In the implicit directional spatial coding (e.g., SNARC effects), participants' behavior indicates the activation of spatial information that modulates their decision-making. However, in laboratory test situations, spatial information is neither available in the stimulus material (which consists of centrally presented words or symbols) nor is a spatial code directly involved in the decision task (such as classifications of small vs. large, early vs. late, odd vs. even). Eventually, spatial information is merely required in the decision, based on the arbitrary assignment of a classification to the respective left-hand or right-hand key. The association with magnitude happens without being actually relevant to the task behavior, in contrast to other experimental procedures such as number line estimation or production tasks. Intriguingly, implicit and explicit access to mental number space were impaired independently from each other in a group of neglect patients (Priftis et al., 2006). Seemingly implicit spatial associations of relative numerical magnitude were also observed in chicks and monkeys (Adachi, 2014; Rugani et al., 2015), but it is hard to estimate whether the same number-space mapping principle(s) can be assumed for humans as well (Patro & Nuerk, 2016).

The seminal experimental research that led to the working memory account of the SNARC effect (van Dijck & Fias, 2011; see previous section) is incorporated in the taxonomy as a separate spatial association of ordinal information. This conception presents a critical departure from the previous hypothesis that spatial associations are predominantly based on their position relative to their activated set origin (Abrahamse et al., 2016). Indeed, it is often ambiguous whether spatial-numerical associations are based on cardinality or ordinality, because it is always possible to sort numbers based on their magnitude, thus interrelations are hard to avoid (Cipora et al., 2015). Nevertheless, a divided presentation allows for more precise attribution of the presumably different cognitive processes which devise spatial associations in either case. The separation in the taxonomy also highlights the fact that actually two separate mathematical constructs are described by ordinality and cardinality, which refer to properties of order and set size, respectively. The ordinality-cardinality distinction, although relatively trivial to most educated adults, also employs a relevant psychological meaning which becomes apparent in the difficulties of patients suffering mathematical difficulties (Rubinsten & Sury, 2011). In lesion patients with calculation deficits (i.e., who are capable to read and write numerals, but have problems in solving simple calculation problems), it was additionally observed that arranging non-numerical sequences according to their order can be dissociated from quantitative number processing performance (Dehaene & Cohen, 1997). But also in healthy participants, the two concepts can be dissociated by different electrocortical responses (Rubinsten, Dana, Lavro, & Berger, 2013).

With regards to a (temporary) mental representation in space as indexed by the SNARC effect, however, it is not clear whether all numerical and non-numerical sequential items are arranged according to their sequential order by a single shared neurocognitive process or by multiple different processes. In general, neuroimaging studies pointed to distinct magnitude processing mechanisms for relatively long time (Cohen Kadosh, Lammertyn, & Izard, 2008; Wood et al., 2008). The taxonomy of the SNARC effect provides clear sub-divisions for spatial associations, which will be considered in the upcoming composition of research.

The Neuromodulation Approach: Electric Stimulation of the Brain

The approach to change thought and action by conducting electricity through brain regions has a fairly long tradition even dating back before the formal emergence of (neuro)psychology, since treatments of several medical conditions (such as depression, pain, headaches, epilepsy, and arthritis) using the electric torpedo fish were promoted already before the 17th century (Stillings, 1975). The *Torpedo Torpedo* and *Torpedo Nobiliana* were known for their capability to produce electric discharge and therapeutic applications of the fish by physicians are mentioned throughout Roman, Arabic, and Medieval inscriptions, with possible links dating back to the Egyptian period (Zago, Priori, & Ferrucci, 2016). With the discovery of electricity, transcranial electric stimulation sporadically found its way into medical applications, with the first reports on good results with melancholia patients in the 18th century. Early pioneers systematically approached the interactions between electricity and mental operations in human and animal experiments (Zago, Ferrucci, Fregni, & Priori, 2007). Continuous scientific progress in the fields of physics, medicine, biology, neuroscience, and psychology has set the rudiment for seemingly targeted applications in contemporary stimulation applications. In its essence, an efficacy of this approach nowadays seems very natural, considering the elementary signal transmission by electric action potentials within the central nervous system.

Contemporary approaches of transcranial brain stimulation encompass a variety of techniques with a subcategory that can be classified as transcranial electric stimulation (tES). Some of these techniques including tES are also referred to as non-invasive brain stimulation,[4] which basically contrasts the external application of tES through head surface areas with the neurosurgical implantation of electrodes for deep brain stimulation. Transcranial electric stimulation produces only relatively weak subthreshold resting membrane potential changes and, accordingly, tES does not externally induce neural activity in terms of action potentials, in contrast to non-invasive transcranial magnetic stimulation (TMS). Instead, to enfold measurable neuromodulation effects, tES interacts with ongoing or task-induced brain activity.

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[4] I will avoid the term “non-invasive brain stimulation” in line with the argumentation of Davis & Koningsbruggen (2013): Although administrations of tES do not meet common criteria of invasiveness such as incisions or insertions into the body, the term obscures the facts that electric currents enter brain areas and that actual effects must not be necessarily mild or less effective than invasive procedures, e.g., deep brain stimulation.

Most basic principles of tES mechanisms were factually established by the groundbreaking innovation of TMS (Barker, Jalinous, & Freeston, 1985). In brief, TMS is based on Faraday's law of electromagnetic induction, which is being utilized to induce electric currents in brain regions through external magnetic fields that could pass the skull. Single-pulse TMS was the first technology to externally induce movement through stimulation of the motor cortex, but many more paradigms and effects are known to date (see Barkin, Ekhtiari, & Walsh, 2015, for a good primer on research in cognitive neuroscience). Evaluation of TMS-induced motor evoked potentials (MEP) is also the most prominent evaluation of the effects of tES, by means of the measurement of a motor response (e.g., finger movement) after a directed TMS puls was delivered to the primary motor cortex. Modulations of MEP magnitudes reflect changes in cortical excitability by tES.

Different variants of TMS (such as single-pulse or double-pulse) are predominantly used to study the central nervous system, causality of brain-behaviour relationships, and their timings by interrupting or exciting neural circuits. Other variants of TMS (such as repetitive TMS, including intermittent vs. continuous theta burst) can be used therapeutically to alter cortical activity and/ or induce neuroplastic processes. By means of TMS coil design (e.g., figure-of-eight, Deep TMS), it is possibly to achieve relatively precise targeting in terms of timing and spatial resolution. Nevertheless, the basic principle of TMS is an active interference with ongoing neural transmission through induction of action potentials and respective neuroplasticity. In contrast to this mechanism, stimulation with tES draws exclusively on *neuromodulation*, i.e., on the modification of ongoing neural activity by changing resting membrane thresholds.

Within tES techniques, electricity can be administered through the scalp in the form of direct current (tDCS), in the form of alternating currents with a predetermined frequency (tACS), or in the form of alternating currents with randomly changing frequencies selected out of a uniformly distributed range (tRNS). Although this classification and administration of neuromodulation techniques with tES is rather novel,[5] tDCS was already administered in a broad range of studies and can be considered to be bolstered by some literature, although

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[5] Heuristically, the recent surge of interest in tES is based on its re-discovery of polarity-specific excitability changes in 1998 (Nitsche & Paulus, 2000; Priori et al., 1998) and there are only ~50 earlier publications on tES, but more than 2000 research reports that were conducted since then.

certainly its validation and exploration of underlying basic principles is still ongoing, particularly in the cognitive domain. A large range of technical parameters can be identified to further determine the effects of tDCS, the most prominent being current intensity and direction, electrode placement, stimulation duration (Nitsche et al., 2008; Nozari, Woodard, & Thompson-Schill, 2014), or individual differences variables such as genetic imprint (Wiegand, Nieratschker, & Plewnia, 2016). Moreover, there are even more potentially relevant parameters that are either unidentified or not systematically assessed, such as hair thickness, sweat, and attachment methods (Horvath, Carter, & Forte, 2014). What is known about the working mechanisms of tDCS – in relevance to the experimental modulation of cognitive performance – will be outlined in the following.

Neuromodulation with transcranial Direct Current Stimulation (tDCS)

In tDCS, direct currents of a weak intensity (between 0-3 mA) are administered transcranially to cortical structures through two (or sometimes more) surface electrodes. Dependent on the current direction relative to neural populations within the electric field, cortical excitability is assumed to be increased underneath the anode and to be decreased underneath the cathode, which is referred to as *polarity-specificity*. Note that this simple dichotomous model classification relates to the net effect of summation of many different modulated neurons, which can become actually modulated in opposite directions during the same stimulation because of their individual orientations or cell morphologies (e.g., Bestmann, de Berker, & Bonaiuto, 2015). Nevertheless, the anodal-excitatory cathodal-inhibitory rationale was examined by stimulation of primary motor cortex (M1) and subsequent quantification of motor-evoked potentials (MEP) with TMS (Nitsche & Paulus, 2000; Priori, Berardelli, Rona, Accornero, & Manfredi, 1998).

TMS-MEP includes repeated assessments of surface electromyography most commonly in one of the small hand muscles after a single-pulse to the contralateral M1 paralleled by the application of different tDCS conditions. In this classical paradigm, both TMS and tDCS target M1 and the respective changes in MEP altitude are established indicators of cortical excitability. During anodal tDCS (returned at the contralateral supraorbital region), larger MEPs were observed. In line with polarity-specificity, during cathodal tDCS, smaller MEPs were observed at constant TMS intensity (Nitsche & Paulus, 2000). These observed excitability changes were replicated in TMS-induced visual evoked potentials during stimulation of primary visual cortex (Antal, Kincses, Nitsche, Bartfai, & Paulus, 2004). Furthermore, cathodal tDCS of visual and sensorimotor cortices impaired respective discrimination in tactile and visual tasks (Antal, Nitsche, & Paulus, 2001; Rogalewski, Breitenstein, Nitsche, Paulus, & Knecht, 2004).

Moreover, after-effects of the stimulation can indicate prolonged neuromodulation due to neuroplasticity. For example, excitability increases from anodal tDCS were found to outlast up to 1 hour after stimulation. The neuroplastic mechanisms underlying after-effects do not linearly scale with stimulation intensity and duration, and after-effects are likely subject to rather complex interactions between LTP- / LTD-like effects, neurochemical modulations, and compensatory and homeostatic regulation (Jamil et al., 2017). However, for experimental psychology studies, after-effects of tDCS are less relevant and mostly negligible in the current thesis, because I will examine *online* effects exclusively, i.e., tasks are performed concurrent to the application of tDCS and no assessments are collected after the stimulation has terminated.

Both online tDCS effects and offline after-effects are thought to depend on the current direction (polarity specificity) and on the administered dose, which is mostly determined by stimulation intensity and duration. However, already at the physiological level, the relations between DC intensity, duration, and effect are not linear. For example, non-linear modulations of cortical excitability were found from stimulations of M1 and, paradoxically, 2 mA cathodal tDCS increased cortical excitability, but 1 mA cathodal tDCS decreased excitability (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013). Further, after-effects of both anodal and cathodal tDCS were most pronounced for 0.5-1 mA, but not for higher intensities up to 2 mA (Jamil et al., 2017) and after-effects of a second session of cathodal tDCS were abolished when preceded by a first session 3- or 24-hours ago, but not for short breaks of 3- or 20-minutes (Monte-Silva et al., 2010). Interestingly, neurotransmitter levels can further influence the effectivity of different tDCS configurations such that deprived smokers showed no response unless their nicotine levels were restituted (Grundey et al., 2012). These (and other) basic interactions render certain tDCS configuration windows effective, when designated concentration levels are optimal,[6] but a change in only one parameter such as duration can reverse after-effects (Monte-Silva et al., 2013). Non-linear tDCS effects are even more complex for cognitive processes,

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[6] A comparable proposal in the domain of tACS is described by the Arnold tongue (Ali, Sellers, & Fröhlich, 2013). For certain frequencies, regulatory brain mechanisms facilitate effects of tACS such that an optimal feedback loop is created and less intense stimulations can have optimal effects.

because paradoxical beneficial effects in cognitive tasks can result from physiologically (mostly) inhibitory stimulation with cathodal tDCS (Schroeder & Plewnia, 2016).

Finally, it is important to note that tDCS targets the membrane voltage of larger numbers of cortical neurons, rather than a single brain region. Although the electrical field is assumed to be normally distributed underneath the stimulating electrodes, current direction can vary with structural properties of the stimulated brain region. Also, individual neuron orientation can vary substantially in neuronal cohorts within a superimposed DC field, which is important because the induced depolarization or hyperpolarization in cell compartments is relative to the electric current direction (Bikson et al., 2004). Already a seemingly precise quantification of cortical excitability implies rather rough net effects of plenty modulated cortical units averaged across the individual cortices from recruited participants.

Effects of tDCS on Cognition

Further physiological studies, animal models, biophysical computational models, as well as conceptual models of behavioral change are still required to better understand the effects of tDCS (Bestmann, de Berker, & Bonaiuto, 2015; Fertonani & Miniussi, 2016). Nevertheless, modulations of cognitive behaviors and of clinical symptoms were also investigated from early on. Studies of cognition with tDCS can also inform basic principles and likewise indicate open and unresolved questions for neurophysiological studies. However, the basic rationale for most previous neurocognitive tDCS studies is certainly paralleled by the scientific inferences possible from patient studies in neuropsychology, trying to resolve causal brain-structure relations through brain lesions or modulations of targeted cortical structure.

However, and in stark contrast to TMS studies in cognitive neuroscience, the “virtual lesion” conception of tDCS effects presents some severe shortcomings. First, as outlined above, tDCS does not abolish or produce activity in one area of the brain, but modulates subthreshold activity of resting membrane potentials. This mechanism of action can alter firing pattern likelihoods, at best, but not simply enhance or disrupt neural function. The cortical outcome of tDCS is better characterized by more or less likely spontaneous firing than by the transient activation or deactivation of functional tissue (i.e., a probabilistic rather than a mechanistic approach; Miniussi, Harris, & Ruzzoli, 2013). Second, the spatial resolution of tDCS is rather low and, even more critically, tDCS is likely to produce cross-cortical remote effects also in other brain regions. For example, when the effects of 2 mA anodal or cathodal tDCS on resting state connectivity were examined with fMRI, changes in BOLD signal were observed in at-rest networks also in distant brain regions (Keeser et al., 2011). The remote tDCS effects can include the same or orthogonally directed modulations of connected cortical or subcortical brain regions (Polanía, Paulus, & Nitsche, 2012; Stagg et al., 2009). Third, tDCS effects may provoke regulatory – and potentially compensatory – responses that can preclude simple causal inferences. Note that cross-cortical and regulatory responses need to be considered in TMS studies as well, if possible, through concurrent neuroimaging (Driver, Blankenburg, Bestmann, Vanduffel, & Ruff, 2009). Eventually, the basic principles that produce behavioral changes from tES could differ to some degree from motor cortex studies, which calls for combined models and integrative stimulation rationales (Bestmann et al., 2015).

Nevertheless, some optimistic results were gathered that pointed to the effectiveness of tDCS also in the cognitive domain. In a highly influential study, researchers from Oxford University administered tDCS concurrent to a learning paradigm and could show 6-month-lasting arithmetic learning improvements after only 6 days of training (Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010). Limitations of this seminal study included small group sizes (N = 5 each), opposite stimulation of a contralateral region underlying the return electrode, and stimulation effects on the neutral Stroop condition in the active control group. Recently, in a much larger cohort and discriminating between verbal and spatial components of WM, comparable long-term effects from prefrontal tDCS were observed to augment a WM training paradigm (Ruf, Fallgatter, & Plewnia, 2017). In cognitive training studies, it is particularly interesting to observe long-term effects after several months and to also assess transfer task performance to examine generalizability of learning and performance gains, which was also available in the latter study.

In single-session experiments, the potential of tDCS in the study of human cognition can be utilized. Early on, it was observed that tDCS could modulate perception (Antal et al., 2001), implicit motor learning (Nitsche, Schauenburg, et al., 2003), and working memory (Fregni et al., 2005). Later, more empirical evidence was gathered on possible effects of tDCS on higher-order cognitive functions such as planning ability (Dockery, Hueckel-Weng, Birbaumer, & Plewnia, 2009), selective attention (Gladwin, den Uyl, Fregni, & Wiers, 2012), emotional processing and calculation speed (Plewnia, Schroeder, Kunze, Faehling, & Wolkenstein, 2015), or executive functions (Boggio et al., 2007).

Amid the first promising results, a large number of negative results recently called into question the general efficacy of tDCS, and it can be assumed that even more negative results are not available due to publication biases and/ or selective reporting (e.g., Horvath, Forte, & Carter, 2015). Some of these issues are elaborated on in Chapter V which also discusses mixed evidence obtained in the conducted research. In my view, the interactions involving tDCS effects in cognition are much more complicated than initially thought and many systematic moderator and mediator variables have yet to be exposed. For example, interestingly, the polarity-specificity of tDCS did not produce symmetrical modulations in behavioral studies, but anodal stimulation appeared more effective on a meta-analytic level (Jacobson, Koslowsky, & Lavidor, 2012). The origin of such asymmetric effects is currently unclear.

Moreover, a stimulation rationale based on previous neuroimaging results may not always provide sufficient motivation for tDCS studies. Negative findings could not refute according neurocognitive theories (even if the absence of evidence was rated in Bayesian analyses), since tDCS produces subthreshold modulations, cross-cortical effects, and compensatory mechanisms. Instead, it must be acknowledged that the current tDCS studies on cognition are still relative explorative (rather than confirmatory) and potential stimulation mechanisms are much more variable than often described. For instance, a mechanistic understanding could be misleading, but tES can still reveal important insights and advance neurocognitive theories in probabilistic frameworks (Miniussi et al., 2013).

Critically, the effects of return electrodes should not be neglected, since cathodal tDCS modulations could either contribute to the examined stimulation outcome or even produce unknown cognitive side effects in another function which was not tested in a given study (Iuculano & Cohen Kadosh, 2013). Also a change in return electrode size (35 cm^2 vs. 100 cm^2) of an otherwise identical tDCS configuration can lead to substantially different effects, and only the unihemispheric configuration effectively changed switch costs in a previous observation (Leite et al., in press).

Moreover, the area between electrodes is relevant as well. In a highly illuminating study only recently posted, it was examined whether motor cortex excitability could be changed by targeting the TMS motor cortex hotspot with adjacent tDCS electrodes placed around, but not above M1 (Rawji et al., 2017). The authors observed that MEP measurements were indeed modulated although electrodes were placed at a distance of each 3.5 cm from the assumed hot spot of M1, i.e., which was also the TMS target location. More generally, although the relatively diffuse perpendicular current flow in areas between electrodes may not hyper- or depolarize all neuron soma (Radman, Ramos, Brumberg, & Bikson, 2009), its presence and relevance should still be evaluated. The next section discusses general practical considerations for tDCS configurations inherent to the present work.

Another issue that deserves appreciation is the fact that initial brain states critically render the responsiveness to external impulses, which can be exemplified by individual differences in brain structure and functionality (Plewnia, Schroeder, & Wolkenstein, 2015) as well as by different demands of a task (Zwissler et al., 2014). Only recently, concurrent fMRI recordings demonstrated this activity-dependent behavior at a neural level by showing that BOLD responses to region-specific stimuli are modulated by tDCS, but not the general activity level. More precisely, in this study, the preference of inferior parietal lobe response to visual presentation of tools vs. faces was modulated following anodal and cathodal tDCS of the same region, respectively (Almeida et al., 2017). Conversely, stimulation efficacy could depend on task-induced activity, which is illustrated in Chapter IV by inclusion of separate task instructions for different a-priori activations of spatial associations.

Eventually, electric brain stimulation still contains much room for technical and procedural improvement. The basic principles of physiological as well as behavioral effects can be considered in the design of cognitive training and remediation protocols. However, given the low spatial resolution of tDCS, task-specific targeting as employed in this thesis may allow for broader and more effective implementations than variations of electrode configurations, particularly for investigations of large-scale bilateral fronto-parietal number networks.

Throughout the present work, polarity-specific tDCS in a prefrontal unilateral configuration (which was previously observed to effectively modulate verbal working memory) is used as experimental manipulation of prefrontal network and combined with different task-induced activities to investigate the neuropsychological theories on implicit biases as modelled by the SNARC effect.

Practical Considerations

Motivation and Safety of Extracephalic Reference Stimulation

Throughout this work, I administered tDCS at an intensity of 1 mA to the left prefrontal cortex with relatively large rubber electrodes (5 × 7 cm^2) and with an extracephalic return electrode placement. This type of configuration has substantial advantages over bicephalic configurations (e.g., which usually utilize [larger] suborbital return electrode placements) and allowed me to inject polarity-specific DC without altering activity in another brain region underneath the return electrode. Thus, the extracephalic return placement minimizes the risk of interference by return electrode modulations of other cortical areas which could be involved in a task under scrutinity, or which could exaggerate unexpected interhemispheric interactions. On the flip side, the extracephalic configuration may also lead to less dense current fields due to larger target-return electrode distance (Moliadze, Antal, & Paulus, 2010) and to uncontrolled diffuse tangential currents in the regions scattered from target to return (Rahman et al., 2013). Nevertheless, waning the very complex and adaptive dynamics of electric brain stimulation interactions, a single cerebral stimulation site allows for the full exploitation of polarity-specific anodal vs. cathodal tDCS effects. At least in a standard head model, I will show that electric field intensities are negligible in parietal regions potentially involved in the implicit spatial-numerical associations under study (Chapter IV; note that this does not rule out the possibility of cross-cortical remote effects). Although explorations into various possible tES montages and parameters can also innovate its effective applications, the present tES research avoids this kind of heterogeneity in terms of configurations, timings, and intensities. Various tES configurations were already explored in the domains of arithmetic performance and trainings (Chapter I).

Extracephalic return electrode placements were often avoided by tDCS researchers because additional risks or adverse effects were suspected, e.g., in line with an early observation of respiratory depression in a subject receiving 3 mA tDCS with an extracephalic montage (Lippold & Redfearn, 1964; Redfearn, Lippold, & Costain, 1964). Thus, safety concerns of the unilateral montage were frequently raised (e.g., Ziemann et al., 2008). In particular, brainstem function modulations are expected from directing external current circuits from cephalic to extracephalic locations. Possible adverse effects were expected regarding autonomic nervous system (ANS) functioning. In a controlled study, however, such adverse effects were not detected in multivariate physiological measures (see also: Baker, Rorden, & Fridriksson, 2010; Vandermeeren, Jamart, & Ossemann, 2010). Precisely, when 1 mA anodal or cathodal tDCS were administered for 20 minutes with a midline-frontal target electrode and an extracephalic return electrode placed over the right tibia, Vandermeeren et al. (2010) did not observe any effect of the stimulation (compared to sham tDCS) on respiratory frequency, blood pressure, and heart rate. Conductance of tDCS in a medical environment is reassuring given these potential adverse events, but to date, most of these concerns were waived (Bikson et al., 2016).

Finite elements modelling further alleviated the concerns of brainstem polarization by extracephalic tDCS reference placements by demonstrating that currents in the brain stem are approximately 5 times less dense than in targeted cortical areas (Noetscher, Member, Yanamadala, & Makarov, 2014). From their numerical modelling, it was additionally observed that extracephalic tDCS configurations produce larger current densities in deeper (white matter) brain regions and produce less bi-frontal fluctuation than placements with contralateral supraorbital return placements, thus rendering the montage better suited for targeted modulations of less shallow brain regions and investigations of frontal network hubs. Interestingly, ANS modulations from prefrontal tDCS (with cephalic and extracephalic montages) in corresponding emotional tasks can be detected (Schestatsky, Simis, Freeman, Pascual-Leone, & Fregni, 2013; Schroeder, Ehlis, Wolkenstein, Fallgatter, & Plewnia, 2015), but rather built on the regulation of emotional processing underneath targeted prefrontal areas (Ochsner & Gross, 2005; Plewnia, Schroeder, & Wolkenstein, 2015).

Motivation and Description of Attachment Method with Ten20© Conductive Paste

The physical connection between electrode and skin is a prerequisite for current flow in tDCS. Traditionally, electrode pads can be placed in sponges soaked in electrolyte solution (NaCl). This procedure can lead to uncontrolled flow of NaCl solution over the head and it is not clear whether current enters the cortex or is shunted over the skin. To avoid this potential confounding in the current research, in the tradition of the laboratory of the Dept. of Psychiatry and Psychotherapy in Tübingen, I used adhesive conductive Ten20® EEG paste directly on the tDCS electrodes, which achieves comparable impedances below 10 kΩ. Brief application of alcohol and skin preparation can be accompanied by appropriate structuring of hair at the electrode target location, e.g., by parting hair at the previously sized and marked location. Another practical advantage of this attachment method is the fact that electrodes stick to the scalp and the firm and uncomfortable head straps could be replaced with elastic rubber caps.

Although such discussion may appear trivial at first, it was assumed also earlier that saline-soaked sponges were relatively imprecise and that large amounts of current were being shortcircuited across the head without entering the cortex. Luckily, invasive electric recordings in non-human primates and human epilepsy surgery patients could show only recently that a percentage of ~10% of current actually enters the cortex during tDCS and produces intracortical electric fields at targeted regions (Opitz, Falchier, Yan, Yeagle, & Linn, 2016).

Technical Parameters

Most remaining parameters in the current studies were chosen to conform to both the most effective and most established state-of-the-art. For both anodal and cathodal tDCS, stimulation intensity of 1 mA was acceptable and also most effective in studies on cortical excitability (Batsikadze et al., 2013; Jacobson et al., 2012). Relatively large 5 × 7 cm electrodes were used due to their successful application in modulations of other cognitive operations such as WM

(Wolkenstein, Zeiller, Kanske, & Plewnia, 2014; Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011); for an overview of different electrode sizes used in modulations of numerical and arithmetic tasks, please refer to Chapter I. The duration of stimulation varied slightly between 20-30 minutes across experiments dependent on the duration of the administered tasks. I examined online effects exclusively due to the probabilistic interaction model (e.g., to achieve tDCS interactions with task-induced activity) and to relate my observations to online excitability changes rather than after-effects, which are less clear and subject to several plasticity mechanisms (particularly in the cognitive domain). Because adverse sensations are most intense in the beginning of a stimulation session and because some participants are sometimes slightly agitated then, I always imposed a 5-minute resting interval before tasks were performed and behavioral data was collected. Although not directly a technical parameter, I consistently assessed adverse effects and mood in all conducted experiments according to the questionnaire developed by Brunoni et al. (2011).

Shortly after the beginning of my thesis, concentric montages (e.g., HD-tDCS) became an interesting replacement of the typical bicephalic or extracephalic configurations. Particularly, more evidence was gathered that concentric tDCS configurations were at least as effective as conventional pad configurations (with a supraorbital return electrode; Kuo et al., 2013), had tolerable side effects (Borckardt et al., 2012), and better focal resolution (Bortoletto, Rodella, Salvador, Miranda, & Miniussi, 2016; Edwards et al., 2013). A recent study also showed that dlPFC stimulation with HD-tDCS could modulate cognitive control in the congruency sequence effect during a visual flanker conflict task (Gbadeyan, McMahon, Steinhauser, & Meinzer, 2016). Thus, a behavioral effect predicted from neuroimaging studies and computational modeling was obtained. However, in keeping with the previous studies that modulated working memory with cathodal tDCS (Wolkenstein et al., 2014; Zaehle et al., 2011), the present work consistently involves “traditional” tDCS with two 5 × 7 cm pad electrodes, where one of them targets cortical region (the left prefrontal cortex) and the other return electrode rests on the contraletaral upper arm. Pending more evaluations also of network modulations and behavioral effects, HD-tDCS remains a promising improvement of conventional tDCS, because the ring electrode configuration improves spatial resolution and removes uncertainty about return electrode placements.

Prefrontal Cortex Contribution to Spatial-Numerical Associations

In numerical cognition research, posterior parietal brain areas are established to subserve arithmetic and numerical magnitude processing, particularly including (horizontal) intraparietal sulcus, angular gyrus, and posterior superior parietal lobe (Dehaene, Piazza, Pinel, & Cohen, 2003; Hubbard et al., 2005). For spatial associations of numbers, also frontal areas were outlined to contribute causally in right-hemisphere brain damaged patients (Doricchi et al., 2005) and following stimulation with rTMS (Rusconi, Bueti, Walsh, & Butterworth, 2011; Rusconi, Dervinis, Verbruggen, & Chambers, 2013). It was assumed that frontal areas would allow for spatial orienting along the mental number line. However, interestingly, physical line bisection was dissociated from mental number line bisection in brain-damaged patients (Doricchi et al., 2005). In recent fMRI studies, it was possible to also track white-matter connections with diffusion tensor imaging, which revealed parieto-frontal arithmetic and number processing networks (Klein et al., 2016). Both model and imaging results particularly showed activation patterns in left-hemispheric prefrontal clusters (Ares 44, 45, and BA 47), consistent with the notion of verbal processes (e.g., see also Dehaene et al., 2003).

In non-human primates, single-cell recordings demonstrated number-selective neurons in both parietal and prefrontal brain areas (Nieder, 2016). Thus, updated theories on number representations in the brain typically encompass prefrontal-parietal networks (Nieder & Dehaene, 2009). Interestingly, only prefrontal cell firings consistently mapped empty sets to a numerical continuum (Ramirez-Cardenas, Moskaleva, & Nieder, 2016). Possibly, the implicit spatial association of number implies a comparable abstract operation for effective task handling and builds on prefrontal involvement as well, next to the established roles of bilateral parietal structures such as the intraparietal sulci, angular gyri, and posterior superior parietal lobes (Klein et al., 2016; Arsalidou et al., 2011).

Consideration of Laterality

Based on the hypotheses presented above, the most relevant electrode configuration for the present thesis includes stimulation of the left prefrontal cortex without opposite polarization of another brain region by means of extracephalic return electrode placement. Previous studies have shown that this electrode configuration was effective to modulate verbal working memory (Wolkenstein et al., 2014; Zahle et al., 2012; Ehlis et al., 2016; Plewnia et al., 2017). Moreover, imaging studies of numerical cognition demonstrate the involvement of left prefrontal areas, as argued above (Klein et al., 2016; Nieder et al., 2015). However, it is important to stress the scope of the presented project, which never empirically tested elicited activation patterns in different brain regions or the possibility of cross-hemispheric compensation by means of concurrent imaging in fNIRS or EEG. Rather, the present studies confronted participants during anodal vs. cathodal stimulation protocols delivered by an identical electrode configuration with different types of tasks and stimuli presumably addressing the same construct. Therefore, a single brain network neuromodulation was probed systematically for its behavioral effect in combination with different cognitive stimulations.

Notably, in different study designs used to test hemispheric lateralization, due to possible cross-cortical stimulation effects (e.g., Clemens et al., 2013), it is not necessarily clear how large tDCS laterality effects actually are, especially in tasks that elicit cross-cortical multiple coding networks. For example, in a recent study on cognitive control in the flanker task testing 120 healthy participants, left-side and right-side polarization were not statistically different (Gbadeyan et al., 2016). Also in the domain of numerical cognition, bilateral activation patterns are observed to corroborate arithmetic tasks and involvement of the right prefrontal cortex can be assumed as well (Klein et al., 2016; Rusconi et al., 2013). Moreover, already neural responsiveness to tDCS is subject to large individual variability, further complicating the study design to probe different tDCS configurations. In my opinion, prior to testing different stimulation configurations in large study samples needed to detect small effects, the behavioral outcome of a single tDCS configuration should be established, replicated, and theoretically elaborated. Moreover, task-specific targeting of neuromodulation effects may provide equal or even superior specificity than neuroanatomically guided targeting, which is difficult to achieve due to the low spatial resolution of tDCS. Therefore, electrode configuration was not varied in the present research, but task characteristics were manipulated systematically to challenge the robustness of stimulation effects and probe its cognitive fundaments as well as possible moderating variables such as task relevance, as implemented in different task instructions.

Thus, although left-hemispheric excitation was based on several theoretical assumptions, this factor was not assessed empirically in this work. Based on the present results, future studies could validate a corroborated rationale for laterality specificity in different study designs.

Overall Rationale of the Presented Research

Several lines of research motivate involvement of PFC in the maintenance of spatial associations, which relates differentially to previous theories on the SNARC effect as sketched above. In fact, active interventions with transcranial magnetic stimulations (Rusconi et al., 2011, 2013) already outlined causal contributions of frontal areas to spatial associations, but previous studies mainly focused on numerical stimuli, thus reflecting both ordinal and cardinal information. Since neuromodulation with tDCS is a relatively novel and controversial technique, results from tDCS studies can be informative to distinguish the presented theories on the SNARC effect. As argued above, systematic variation of task characteristics and instruction are important tools to guide task-specific targeting of tDCS. Furthermore, by testing the conditions that produce behavioral changes, the neuromodulation results can further advance the possibility to change PFC-hosted WM processes (Botvinick & Cohen, 2014; D'Esposito & Postle, 2015) relative to the generation and/ or maintenance of implicit biases.

In this thesis, I administered tDCS to the left prefrontal cortex with either anodal or cathodal configuration. Other possible electrode configurations are reviewed in Chapter I. Within and across studies, I varied the tasks that were performed during the stimulation by changing stimuli, instructions, or even complete task procedures. These manipulations in cognitive parameters allowed me to discriminate different theoretical aspects, but also to document the task-specific targeting in the PFC tDCS protocol previously established to modulate verbal working memory. Figure 0.2 displays a graphical overview of the studies incorporated in the present work, which elaborate the possibility of a PFC-guided cognitive origin of the SNARC effect along the taxonomy of spatial-numerical associations. Finally, departing from spatial to non-spatial implicit associations, I present first evidence for a generalizable stimulation rationale comprising also implicit associations in the IAT paradigm.

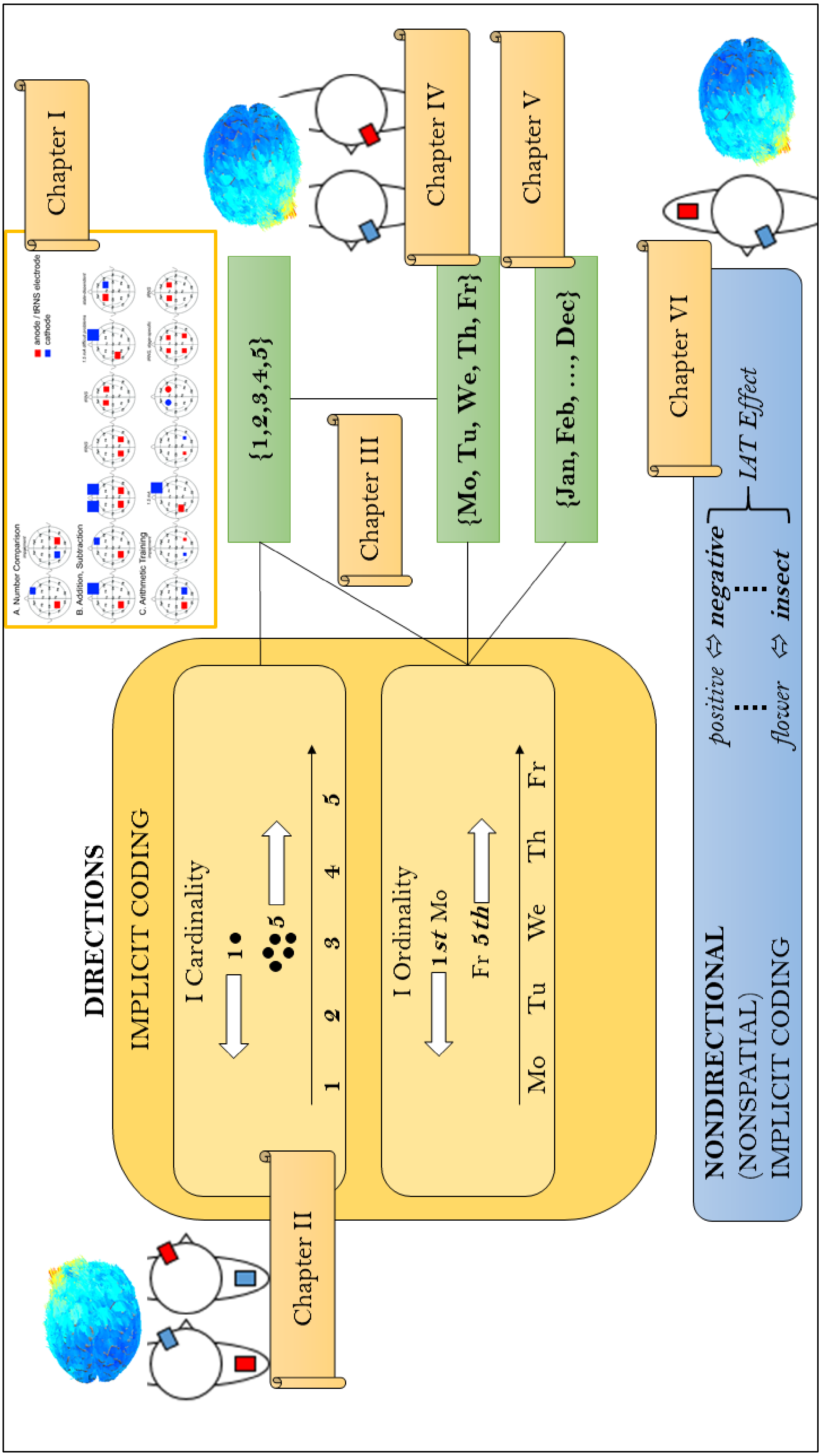
DIRECTIONS
IMPLICIT CODING
I Cardinality
1
5
1 2 3 4 5
I Ordinality
1 st Mo
Fr 5 th
Mo Tu We Th Fr
{1,2,3,4,5}
{Mo, Tu, We, Th, Fr}
{Jan, Feb, ..., Dec}
Chapter I
Chapter II
Chapter III
Chapter IV
Chapter V
Chapter VI
A. Number Comparison
B. Addition, Subtraction
C. Arithmetic Training
anode / tRNS electrode
cathode
NONDIRECTIONAL
(NONSPATIAL)
IMPLICIT CODING
positive ⇔ negative
flower ⇔ insect
IAT Effect

Figure 0.2. *Overview of empirical investigations in the current thesis. The focus is on implicit coding of directional spatial associations. Chapter I provides a review on neuromodulation studies in the domain of numerical cognition in general. Chapter II tests neuromodulation effects with anodal and cathodal tDCS to the prefrontal cortex on the implicit coding of cardinality in the SNARC effect obtained in parity-judgment task and magnitude judgment task. Chapter III compares SNARC effects that are based on ordinality exclusively (weekdays Mo-Fr) with SNARC effects that are based on ambiguous ordinality and cardinality information (numbers 1-5). Chapters IV and V investigate neuromodulation effects with numerical and purely ordinal sequences. Finally, Chapter VI provides a first generalization of the obtained stimulation effects of implicit coding to a nondirectional and non-spatial implicit association effect obtained in the implicit association test (IAT). The displayed electric current modelling of transcranial direct current stimulation electrode configuration is introduced and described in more detail in Chapter IV.*

OBJECTIVES AND OVERVIEW

The presented empirical work investigates the neuropsychological underpinnings of SNARC effects based on markedness correspondence within a working memory (WM) framework by administration of prefrontal tDCS. I begin with a mini-review of existing literature on neuromodulation effects with tDCS and tRNS for enhancements of numerical and arithmetic processes (**Chapter I**). In the following, I employ prefrontal tDCS concurrent to different tasks and stimuli to juxtapose predictions from the different theories on the SNARC effect.

In the chapters, I describe the collected evidence favoring the augmented WM account of the SNARC effect in two lines of study. In single-task experiments, I show that spatial-numerical associations are specifically reduced by a tDCS configuration that is typically used for reduction of WM processes (**Chapter II**). Visual spatial conflicts are not modulated.

The following series of experiments critically complements the notion of a unified WM process. In an individual differences approach, SNARC effects for single-digits and for weekdays are hardly correlated, showing insufficient convergent validity (**Chapter III**). Next, concurrent modulation effects are opposite for the two sequences. Encompassing also previous patient studies, I introduce and elaborate a hybrid multiple-coding model and the possibility of linguistic markedness correspondence effects (**Chapter IV**). Finally, the generalizability of the stimulation rationale is tested based on the idea that any effect including on markedness correspondence should respond to the prefrontal stimulation (**Chapters V & VI**). Results show effectivity also in the implicit association task, in line with the theoretical proposal of salience asymmetries also in this task (**Chapter VI**).

In sum, the results are hardly accounted for by a single cognitive mechanism that arranges all items alike in space. Consistent with results from other research groups, I present a hybrid and augmented multiple-coding WM account also considering markedness principles.

EMPIRICAL CHAPTERS

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I. MINI-REVIEW: NEUROMODULATION IN NUMERICAL COGNITION

Cognitive enhancement of numerical and arithmetic capabilities: A mini-review of available transcranial electric stimulation studies

The following chapter is published as:

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Abstract

Arithmetic capabilities are complex cognitive skills essential for handling requirements of the modern world. At the same time, educational institutions are challenged with math-related problems, e.g., developmental dyscalculia, math anxiety, and also with less severe difficulties of arithmetic understanding. Thus, non-invasive techniques for cognitive enhancement have attracted researchers' and practitioners' interest in the fields of education, psychology, and neuroscience. Particularly, studies employing transcranial electric stimulation (tES) in arithmetic learning, problem solving, and performance in numerical tasks and operations have shaped an optimistic perspective of cognitive enhancement in these domains, building on the fronto-parietal correlates of healthy and deficient arithmetic performance and learning. However, the heterogeneity of stimulation approaches in numerical cognition research – with different electrode montages, stimulation protocols, tasks, outcomes, and combinations thereof – may also showcase a variety of parameters relevant more generally to the cognitive domain. Here we present a short overview of the different tES approaches to enhance numerical and arithmetic capabilities in performance and training within the general framework of cognitive enhancement. We conclude that performance and training gains can be obtained from different strategical tES configurations, but more standardization, better translation between neurodevelopmental perspectives and tES principles, as well as pre-registered and controlled studies in critical populations are needed.

Introduction

Basic numerical and arithmetic abilities are critical for numerous activities and societal functioning. Yet, a substantial amount of the general population (e.g., up to 22% in the UK) shows mathematical deficits which are often specified in developmental trajectories, cognitive disabilities, or comorbidities (Kaufmann et al. 2013) and which can result in occupational and economic disadvantages (Bynner & Parsons 1997). Both domain-general and domain-specific functions supplement the successful operation on numerical quantities in everyday life. These cognitive functions include magnitude representation, retrieval of, and operation on arithmetic facts on the domain-specific side, and working memory, executive functions, and attention on the domain-general side. The variety of involved domain-general and domain-specific cognitive functions thus also increases the dimensionalities of possible mathematics training strategies (Looi & Cohen Kadosh 2016).

Arithmetic processing is mainly subserved by the fronto-parietal network of the brain (Klein et al. 2014; Matejko & Ansari 2015; Nieder 2016): Different parietal circuits are particularly relevant for magnitude representations (Dehaene et al. 2003) and arithmetic operations often produce additional prefrontal activations (Arsalidou & Taylor 2011). By modulating activity in these brain areas, arithmetic performance could be changed. Accordingly, investigations with transcranial stimulation can causally bolster the correlational evidence from neuroimaging, because brain activity becomes an independent, manipulable variable rather than a dependent, measurable variable. Going beyond causal reasoning, neuromodulation has also been proposed as effective strategy to improve arithmetic capabilities over and above behavioral cognitive training.

In particular, transcranial electric stimulation (tES) has become a promising tool to enhance various arithmetic tasks and trainings. However, the complex neurocognitive functions required in different arithmetic tasks have sparked different approaches within recent tES studies. Moreover, the neuromodulatory technique itself also allows for different implementations with critical consequences for assumed neurophysiological and behavioral effects. Thus, heterogeneity (anatomically, parametrically, and content-wise) is the norm and it is hard to get a conclusive overview even on this small field. In this mini-review, we provide an overview of studies employing tES on numerical processing and learning disentangling above factors. Our particular focus is to discuss basic methodological and translational aspects of tES approaches in the general framework of cognitive enhancement that may contribute to the current heterogeneity.

Stimulation for Enhancing Arithmetic Capabilities

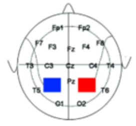
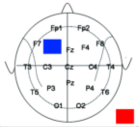
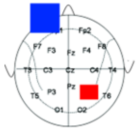
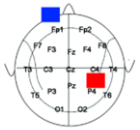
The current review focuses on tES methods, but numerical cognition research is also informed by extensive previous work with transcranial magnetic stimulation (TMS) examining the causal structure-function relations underlying arithmetic skills with high focality (Salillas & Semenza 2015) or the mechanisms underlying place-value integration in multi-digit number processing (Knops et al., 2006). Advantages of administering weak currents through scalp electrodes with tES over active interference with electromagnetic TMS pulses are the possibility of modulating brain activity online (that is: concurrent to a behavioral task or training) without auditory and sensory distraction, the establishment of sham and active control stimulation conditions with indistinguishable sensory artifacts, portability, economic efficiency, and easy implementation in outpatient interventions (Priori et al. 2009; see also: Duecker & Sack 2015).

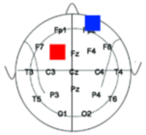
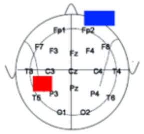
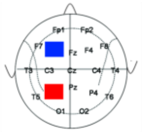
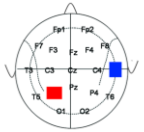
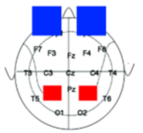
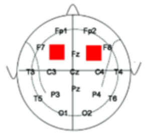
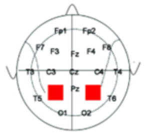
Within tES applications for the enhancement of numerical cognition, the most prominently investigated methods are transcranial direct current stimulation (tDCS) and transcranial random noise stimulation (tRNS). For both techniques, two (or more) surface electrodes are fixed over brain regions and a weak current is applied (mostly 1-2 mA). Using direct currents in tDCS, cathode and anode electrodes differ in their neurophysiological effect. It is assumed that in the human brain underneath the anode, depolarization mostly produces excitatory shifts of resting membrane potentials whereas underneath the cathode, hyperpolarization mostly modulates neuronal activity in inhibitory ways (Nitsche & Paulus 2000; see also: Jacobson et al. 2012). In contrast to TMS, these subtle neuromodulatory shifts are not capable to induce action potentials on their own. However, tES can emphasize or attenuate inherent neural activity and thus also produce cross-cortical network responses (Pope & Miall 2012). Any modulation of behavioral effects thus rests on the current network activity (state-dependency) and on neural activations as induced by a task (Silvanto & Pascual-Leone 2008; Bikson & Rahman 2013).

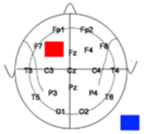
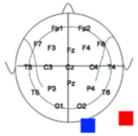
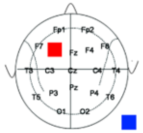
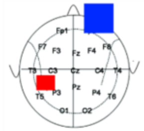
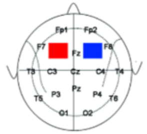
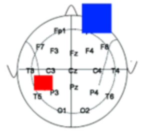
Often, only the effect under one ‘target’ electrode is desirable. However, ‘return’ electrode placement (typically of the cathode electrode) is highly relevant, because its placement also affects current flow and current fields underneath the target electrode, e.g., due to target-return distance and direction, shunting over the scalp, or network dynamics (Bikson et al. 2010; Moliadze et al. 2010). In addition, regions between the electrodes are flooded by tangential current, which can modulate additional synaptic efficiency of some neuronal populations (Rahman et al. 2013). This is a particular problem in numerical cognition, because – as outlined above – domain-general functions also contribute to numerical functioning. It is not sufficient to avoid number-related brain areas for the placement of the return electrode, because a domain-general function underlying the overall current flow may also exert its influence on numerical processing. Furthermore, an opposite polarization in another brain region may be of theoretical interest (e.g., in oppositional placements). However, in most cases of unilateral placement with one theoretically motivated target electrode, the return and intermediate area activity is neglected and accordingly, large return pads are used that produce less dense current fields or return electrodes are placed on extracephalic locations.

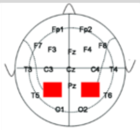
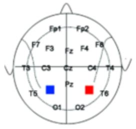
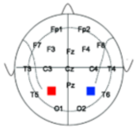
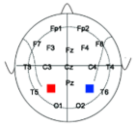
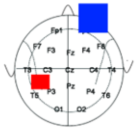
In contrast, alternating currents are used in tRNS with (high) frequencies randomly picked from a normally distributed range of predefined oscillations. What is known about tRNS mechanisms is that its intensity- and frequency-dependent administration can enhance cortical excitability underneath both surface electrodes (Terney et al. 2008). Furthermore, tRNS can facilitate subthreshold detection processes according to stochastic resonance principles (Antal & Herrmann 2016; van der Groen & Wenderoth 2016). Note that tRNS mechanisms are likely to differ from the fixed application of a single oscillation in transcranial alternating current stimulation (tACS), which is thought to act by entrainment and phase-locking (Ozen et al. 2010; Battleday et al. 2014). The excitatory effect of tRNS tended to be larger, yet shorter, compared to anodal tDCS, in motor cortex evaluations (Moliadze et al. 2014). In cognitive tasks, mixed results were obtained and some studies report on the lack of performance modulations in working memory tasks (Mulquiney et al. 2011; Holmes et al. 2016). However, numerous studies also report on effective performance and learning modulations by tRNS in numerical tasks and trainings (Cappelletti et al. 2013; Snowball et al. 2013; Pasqualotto 2016; Popescu et al. 2016). Little direct behavioral outcome comparisons between the two techniques exist to date. Yet, their different characteristics could imply better targeted implementations: For instance, the after-effects of tRNS appear NMDA receptor independent, in contrast to anodal tDCS (Chaieb et al. 2015). Thus, different neuroplastic (long-term) consequences of tRNS and tDCS could further augment and specify training effects.

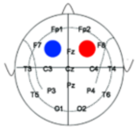
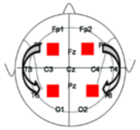
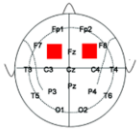
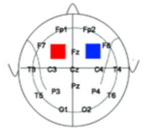
Table 1.1. Overview of original tES studies on numerical and arithmetic processes in performance and training paradigms. The majority of studies administered tES online to the behavioral task, in healthy student populations (mixed-sex aged 18-42 y) and deviations from these parameters are explicitly stated below. Anode and cathode target regions refer to the international 10-20 system for electrode placements. For tRNS, both anode and cathode deliver current (reported: peak-to-peak intensity) in negative and positive direction and are assigned randomly (no study employed DC offset). Cross-over design refers to repeated measurement of different stimulation conditions in counterbalanced order. Green and red colors indicate electrode configurations that elicit the described beneficial and detrimental effects, respectively. Comparison signs in results column point to performance enhancements, which may be indicated by relatively smaller measured response times.

Study	**tES Method** (group), anode, cathode, current *Duration, electrode size, AC range*	**Sample & Design**	**Task(s)** *color code*: enhancement, impairment, null effect	**Result** [measure] + physiological effects # transfer, additional measures	**Effect Size**	**Successful Montage**
1. Cognitive Enhancement of Performance **1.1. Numerical Processes**						
Li et al., 2015	**tDCS** online (LA-RC) P3, P4, 2mA (RA-LC) P4, P3, 2mA (S) sham *30 min, 5x5 cm*	N=18 cross-over	number comparison, spatial attention (modified Posner task), continuous attention (CRT), vigilance level	(S)>(RA-LC) [NDE; RT], no modulation of spatial attention, (RC-LA)>(RA-LC) [RT in final CRT block]	d=0.61 d=0.83	
Schroeder, Pfister, Kunde, Nuerk, & Plewnia, 2016	**tDCS** online (1) extracephalic, F3, 1 mA and sham (2) F3, extracephalic, 1 mA and sham *25 min, 5x7 cm*	N_1=24, $N_{1\text{-rep}}$=24, N_2=24 separate cross-over	spatial-numerical associations (SNARC effect), stimulus-response conflict	(1)>(2)=(sham) [RT], no effect on explicit conflict, no modulation of NDE # conceptual replication	d=0.49 d=0.56	
1.2. Arithmetic Processes						
Artemenko, Moeller, Huber, & Klein, 2015	**tDCS** online (LA) P3, SO, 1mA (RA) P4, SO, 1mA (LC) SO, P3, 1mA (RC) SO, P4, 1mA (S) sham *20 min, 5x5 parietal & 10x10 cm SO*	N=25 cross-over	addition 2AFC, color-word Stroop (control)	(RA)>(RC) [carry effect; RT] no effect on Stroop place-value lateralized in right IPS	d=0.36^1	
Clemens, Jung, Zvyagintsev, Domahs, & Willmes, 2013	**tDCS** online (1) CP4, SO, 2mA and sham *20 min, 5x7 cm*	N=10 male within (pre-post)	simple multiplication verification	no behavioral effect [RT/efficiency] + fMRI pre/post tDCS during + task: AG activity increase	d=1.85-2.94^1	

Study	**tES Method** (group), anode, cathode, current *Duration, electrode size, AC range*	**Sample & Design**	**Task(s)** *color code*: enhancement, impairment, null effect	**Result** [measure] + physiological effects # transfer, additional measures	**Effect Size**	**Successful Montage**
Gill, Shah-Basak, Hamilton, 2015	**tDCS** offline (1) F3, SO, 2 mA and sham *20 min, 5x5 cm*	N=22 (collapsed) cross-over	PASAT addition after an easy (N=11) or difficult (N=11) online verbal WM task WM task (1-back, 3-back)	(1)>(sham) [PASAT PE] if preceded by difficult WM task (3-back) no effect on WM tasks [PE]	$d=0.69^{1}$	
Hauser et al., 2016	**tDCS** online→offline (1) P5-CP5, SO, 1 mA or (2) sham *first 30 min of task, 5x7 cm anode & 5x10 cm cathode*	N_1=20, N_2=20 between	complex subtraction 3AFC repeated vs. novel problems	no group differences in learning and problem solving (ceiling effect) + tDCS nullified novelty- + related right prefrontal + deactivation [fMRI]	$d=2.01^{1}$	
Houser, Thoma, & Stanton, 2014	**tDCS** offline (1) P3, F3, sham, (2) 1mA, or (3) 2mA *20 min, 5x7 cm*	N_1=14, N_2=15, N_3=13 between	statistical problem (calculation of non-parametric-Kruskal-Wallis after instructional video)	sham = 1mA, 1mA > 2mA [Calculation Score]; Instruction and calculation time covary with task success; possible effect of prefrontal cathode	$d=0.41^{1}$	
Houser, Thoma, Fonseca, O'Connor, & Stanton, 2015	**tDCS** offline (1) P3, T4, sham, (2) 1mA, or (3) 2mA *20 min, 3x5 cm*	N_1=13, N_2=10, N_3=9 between	statistical problem (calculation of non-parametric-Kruskal-Wallis after instructional video)	1mA & 2mA > sham [Calculation Score]; time covariate	$d=1.51\text{-}1.27^{1}$	
Klein et al., 2013	**Bi-tDCS** online (1) P3+P4, SO+SO, 1mA (2) SO+SO, P3+P4, 1mA (3) sham *20 min, 5x5 parietal & 10x10 cm SO*	N=24 cross-over	addition 2AFC color-word Stroop (control)	(1)<(2) [RT distractor distance effect], no effect on Stroop	$d=0.46^{1}$	
Pasqualotto, 2016	**tRNS** online (F) F4, F3, 1mA (P) P4, P3, 1mA (S) sham *20 min, 5x5 cm, AC: 100-600 Hz*	N_F=18, N_P=18, N_S=18 within-between	subtraction verification word categorisation	(F)=(P)>(S) Improvement [RT block 4 – block 1] no effect on categorization # 1w follow-up: (F)=(P)>S # [PE trained and novel # problems]	$d=0.59\text{-}0.93^{1}$ -	 

Study	**tES Method** (group), anode, cathode, current *Duration, electrode size, AC range*	**Sample & Design**	**Task(s)** *color code*: enhancement, impairment, null effect	**Result** [measure] + physiological effects # transfer, additional measures	**Effect Size**	**Successful Montage**
Plewnia et al., 2015	**tDCS** online (1) F3, extracephalic, 1 mA and sham *20 min, 5x7 cm*	N=28 male between	Adaptive PASAT addition	(1)<(sham) for performance [number of trials and speed] and negative affect [PANAS self-report]	d=0.94 d=1.37	
Pope et al., 2012	**tDCS** offline (A) cerebellum, extracephalic, 2mA (C) extracephalic, cerebellum, 2mA (S) sham *20 min, 5x5 cm*	N_A=22, N_C=22, N_S=22 between (pre-post)	PASAT addition and subtraction; verb generation	(C)>(S)=(A) [PE and RT subtraction; RT in verb generation]	-	
Pope et al., 2015	**tDCS** offline (A) F3, extracephalic, 2mA (C) extracephalic, F3, 2mA (S) sham *20 min, 5x5 cm*	N_A=20, N_C=20, N_S=19 between (pre-post)	PASAT addition and subtraction	(A)>(S)=(C) [PE decrease subtraction]	-	
Rütsche, Hauser, Jäncke, & Grabner, 2015	**tDCS** offline (1) P5-CP5, SO, 1.5 mA and sham *30 min, 5x7 parietal & 10x10 cm SO*	N=23 cross-over	small arithmetic problems large arithmetic problems (verbal production)	(1)<(sham) [PE small problems], (1)>(sham) [RT large problems] + EEG during task: + alpha & theta modulations	d=0.51 d=0.45 d=0.47-0.72	
Sarkar, Dowker, & Kadosh, 2014	**tDCS** online (1) F3, F4, 1mA and sham *30 min, 5x5 cm*	$N_{\text{high math anxiety}}$ =25, $N_{\text{low math anxiety}}$=20 mixed cross-over	affective priming+ arithmetic verification, attention (ANT)	(1)>(sham) high anxiety, (1)<(sham) low anxiety, (1)>(sham) executive control scores [RT] + modulation of salivary + cortisol (pre-post)	d=5.69[1] d=4.13[1] d=1.03[1]	
1.3. Numerical & Arithmetic Processes						
Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013: Exp. 1	**(Bi-)tDCS** offline (1) P3, SO, 1mA (2) P3+P4, SO, 1mA (3) SO, P3+P4, 1mA (4) sham *25 min, 5x7 target & 10x10 cm return electrodes*	N=21 cross-over	number comparison, subtraction 3AFC	P3 > sham [PE] P3 > sham [RT] unilateral left parietal tDCS enhanced performance no modulation of NDE	d=0.76 d=0.51	
Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013: Exp. 2	**tDCS** offline (1) P4, SO, 1mA and sham *25 min, 5x7 target & 10x10 cm return electrodes*	N=16 cross-over	number comparison, subtraction 3AFC	no effects (control experiment; laterality specificity)		

Study	**tES Method** (group), anode, cathode, current *Duration, electrode size, AC range*	**Sample & Design**	**Task(s)** *color code*: enhancement, impairment, null effect	**Result** [measure] + physiological effects # transfer, additional measures	**Effect Size**	**Successful Montage**
2. Cognitive Enhancement of Training and Learning **2.1. Numerical Training**						
Cappelletti et al., 2013	**tRNS** online → offline (P) P3, P4, 1mA (PNT) P3, P4, 1mA, no training (M) C3, C4, 1mA (ST) sham & training *20 min for 5 d, 5x7 cm, AC: 0-250 Hz*	N_P=10, N_{PNT}=10, N_M=10, N_{ST}=10 Between	dot-array numerosity discrimination training (5d) transfer: continuous magnitudes discrimination, arithmetic, attention, executive, Stroop (control)	(P)>(M)=(ST)>(PNT) [number acuity *wf*], (P) improved continuous magnitude discrimination [RT/PE], no effects on arithmetic & control tasks + (P) displayed sustained + discrimination acuity after + 16 weeks	d=1.12-1.25^1	
Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010	**tDCS** online → offline (LA-RC) P3, P4, 1mA (RA-LC) P4, P3, 1mA (S) sham *20 min for 6 d, 3x3 cm*	N_{LA-RC}=5, N_{RA-LC}=5, N_S=5 Between	training with artificial numerical symbols (6d) numerical stroop number-to-space (MNL)	(RA-LC)>(S)>(LA-RC): faster automaticity [RT] (RA-LC): linear MNL + sustained automaticity + (RA-LC) after 6 months	-	
Iuculano & Cohen Kadosh, 2013	**tDCS** online → offline (PPC) P3, P4, 1mA (DLPFC) F4, F3, 1mA (S) sham *20 min, 3x3cm*	N_{TOTAL}=19 Between	training with artificial numerical symbols (6d) numerical stroop digit stroop	(PPC)>(S)>(DLPFC) [learning slope] (DLPFC)>(S)>(PPC) [numerical stroop RT] digit stroop: no transfer Dissociation of learning and automaticity	d=2.0^1 d=1.45^1	
Iuculano & Cohen Kadosh, 2014	**tDCS** online→ offline (LA-RC) P3, P4, 1mA (RA-LC) P4, P3, 1mA *20 min, 3x3 cm*	2 patients with developmental dyscalculia between single-case	training with artificial numerical symbols (6d) numerical stroop number-to-space	(LA-RC)>(RA-LC) [numerical stroop RT] automaticity and linear number-to-space mapping	-	
2.2. Arithmetic Training						
Grabner, Rütsche, Ruff, & Hauser, 2015	**tDCS** online → offline (PA) P5-CP5, SO, 1.5 mA (PC) SO, P5-CP5, 1.5 mA (S) sham *30 min for 1 d, 5x7 cm*	N_{PA}=20, N_{PC}=20, N_S=20 Between	multiplication and subtraction facts (1d)	(PA)=(S)>(PC) [RT slope] (PA)>(S)=(PC) [PE slope subtractions] + (PA)=(S)>(PC) for trained + problems after 1 day [RT]	d=0.85 d=0.71 d=0.55	

Study	**tES Method** (group), anode, cathode, current *Duration, electrode size, AC range*	**Sample & Design**	**Task(s)** *color code*: enhancement, impairment, null effect	**Result** [measure] + physiological effects # transfer, additional measures	**Effect Size**	**Successful Montage**
Looi et al., 2016	**tDCS** online (FT) F4, F3, 1mA (FNT) F4, F3, 1mA+placebo training (S) sham *30 min, 25cm² electrodes*	N_{FT}=10, N_{FNT}=10, N_S=10 between	adaptive body-tracking video-game on fractions (2d) verbal WM	(FT) better performance (sham+placebo training) transfer to verbal WM better tES effect for lower baseline ability + long-term effects and + sustained transfer after 2 + months	- - d=0.63-0.72	
Popescu et al., 2016	**tRNS** online (tRNS) F3, F4, 1mA (days 1-3) (tRNS) P3, P4, 1mA (days 4-5) (S) sham (days 1-5) *20 min, 4x4cm, AC: 100-640 Hz*	N_{tRNS}=16, N_S=16 Between	training (5d): calculation and time-pressured drill, old & new arithmetic problems (d5) attention (ANT)	(tRNS)>(S) [RT difficult problems, training+test] (tRNS)>(S) [PE new & easy problems] no effect on ANT	d=1.39 d=1.16 d=1.46	
Snowball et al., 2013	**tRNS** online (tRNS) F3, F4, 1mA or (S) sham *20 min, 5x5cm, AC: 100-600 Hz*	N_{tRNS}=13, N_S=12 Between	training on arithmetic problems (6d): calculation and (time-pressured) drill mental rotation, attention (ANT)	(tRNS) steeper calculation and drill learning rates [RT] no effects on mental rotation and ANT + sustained calculation + performance after 6 + months # pre-post NIRS: prefrontal # hemodynamic response # mirrors behavioral results	- d=1.09	
Vanderhasselt et al., 2015	**tDCS,** online (1) F3, F4, 2mA or (S) sham *30 min, 5x5cm*	N_1=19, N_s=14 depressed patients Between	Training (5d) on adaptive PASAT addition Depressive brooding (rumination)	(1)<(2) [pre-post speed difference] # reduction of rumination # associated with training	d=0.72[1]	

Notes: 2AFC=two-alternative forced choice, AC=alternating current, AG=angular gyrus, IPS=intraparietal sulcus, NDE=numerical distance effect, PASAT=Paced Auditory Serial Addition Task, PE=percentage of errors, PFC=prefrontal cortex, RT=response times, SO=(contralateral) supraorbital region. Cohen's d: 0.2=small effect, 0.5=medium effect, 0.8=large effect. [1] Effect sizes are computed and transformed according to Cohen (1988) from reported sample size, means and standard deviations, *t*-values, and *F*-values, for two means and for more than two means with a significant linear trend.

Short Overview of Reviewed Studies

Acknowledging the involvement and relevance of different domain-specific and domain-general functions, associated brain areas, and networks in numerical and arithmetic processes would exceed the scope of this mini-review, and elaborated descriptions are available elsewhere (Arsalidou & Taylor 2011; Looi et al. 2016b). So far, various combinations of tasks, study designs, and electrode configurations have been investigated using tES methods. Table 1.1 presents an overview of the reviewed studies.[7]

Numerical Performance Modulations

The available study results corroborate the importance of bilateral parietal brain regions for numerical processing, but active control stimulations and tasks also indicate distinct lateralization and state-dependency.

For comparing the magnitudes of two-digit numbers, unilateral left-side parietal anodal tDCS generally led to more accurate responses (Hauser et al. 2013). Conversely, a bipolar oppositional placement with right anodal, left cathodal parietal stimulation impaired response times for single-digits close to the comparison referent (Li et al. 2015). Thus, the bipolar stimulation modulated the increasing difficulty to distinguish closer digits, termed numerical distance effect (NDE; Moyer & Landauer 1967). Considering the state-dependency principle of tES effects, this modulation of NDE could be either domain-specific for magnitude representations or it could be driven by the higher level of task difficulty and neural activation in critical trials. In other words, higher demands for discriminating close targets, but also for processing multi-digit numbers could encompass more task-induced activity ready for neuromodulation. NDE in multi-digit comparisons was unaffected by several tDCS configurations of Hauser et al. (2013), but the distractor-distance effect for selecting correct two-digit addition results was monotonically modulated by a bilateral-bicephalic parietal stimulation (Klein et al. 2013). In contrast to the effect of tDCS on the parietal lobe, when

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[7] A PubMed search (tDCS/tRNS AND arithmetic/numerical cognition) identified 34 papers that were manually screened for original results and new cross-referenced studies.

the prefrontal cortex was stimulated both NDE and single-digit accuracy rates were unaffected. Instead, spatial-numerical associations were blocked by cathodal tDCS (see the next Chapter II and Schroeder et al. 2016).

Arithmetic Performance Modulations

Performing even simple arithmetic operations requires domain-general working memory and executive functions involvement to maintain operation components, yet to different extents depending on the exact task. Most studies employed supraorbital or prefrontal return cathodes without necessarily highlighting potential effects on such domain-general functions. Interestingly, for novel and complex subtractions, left-parietal tDCS prevented characteristic prefrontal deactivations below the right-prefrontal cathode as captured with simultaneous fMRI (Hauser et al. 2016) and this configuration improved reaction times (Hauser et al. 2013). In another paradigm, after viewing an instructional video, administering a complex statistical procedure was enhanced from left-parietal anodal tDCS with temporal cathode (Houser et al. 2015), but not with prefrontal cathode placement (Houser et al. 2014). Also considering neurodevelopmental studies, the accumulation of arithmetic proficiency may be accompanied by a shift from broad prefrontal to precise parietal activations (Zamarian et al. 2009). In this line, both frontal and parietal excitatory tRNS generated greater speed improvements over the course of an experiment in subtraction verifications, but not in word classifications (Pasqualotto 2016).

Furthermore, tDCS to one area can lead to altered activations over wide-spread networks in the brain and to effects on cognitive functions related to areas distant from the stimulated area. For example, cathodal stimulation of the cerebellum led to improvements in paced auditory serial subtraction by disinhibition of prefrontal activity (Pope & Miall 2012), and comparable results were obtained with prefrontal anodal tDCS (Pope et al. 2015). In clinical research, a variant of the serial addition WM task is often used in conjunction with tDCS to enhance domain-general functions and emotional processing in depressive patients (Vanderhasselt et al. 2015): Repetitively solving additions at increasing speed frustrates participants and elicits negative affect, but anodal prefrontal tDCS can concurrently improve emotional responses and arithmetic performance (Plewnia et al. 2015). Correspondingly, low- and high-math anxiety individuals show impaired and improved arithmetic performance, respectively, following tDCS above the prefrontal cortex (Sarkar et al. 2014). These results also highlight the importance of emotion for math-related cognitive processing, for which behavioral correlations have often been reported (Suárez-Pellicioni, Macarena, Núñez-Peña, María Isabel, & Colomé 2016).

Also domain-specific effects in multi-digit processing could be modulated: Left-parietal anodal tDCS with 1.5 mA was beneficial for solving problems with larger operands (problem size effect; sums exceeding 10 and including carries), but decreased accuracy in small problems (Rütsche et al. 2015). These differential (beneficial and detrimental) effects seem to be incompatible with a simple domain-general explanation, such as attention, working memory or response preparation processes. Furthermore, whereas the latter result of impaired accuracy from anodal tDCS is counterintuitive, system noise injection by anodal tDCS could skew arithmetic retrieval precisions and this conception was corroborated by concurrent EEG theta measurements (Rütsche et al. 2015; see also Fertonani & Miniussi 2016). Regarding place-value effects (e.g., carrying unit-digits), right-side anodal vs. cathodal parietal tDCS prolonged latency increases for carry operations in a two-digit addition task out of a series of unilateral placements (Artemenko et al. 2015).

Numerical Training Modulations

Whereas tRNS was used only selectively in studies on performance, the technique appears more appealing for numerical and arithmetic training. Highlighting the role of concurrent (‘online’) stimulation during cognitive training, Cappeletti et al. (2013) assembled comparisons between the combinations of training with parietal, motor, and sham tRNS over five days, but also with a parietal tRNS during rest. Number acuity in dot-array discrimination improved most from the parietal stimulation combined with training, but no transfer to arithmetic tasks was observed.

To investigate numerical learning in adults, a prominently investigated paradigm is the artificial symbols training where arbitrary, meaningless figures are assigned to numerical magnitudes. Repeated feedback-guided magnitude comparisons with the artificial symbols (training phase) produce automatic number evaluations that interfere with physical size presentations and map onto space (test phase; Tzelgov et al. 2000). In this paradigm, oppositional parietal tDCS (right anodal, left cathodal) produced faster automaticity and more linear mapping of artificial symbols in a training over 6 days, with sustainability after 6 months (Cohen Kadosh et al. 2010). For the opposite placement, an impaired automaticity was detected, but here the stimulation also produced steeper learning curves superior to prefrontal and sham stimulations (Iuculano & Cohen Kadosh 2013). Interestingly, when the numerical training paradigm was administered in two individuals with severe arithmetic problems, only the left-anodal right-cathodal configuration, which led to impairment in typical participants, led to behavioral improvements (Iuculano & Cohen Kadosh 2014). Although certainly larger samples are required to confirm this pattern, the application of tDCS-combined trainings may provide effective rehabilitation and treatment prospects for numerical deficits.

Arithmetic Training Modulations

With artificial symbols depicting calculation algorithms for arithmetic operations, drill and calculation training combined with prefrontal tRNS improved learning rates, led to sustained calculation performance 6 months later, and generalized to untrained calculation problems (Snowball et al. 2013). In addition, hemodynamic recordings captured short-term and long-term physiological tRNS effects. More recently, an interesting combination of prefrontal tRNS on days 1-3 and parietal tRNS on days 4-5 was observed to improve performance in difficult math problems and accuracy in new and easy problems (Popescu et al. 2016). But also targeting the left parietal cortex with 1.5 mA in a single-day training study on multiplication and subtraction facts, polarity-specific and operation-specific subtraction learning improvements were found and performance differences were sustained in 24h follow-up (Grabner et al. 2015).

In combination with an adaptive body-tracking video-game on fractions, prefrontal bipolar-balanced tDCS (left anodal, right cathodal) resulted in improved and sustained task performance and transferred also to domain-general functions (verbal working memory span) (Looi et al. 2016a).

These first studies demonstrate the potential of tES for enhancing arithmetic training effects in healthy adult subjects and they already incorporate assessments of additional informative indices such as learning curves, specific and general transfer to non-trained stimuli and tasks, long-term effects, and neurophysiological profiles, although effects on domain-general functions are less well discriminated. In contrast, studies employing tES-augmented trainings in atypical populations are scarce and potentially restrained by unknown physical and cognitive side effects (Krause & Cohen Kadosh 2013). Different neurophysiological profiles of individuals or groups at certain development stages (e.g., dyscalculia, stroke patients, children) most likely necessitate tailored parametrical and training-related adjustments, e.g., to also consider specific numerical, arithmetic, and/ or domain-general impairments such as working memory capacity. In this respect, tES research is still in its infancy. Moreover, most conclusions are based on single studies, researchers implement dissimilar tES configurations, and the interdependence of different brain areas and effects in certain tasks is not completely clear. In order to further integrate these partially heterogeneous findings, interpretations of different modulations by tES must also consider and build on the ongoing validation of its very basic principles.

tES Configurations

According to physical arrangements classification (Nasseri et al. 2015), successful modulations of numerical performance utilized unilateral monopolar placements with large return electrodes, bilateral bipolar-balanced and non-balanced, as well as the dual-channel bilateral double-monopolar arrangement by Klein et al. (2013). Most studies focus on parietal placements with 1 mA, but also prefrontal placements appear effective with tRNS (Pasqualotto 2016) and produce significant modulations of spatial-numerical associations (Schroeder et al. 2016) and of math-related emotional processing (Sarkar et al. 2014; Plewnia et al. 2015).

All studies with tRNS used a bilateral bipolar-balanced placement with electrodes either targeting left and right prefrontal areas (e.g., F3 and F4) or parietal areas (e.g., P3 and P4). We wish to highlight once more that these placements are taken to increase excitability over both targeted areas and there is no need of an additional return electrode. Thus, in contrast to (single-channel) tDCS, the bipolar-balanced placement in tRNS is less likely to modulate hemispheric activity dominance and may prove useful for bilateral magnitude processing. Yet, its exact neurophysiological principles are different from (anodal) tDCS and currently not completely understood (Antal & Herrmann 2016).

An interesting concept is the modulation of distinct learning phases over different cortex regions as implemented by Popescu et al. (2016). Future research needs to validate this approach by individualized transcranial stimulation or by comparing different configuration changes directly (e.g., switching from prefrontal to parietal stimulation after 2, 3, or 4 days). The potential of an augmentative effect and better targeting of stimulation by considering training phase is also confirmed by the finding that specific tDCS polarity sequences can lead to more effective modulations with long-term sustainability (Dockery et al. 2009). Thus, fundamental research can also inform interventional administrations, although generalizations from healthy volunteers to different clinical populations (e.g., developmental dyscalculia or acalculia after a stroke) should consider all translational aspects (e.g., functional, structural, strategical compensation, and behavioral differences) in corresponding models before selecting tES configuration parameters.

In the literature, prominently debated tES parameters are electrode configuration and sizes, current intensity and duration, and timing of stimulation compared to task performance (online vs. offline). These and other parameters do not seem to work linearly (e.g., higher intensities can exceed optimal stimulation ranges; Batsikadze et al. 2013) and their combination outcomes might critically depend on task and individual characteristics as well as return electrode effects (Schroeder & Plewnia, 2016). Eventually, this variety of possibilities will allow for broad-ranging applications and fine-grained targeting from underlying theoretical models. Currently, however, simplification or even standardization of certain parameters would facilitate cumulative research, and the ongoing development of electric field modelling tools can already be used for selecting stimulation targets (Truong et al. 2014). Regarding numerical processes, stimulations should be administered concurrent to a task and could then achieve neurostructural precision following task-selective recruitment (Clemens et al. 2013; Bikson & Rahman 2013), but effectivity can vary according to individual differences. Based on the available literature, so far, electrode sizes do not appear to produce remarkable effectivity differences in this domain. However, since the anti-proportional relationship between current density and electrode size (at fixed current strength) does not linearly scale for respective distances from the electrode (e.g., scalp-brain distance) and smaller electrodes may not produce as dense fields in deeper regions (Miranda et al. 2009; see also: Ho et al., 2016), this observation will require systematic evaluation in the future. Furthermore, publication biases can impede the development of better stimulation models, because nonsignificant results are dismissed, theories are elaborated post-hoc, and results could lack reproducibility. In this vein, preregistration of according studies and protocols (e.g., https://aspredicted.org or https://osf.io) could facilitate scientific communication and rigorous evaluation of tES methods.

Conclusion

Both tDCS and tRNS can enhance arithmetic capabilities in adult populations and could be promising tools for deviant performance populations. The current literature is coined by heterogeneity in variable parameters such as montage, but effectivity estimation requires better standardization. Studies with (sub-) clinical populations and children are needed to examine the usefulness of tES for at-risk groups. However, having said that, future research must consider their potentially different neurofunctional signatures, examine potential side effects, and discuss neuroethical questions (Cohen Kadosh et al. 2012; Davis 2014). Documentation of (individualized) task-specific brain activity will potentially allow for predictive adjustment of tES configurations and better evaluation thereof, i.e., using fMRI (Clemens et al. 2013), EEG (Grabner et al. 2015), or fNIRS (Snowball et al. 2013). Further tES precision could be obtained from considering a neurodevelopmental perspective, relevant domain-related states, concurrent neuroimaging, and theoretical optimization of task-related brain-structure correspondence in experimental and training studies to improve efficacy and replication (Harty, Sella, & Cohen Kadosh, 2017).

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Post-Publication Supplementary *P*-Curve Analysis

After official publication of the mini-review, I was informed about *p*-curve analysis as a potentially useful tool to investigate publication bias in the domain of neuromodulation of number processing. In short, *p*-curve analysis rests on the observation that a true effect would statistically imply that most *p*-values from multiple different studies are positioned closer to zero than to the significance threshold α. In contrast, if researchers apply questionable research practices such as *p*-hacking and/ or if there is no true effect due to publication biases, it can be expected that more published *p*-values reside close to the significance threshold. Thus, *p*-curve analysis provides an estimate of the evidential value of an assumed effect by inspecting the distribution and skewness of *p*-values across studies (Simonsohn, Nelson, & Simmons, 2014). Only recently, *p*-curve analysis on the effects of tDCS on cognition and working memory revealed negative results and lack of evidential value (Medina & Cason, 2017).

Disregarding the crucial differences in parameters and tasks of the different studies, *p*-curve analysis can provide a benchmark whether publication bias and questionable research biases distort the research field in measurable ways. In the present case, all 27 statistically significant tDCS results from the mini-review were submitted to the *p*-curve analysis. Both the half and the full tests for a right-skewed *p*-value distribution were significant with ps $< .1$, which is argued to indicate evidential value. Moreover, the tests for 33% power also produced acceptable values corroborating evidential value of the studies and the overall power estimate across all studies yielded 75%. The p-curve distribution is visualized in Figure 1.1. Overall, the additional analysis corroborates the conclusions of the mini-review of the generally positive tES effects in the domains of numerical and arithmetic cognition by indicating evidential value in the reviewed studies.

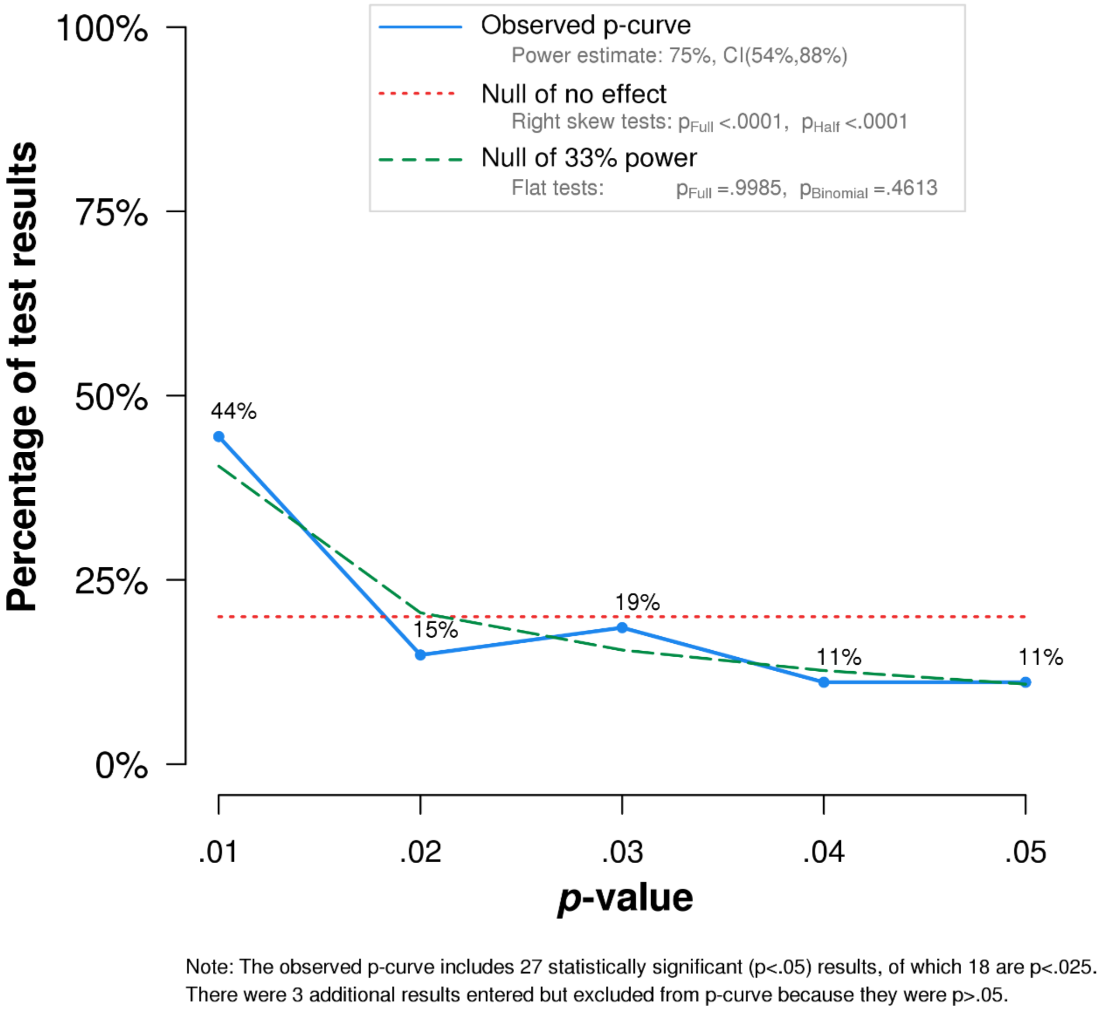

Figure 1.1. *Distribution of p-values in the domain of neuromodulation of number processing, extracted from all studies which are discussed in the mini-review (i.e., p-curve analysis). The statistically significant right-skew tests indicate evidential value of the studies (see also: www.p-curve.com; accessed 11/07/2017).*

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II. SPACE, NUMBER, AND ELECTRICAL STIMULATION

Counteracting implicit conflicts by electrical inhibition of the prefrontal cortex

The following chapter is published as:

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Abstract

Cognitive conflicts and distractions by task-irrelevant information often counteract effective and goal-directed behaviors. In some cases, conflicting information can even emerge implicitly, without an overt distractor, by the automatic activation of mental representations. For instance, during number processing, magnitude information automatically elicits spatial associations resembling a mental number line. This Spatial–Numerical Association of Response Codes (SNARC) effect can modulate cognitive-behavioral performance but is also highly flexible and context-dependent, which points toward a critical involvement of working memory functions. Transcranial direct current stimulation to the PFC, in turn, has been effective in modulating working memory-related cognitive performance. In a series of experiments, we here demonstrate that decreasing activity of the left PFC by cathodal transcranial direct current stimulation consistently and specifically eliminates implicit cognitive conflicts based on the SNARC effect, but explicit conflicts based on visuospatial distraction remain unaffected. This dissociation is polarity-specific and appears unrelated to functional magnitude processing as classified by regular numerical distance effects. These data demonstrate a causal involvement of the left PFC in implicit cognitive conflicts based on the automatic activation of spatial–numerical processing. Corroborating the critical interaction of brain stimulation and neurocognitive functions, our findings suggest that distraction from goal- directed behavior by automatic activation of implicit, task- irrelevant information can be blocked by the inhibition of prefrontal activity.

Introduction

Automatic activation of task-irrelevant and potentially distracting cognitive processes often counteracts effective behavior by blurring attentional and memory resources and luring cognitive processes into the wrong direction. This can happen implicitly, hence without an external stimulus feature directly prompting such processing. A classic example for an implicit cognitive conflict is the spatial association of numbers. Here, although ubiquitous number symbols traditionally convey objective information about the external world, implicit spatial information is automatically activated during number processing (Cipora, Patro, & Nuerk, 2015; Gevers, Lammertyn, Notebaert, Verguts, & Fias, 2006), following left-to-right spatial activations with ascending number magnitude (the SNARC effect; Dehaene, Bossini, & Giraux, 1993; Wood, Willmes, Nuerk, & Fischer, 2008). These spatial-numerical associations can systematically bias overt behaviors such as lateral turns during walking (Shaki & Fischer, 2014) and fair action decisions (Schroeder & Pfister, 2015).

The functional implications of space-number associations are currently controversially discussed: SNARC is sometimes assumed to precede number processing in general (e.g., Rugani, Vallortigara, Priftis, & Regolin, 2015). In contrast, other studies either failed to find correlations between SNARC effects and mathematical ability in human adults (Cipora & Nuerk, 2013; for a review, see Cipora, Patro, et al., 2015) or even suggested that professional mathematicians exhibit diminished rather than increased SNARC effects relative to less mathematically trained participants (Cipora, Hohol, et al., 2015; Hoffmann, Mussolin, Martin, & Schiltz, 2014). Regarding its cognitive foundations, it has been suggested that space-number associations are driven by flexible ordinality representations of the current number set in serial order working memory (WM; van Dijck, Abrahamse, Acar, Ketels, & Fias, 2014; van Dijck & Fias, 2011), possibly emphasized by cultural learning (Patro, Nuerk, Cress, & Haman, 2014; Shaki, Fischer, & Petrusic, 2009). The established neurophysiological view on the representation of number magnitude and its association with space highlights specifically the contribution of parietal areas (Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Cohen Kadosh & Walsh, 2009; Cutini, Scarpa, Scatturin, Dell'Acqua, & Zorzi, 2014; Dehaene, Piazza, Pinel, & Cohen, 2003; Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003; Krause, Lindemann, Toni, & Bekkering, 2014). Only recently, however, studies indicated that prefrontal contributions to advanced numerical cognition might be essential (Arsalidou & Taylor, 2011; Klein et al., 2014), especially in terms of fronto-parietal circuits (Göbel, Johansen-Berg, Behrens, & Rushworth, 2004; Nieder, 2016; Rusconi, Dervinis, Verbruggen,

& Chambers, 2013). Similarly, numeric interval bisection critically deviated in individuals with prefrontal damage (Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005). This corresponds with the idea that WM functions are involved in seemingly basic spatial-numerical processes (van Dijck et al., 2014; van Dijck & Fias, 2011). Yet, the underlying neurophysiological foundations for implicit spatial-numerical conflicts are not resolved.

Empirically, the claim that WM is critically involved in the SNARC effect was motivated from the observations that i) items (i.e., random numbers) at the beginning of a WM list are responded to more quickly with left rather than right responses, with the reversed pattern for items from the end of a WM list. This pattern suggests links between the sequential positions – not necessarily the numerical magnitude – in WM and spatial left-right response codes (van Dijck & Fias, 2011). Further, ii) concurrent WM load from maintenance of non-numerical visuo-spatial or phonological information disrupted SNARC (Herrera, Macizo, & Semenza, 2008; van Dijck, Gevers, & Fias, 2009). Thus, it was suggested that the common left-to-right spatial-numerical alignment is supported by WM functions maintaining a magnitude-ordered number sequence in SNARC tasks, as opposed to a long-term mental number line representation. Indirectly, these considerations postulate that prefrontal activity may guide the ties between space and number. Critically, however, it is now well established that PFC activities corroborate rather broad sets of cognitive functions that could draw on working memory, e.g., as maintenance of internal and possibly distributed representations (D’Esposito & Postle, 2015), but also on cognitive control functions such as conflict detection and inhibition (Botvinick, Cohen, & Carter, 2004; Miller & Cohen, 2001). In SNARC, comparable to other conflict tasks, spatial-numerical associations can activate a spatial response incompatible with a task rule, thus prefrontal control is required to inhibit incongruent activations and select the appropriate action. By experimentally modulating PFC activity during corresponding tasks, the neurophysiological underpinnings of these viewpoints can be investigated.

Building on the idea that mental associations between numbers and space are guided by a WM-related mechanism, we here tested their susceptibility to a noninvasive neuromodulation technique previously used to alter WM performance, while also controlling for online performance on externally available spatial conflicts. In this study, we administered transcranial direct current stimulation (tDCS) to the left prefrontal cortex (PFC) during SNARC and explicit spatial stimulus-response conflict tasks. Particularly anodal, activity-increasing tDCS is known to enhance WM (Fregni et al., 2005; for a review on WM modulations with this montage, see: Brunoni & Vanderhasselt, 2014) and other PFC-related processes (Dockery, Hueckel-Weng, Birbaumer, & Plewnia, 2009; Schroeder, Ehlis, Wolkenstein, Fallgatter, & Plewnia, 2015). Conversely, cathodal, activity-decreasing tDCS has been shown to impair PFC functions including WM (Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011, Wolkenstein, Zeiller, Kanske, & Plewnia, 2014). However, a simple dichotomy of beneficial anodal and detrimental cathodal tDCS does not account for the complexity of interactions between cognitive processes, brain activity and stimulation effects (Jacobson, Koslowsky, & Lavidor, 2012; Plewnia, Schroeder, & Wolkenstein, 2015). Further, distal and network effects can accompany any stimulation that originally targeted the PFC. Such effects may lead to a modulation also of parietal sites, i.e., via frontoparietal connectivity and/ or inhibitory pathways.

Rather, the critical interplay between modulations of cortical excitability and task-induced activity allows for causal inferences regarding the functional involvement of brain regions that might also include remote and interconnected circuits (Fertonani & Miniussi, 2016). In order to assess the specificity of this task-dependent interplay, we tested the effect of concurrent cathodal or anodal tDCS to the left PFC on a spatial-numerical SNARC conflict and on a non-numerical Simon conflict (Hommel, 2011; Simon & Rudell, 1967) as control. Both tasks afford the suppression of either implicitly associated or sensory available spatial information, respectively, and might be mediated by similar mechanisms, i.e., spatial attention (Mapelli, Rusconi, & Umiltà, 2003; Notebaert, Gevers, Verguts, & Fias, 2006) and cognitive control (Notebaert, Gevers, Verguts, & Fias, 2006; Pfister, Schroeder, & Kunde, 2013). Regarding conflict-related processes, a non-specific modulation of both effects can be expected with larger conflicts during PFC attenuation by cathodal tDCS. Following the evidence that spatial and numerical processing predominantly recruits parietal areas, Simon and SNARC conflict effects should be unaffected by the PFC stimulation. However, following the idea that WM is causally involved in linking numbers with space, tDCS should specifically affect the SNARC effect while leaving intact perceptual spatial response conflicts.

Notably, both tasks are not direct tests of WM functioning. Rather, we utilize the modulation by tDCS to test the consequences of a general conflict resolution or a specific WM function implying frontal and/ or fronto-parietal involvements differentially in the two tasks. Also, in a nonspatial IAT task, anodal tDCS was already demonstrated to increase an implicit association bias by accelerating responses to congruently paired categories (Gladwin, den Uyl, & Wiers, 2012). With this study, we aimed at shedding light on the role of PFC in forming implicit spatial-numerical associations during number judgments.

More precisely, from the previous proposal of WM involvement in SNARC (van Dijck & Fias, 2011), we hypothesized cathodal, inhibitory tDCS to impede automatic space-number associations and to thus reduce behavioral conflicts by task-irrelevant implicit spatial information in a parity judgment (Exp. 1) and a magnitude judgment task (Exp. 2). Therefore, a task-specific effect of inhibitory prefrontal cortex stimulation should occur, but neither spatial information processing nor magnitude processing by itself should be modulated. Finally, by administering anodal tDCS in experiment 3, we aimed at exposing the polarity-specificity of this neuromodulatory effect.

Methods

Participants

Seventy-two healthy volunteers (17 male, mean age: 23.9 years, range: 18 – 42 years) were recruited in total, with twenty-four new participants for each of the three experiments. Each individual participated in two experimental sessions on separate days. Participants were consistently right-handed (Edinburgh Handedness Inventory (Oldfield, 1971): $LI > 75$) and scored without pathological findings in preceding screenings for psychiatric disorders and dyschromatopsia (Ishihara, 1917). Further exclusion criteria were: Age < 18 years, epilepsy, neurologic disorders, pregnancy, metallic implants and pacemakers. Participants signed an informed consent as reviewed by the ethical commission of the University Hospital Tübingen (approval id: 215/2014BO2) and received 20 € or course credit as compensation.

Transcranial Direct Current Stimulation

Direct current was generated by a CE-certified stimulator (DC-STIMULATOR MC, NeuroConn, Germany) and delivered with a pair of identical 5 × 7 cm^2 rubber electrodes covered with adhesive paste (10/20 conductive EEG paste, Kappamedical, USA). Stimulation lasted 25 min (including a 5 min pretask idle time) with a current of 1 mA, resulting in a current density of 0.028 mA/cm^2, and impedances were below 10kΩ. Stimulation was faded in and out with a 5 s ramp. For participants of experiments 1 and 2, the cathode electrode was placed over the left PFC (F3 according to the 10–20 EEG system of electrode placement) and fastened with a bathing cap. The reference/anode electrode was placed extracranially on the contralateral upper arm to avoid an opposite polarization of another brain area and thus ensure that tDCS effects could be traced back exclusively to stimulation of the left PFC (Wolkenstein & Plewnia, 2013). For participants of experiment 3, active and reference electrode polarity were exchanged (anode: F3, cathode: upper arm). Both tasks were initiated and completed during active tDCS. Sham stimulation current was faded out after 40s of stimulation (4:20 minutes prior to the beginning of the first task) and accordingly the tasks were initiated and completed without active tDCS. Verum and sham sessions were run on separate days and stimulation order was counterbalanced across participants.

Procedure

All experiments followed a sham-controlled crossover design. Participants were seated in front of a 17” monitor with 60 cm distance to the screen and all stimuli appeared at a size of 2.0° as implemented in PsychoPy software (Peirce, 2007). All sessions consisted of one practice and three test blocks for each of the two tasks. Stimulation sequence (sham / verum) and task order (Simon / SNARC) were counterbalanced across participants, but a fixed response mapping was determined to keep possible influences of parity or color on spatial decisions constant (Elliot & Maier, 2014; Nuerk, Iversen, & Willmes, 2004). Participants were instructed to respond with a right (left) key press to blue / even (yellow / odd) circle targets or single-digits in the respective tasks (Figure 2.1) and thus had to ignore actual positions on screen or spatial-numerical associations in response-incongruent trials (50% of all trials). Cathodal/Sham/Anodal tDCS was applied online to the task to the left PFC [see Figure 2.1C for a computational model of the stimulation effect (Jung, Kim, & Im, 2013)]. After 5 minutes of (sham-) stimulation, onscreen instructions signaled the beginning of the first experimental task.

Both parity judgment (experiments 1 and 3) and magnitude judgment (experiment 2) SNARC tasks comprised single-digit targets 1-9 except 5. In the Simon task, participants judged circle colors (blue vs. yellow) and had to ignore circle locations (distance from central fixation: -4°, -2°, 2°, and 4°). Via onscreen instructions, mapping rules and short encouragements to react correctly as fast as possible were provided and repeated in each short break between the blocks. Additional instructions announced the second experimental task and provided the new task rules. Parity, magnitude, and color judgments were given with the left or right index finger on identically marked keys ‘s’ and ‘l’ of a standard German QWERTZ-keyboard, yielding an inter-key distance of 11.6 cm.

Trials started with a short central fixation (+; 300 ms), followed by a centrally presented white digit in the SNARC tasks or a laterally shifted colored circle in the Simon task. All stimuli were presented equally often in randomized order. Incorrect or late responses (>2000 ms) triggered immediate feedback in form of the German words “Fehler” (Eng. “error”) or “Bitte schneller antworten!” (Eng. “please respond faster!”) for 500 ms. An additional blank inter-trial-interval of 300 ms ended each trial. Responses were regarded congruent (incongruent) if a left (right) response was given to a leftwards positioned circle or a digit < 5, and vice versa. Each experimental block contained 40 congruent and 40 incongruent trials and an error count was provided in each break between blocks.

Questionnaires

We assessed participants’ mood pre- and post-stimulation by the PANAS questionnaire (Watson, Clark, & Tellegen, 1988), adverse effects of tDCS (cf. Brunoni et al., 2011), and blinding efficacy (sham vs. verum stimulation guesses) in all sessions.

Data Treatment

Trials with errors and trials following errors were excluded from the analyses (5.5 %; cf. Rabbitt, 1979), as were stimulus repetition trials (6.4 %; cf. Tan & Dixon, 2011; Pfister, Schroeder, & Kunde, 2013). Outlier trials with response times (RTs) differing more than 2.5 standard deviations from the mean RT of the corresponding design cell were omitted (1.7 %). These criteria left 86.4 % of all trials for the analyses. Mean response times (RTs) and error rates from the SNARC and Simon tasks were submitted to separate 2 ($\mathit{congruency}_{\text{CONGRUENT,INCONGRUENT}}$) × 2 ($\mathit{stimulation}_{\text{CATHODAL,SHAM}}$) repeated measures analyses of variance (ANOVA), followed up by paired t-tests.

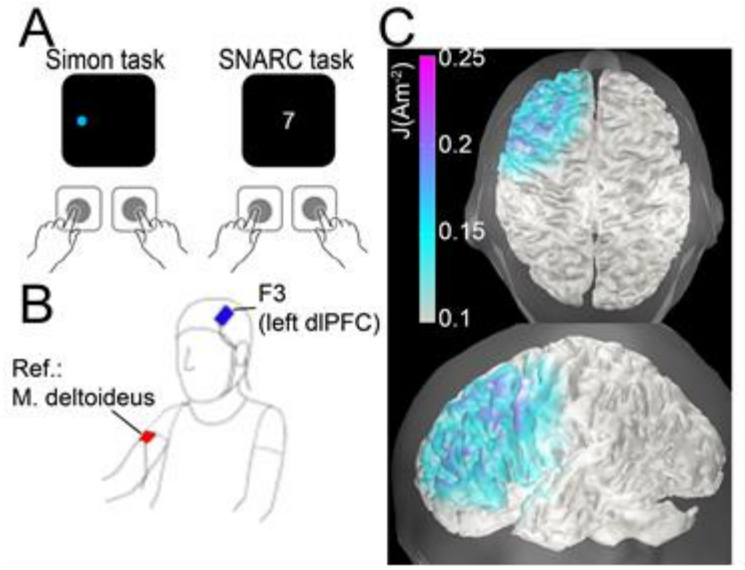

Figure 2.1. *Experimental tasks and electrode montage. (A) Participants judged colors (Simon task) and digit parity (experiment 1 and 3) or digit magnitude (experiment 2; SNARC tasks) by index finger key presses. (B) The active tDCS electrode (cathode) was placed over the left prefrontal cortex (F3) and the reference electrode (anode) was placed on the contralateral upper arm to avoid an opposite polarization of another cortical region (Wolkenstein & Plewnia, 2013; Zwissler et al., 2014). Electrode positions were interchanged for experiment 3. (C) Current density distribution as modeled using the COMETS toolbox (Jung et al., 2013).*

Results

Experiment 1

We tested 24 right-handed participants (mean age = 24.2 years, *SD* = 4.4 years, 3 male) during sham and cathodal tDCS on a color-judgment Simon task and a parity-judgment SNARC task. Mean Response Times (RTs) for both tasks and stimulation conditions are depicted in Figure 2.2 (left panel). For the SNARC task, a significant main effect of $congruency_{\text{CONGRUENT,INCONGRUENT}}$ emerged, $F(1,23) = 5.68$, $p = .026$, $\eta_p^2 = 0.20$, signaling reliable SNARC effects. Importantly, the two-way interaction of $congruency_{\text{CONGRUENT,INCONGRUENT}}$ and $stimulation_{\text{CATHODAL,SHAM}}$ was significant, $F(1,23) = 9.42$, $p = .005$, $\eta_p^2 = 0.29$, whereas the main effect of $stimulation_{\text{CATHODAL,SHAM}}$ was not significant, $F(1,23) = 2.72$, $p = .11$. Follow-up paired *t*-tests confirmed that responses were significantly faster during cathodal stimulation (compared to sham stimulation) in incongruent SNARC trials, $t(23) = 2.33$, $p = .029$, d = 0.49, but not in congruent SNARC trials, $t(23) = 0.75$, $p = .46$.

For the control Simon task, a reliable main effect of congruency$_{\text{CONGRUENT,INCONGRUENT}}$ emerged, $F(1,23) = 99.93$, $p < .001$, $\eta_p^2 = 0.81$, signaling reliable Simon effects. However, neither the main effect of *stimulation*$_{\text{CATHODAL,SHAM}}$, $F(1,23) = 0.08$, $p = .77$, nor the two-way interaction approached significance, $F(1,23) = 0.01$, $p = .91$, suggesting that the tDCS modulation was specific to incongruent SNARC trials. By subjecting the data from both tasks to another repeated measures ANOVA, this hypothesis was substantiated in terms of a significant three-way interaction of *task*$_{\text{SNARC,SIMON}}$, *congruency*$_{\text{CONGRUENT,INCONGRUENT}}$, and *stimulation*$_{\text{CATHODAL,SHAM}}$, $F(1,23) = 8.12$, $p = .009$, $\eta_p^2 = 0.26$.

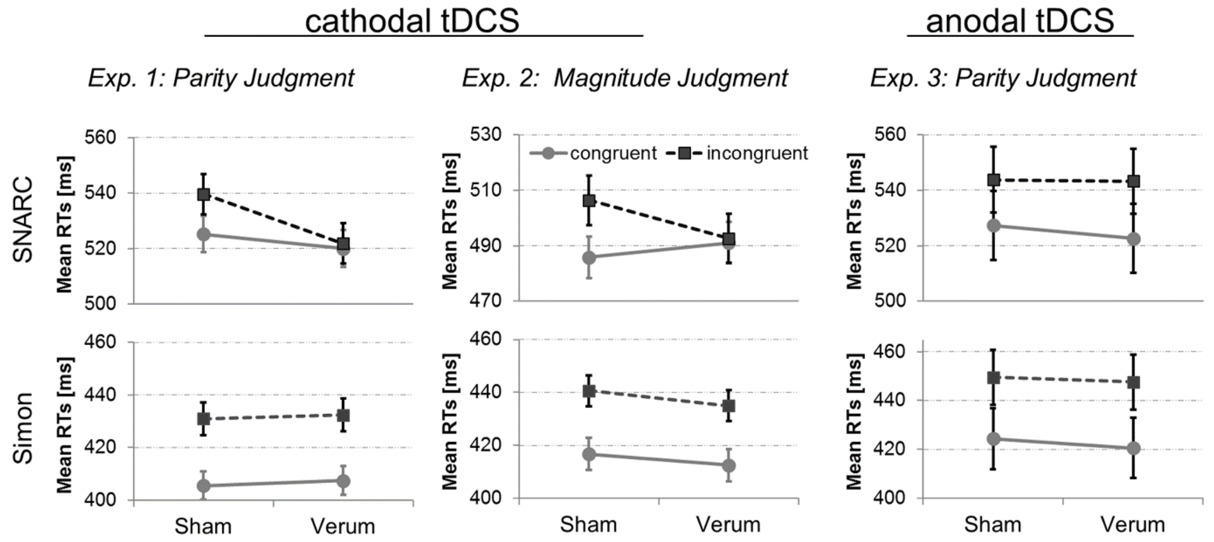

Figure 2.2. *Specific modulation of implicit conflicts by cathodal tDCS. Mean RTs of congruent and incongruent SNARC and Simon trials in verum and sham stimulation conditions of the three experiments. Error bars indicate standard errors of paired differences (Pfister & Janczyk, 2013). During cathodal (experiments 1 and 2) or anodal tDCS (experiment 3), participants judged single-digits by their parity (odd or even) or magnitude (<5 or >5; SNARC tasks) and laterally shifted circles by their color (Simon task).*

In error rates, the 2 × 2 ANOVAs again showed the main effect of *congruency*$_{\text{CONGRUENT,INCONGRUENT}}$ to be significant for the SNARC task, $F(1,23) = 6.82$, $p = .016$, $\eta p^2 = .23$, and for the Simon task, $F(1,23) = 16.67$, $p < .001$, $\eta p^2 = .42$. In contrast to RTs, the *stimulation*$_{\text{CATHODAL,SHAM}}$ × *congruency*$_{\text{CONGRUENT,INCONGRUENT}}$ interaction in the SNARC task was not significant, $F(1,23) = 0.90$, $p = .35$, and neither was the main effect of $stimulation_{\text{CATHODAL,SHAM}}$, $F(1,23) = 2.20$, $p = .15$. The same picture emerged for the Simon task, *p*s > .40.

Experiment 2: Magnitude Judgment

To delineate the relevance of magnitude processing for the formation of the stimulation effect and to cross-validate our results, another group of 24 participants (mean age = 22.8 years, *SD* = 4.6 years, 7 male) was asked to make explicit magnitude judgments in the SNARC task. Experimental design and the control Simon task were identical to experiment 1. In the magnitude judgment task, two blocks of each 240 trials were completed by all participants and the response mapping order (i.e., congruent, left hand [incongruent, right hand] response for digits < 5 in the first block) was counterbalanced across participants, but held constant for the two sessions.

Resembling the data of experiment 1, a significant two-way interaction of $congruency_{\text{CONGRUENT,INCONGRUENT}}$ and $stimulation_{\text{CATHODAL,SHAM}}$ emerged for the SNARC task, $F(1,23) = 10.58$, $p = .004$, $\eta_p^2 = 0.32$, but not for the Simon task, $F(1,23) = 0.19$, $p = .66$ (Figure 2.2, center panel). Again, task-specificity was tested with data from both tasks, which yielded a significant three-way interaction of $task_{\text{SNARC,SIMON}}$, $congruency_{\text{CONGRUENT,INCONGRUENT}}$ and $stimulation_{\text{CATHODAL,SHAM}}$, $F(1,23) = 7.85$, $p = .010$, $\eta_p^2 = 0.26$. Importantly, although the stimulation-driven response *acceleration* in SNARC-incongruent trials was not significant, $t(23) = 1.54$, $p = 0.14$, SNARC *effects* (i.e., the RT difference between congruent and incongruent trials) did not differ significantly from zero during cathodal tDCS, $t(23) = 0.32$, $p = 0.75$, but SNARC effects were pronounced during sham tDCS, $t(23) = 3.06$, $p < 0.01$, d = 0.62. Again, error rates were not affected by the stimulation, all *p*s > .83, which implies that effective magnitude comparison (for instance, correct retrieval of magnitude facts) was not eliminated by PFC down-regulation.

Numerical Distance Effect

Unrelated to the resolution of cognitive conflicts, the difficulty (and, consequently, mean response latency) of a magnitude judgment decreases with the numerical distance between the two compared digits (Moyer & Landauer, 1967). Reflecting the analogue nature of magnitude representations, numerical distance effects are not necessarily linked to a spatial mapping (Bonato, Zorzi, & Umiltà, 2012) and diverge from SNARC effects (Nuerk, Bauer, Krummenacher, Heller, & Willmes, 2005). What is more, while distance effects draw on parietal IPS activation, they might also be related to general response-selection processes (Göbel et al., 2004) as required throughout our tasks. However, if numerical magnitude processing *per se* was affected by the stimulation, the numerical distance effect should also appear modified. We therefore extracted congruency-independent response times for individual target digit distances from the reference digit ‘5’ (|distance| = 1, 2, 3, or 4) from both stimulation sessions seperately and tested for modulatory effects in a 2 ($stimulation_{\mathrm{CATHODAL,SHAM}}$) × 4 ($distance_{1,2,3,4}$) ANOVA (c.f. Holloway & Ansari, 2009). As indicated by Figure 2.3A, reliable distance effects emerged during both sham and cathodal stimulation and gave rise to a significant main effect of $distance_{1,2,3,4}$, $F(3,69) = 42.53$, $p < .001$, $\eta_p^2 = 0.65$. However, neither the main effect of $stimulation_{\mathrm{CATHODAL,SHAM}}$, $F(1,23) = 0.34$, $p = .57$, nor the interaction term approached significance, $F(3,69) = 0.28$, $p = .84$.

These findings indicate that the modulation of SNARC effects by prefrontal cortex stimulation observed in experiment 1 and 2 was not driven by altered magnitude processing, but the modulation was exclusively related to the emergence of (and distraction by) spatial-numerical associations.

Experiment 3: Polarity Specificity

Finally, we repeated experiment 1 with a new group of 24 participants (mean age = 24.7 years, *SD* = 5.1 years, 7 male) and administered 1 mA anodal, activity enhancing tDCS to the left PFC to test whether the previous results were polarity-specific (Figure 2.2). Following our previous findings, we now predicted a task-specific increase in spatial-numerical conflicts from anodal tDCS relative to sham stimulation.

A main effect of $congruency_{\mathrm{CONGRUENT,INCONGRUENT}}$ signaled reliable SNARC effects, $F(1,23) = 11.16$, $p = .003$, $\eta_p^2 = 0.33$. However, we neither obtained a significant main effect of $stimulation_{\mathrm{ANODAL,SHAM}}$, $F(1,23) = 0.57$, $p = .814$, nor a two-way interaction, $F(1,23) = 2.18$, $p = .153$. As with cathodal stimulation, there were no significant stimulation effects on Simon conflict nor in error rates, *p*s > .28. Thus, although descriptively a slight increase in SNARC was observed (see Figure 2.3B), the effect of anodal stimulation alone was not significant.

To resolve the differential effects of cathodal and anodal tDCS on SNARC, we next directly compared the results of experiments 1 and 3 in a between-experiments analysis. The ANOVA on the SNARC task comprised the within-subjects factors $stimulation_{\mathrm{VERUM,SHAM}}$ and $congruency_{\mathrm{CONGRUENT,INCONGRUENT}}$ as well as the between-experiments factor $polarity_{\mathrm{ANODAL,CATHODAL}}$.

A significant interaction of $stimulation_{\text{VERUM,SHAM}}$, $congruency_{\text{CONGRUENT,INCONGRUENT}}$ and $polarity_{\text{ANODAL,CATHODAL}}$ emerged, $F(1,46) = 10.86$, $p = .002$, $\eta_p^2 = 0.19$, which substantiates our polarity-specificity hypothesis.

Joint Analyses: Time Course of Conflict Effects

Since it is conceivable that tDCS effects could have emerged on the basis of overall prolonged responses, we evaluated the effect functions of both tasks (with conflict effects defined as the RT difference between incongruent and congruent trials) by a quantile analysis and splitted the RT data individually into four equally large quartiles of participants' response speed. If the stimulation effect was due to the current time on task, a tDCS modulation of both SNARC and Simon effect functions should emerge for prolonged responses only.

As illustrated in Figure 2.3C, the task-specific impact of tDCS on the SNARC effect was not particularly modulated by response speed as quantified by the quartile split (and there were no significant interactions, *p*s > .34). Interestingly, the magnitude of sham SNARC, at the same time, increased with prolonged responses (*p*s < .04), in line with previous findings (Gevers, 2006). Importantly, and in both experiments employing cathodal stimulation, a significant tDCS effect emerged already in the fastest SNARC trials that also contained the smallest conflict sizes at sham (Exp. 1: $t(23) = 2.44$, $p = .023$, d = 0.56; Exp. 2: $t(23) = 3.00$, $p = .006$, d = 0.60). In contrast, no significant effect was detected for the slowest Simon trials (Exp. 1: $t(23) = 0.12$, $p = .91$; Exp. 2: $t(23) = 0.19$, $p = .85$). For these two quartiles of the respective tasks, mean RTs in the SNARC task (Exp. 1: 443 ms, Exp. 2: 420 ms) were faster than mean RTs in the Simon task (Exp. 1: 507 ms, Exp. 2: 520 ms), all *p*s < .001, which renders unlikely that the modulation depended on response speed or within-task conflict strength.

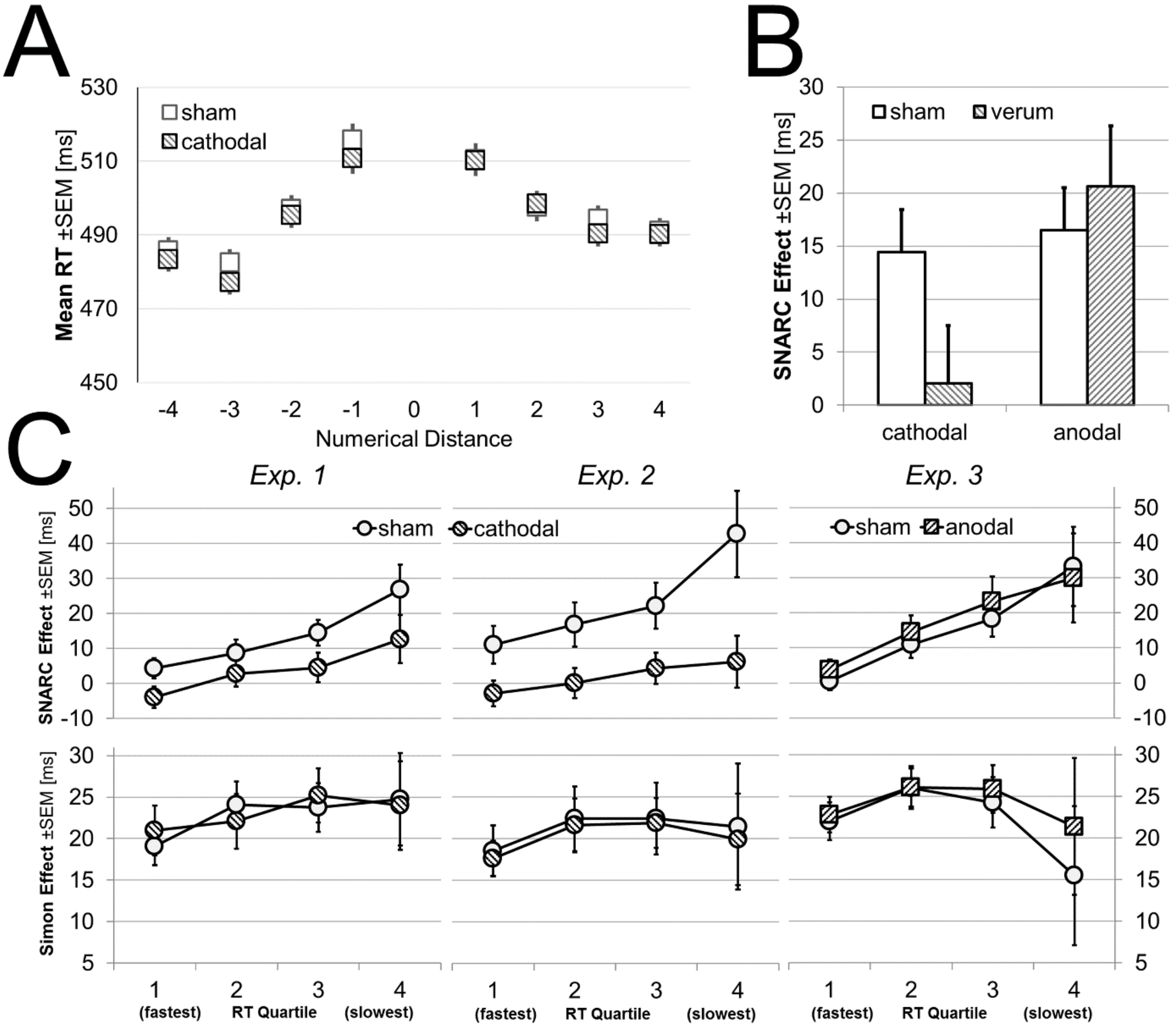

Figure 2.3. *Numerical distance effect, polarity-specificity and time course analysis. Regular numerical distance effects (A) emerged in experiment 2 and independent of tDCS. (B) Polarity-specific modulation of SNARC effects in parity judgment. (C) Time course analyses of SNARC and Simon conflict effects. A modulation by cathodal tDCS was already observed for the fastest SNARC trials, but not for the slowest Simon trials.*

Table 2.1. TDCS adverse effects. Adverse sensations were assessed on a 5-point Likert-like scale after each session (1 = none, 5 = extensive). Ratings from the two sessions were subjected to paired *t*-tests. There were no main effect nor interactions between experiments (*p*s > .21), thus collapsed data are presented.

Sensation	**Verum tDCS** ***M (SD)***	**Sham tDCS** ***M (SD)***	***p***
Tingling at the site of the electrode	2.90 (1.19)	2.34 (1.17)	.001
Tingling elsewhere	1.33 (0.68)	1.18 (0.49)	.16
Exhaustion	1.68 (0.88)	1.39 (0.77)	.007
Itching	2.04 (1.20)	1.64 (0.96)	.003
Headache	1.30 (0.58)	1.28 (0.64)	.73
Nausea	1.07 (0.31)	1.00 (0.00)	.058

Adverse Effects and Blinding Efficacy

Participants experienced weak sensations of tingling and exhaustion in both sham and verum stimulation sessions (Table 2.1). There were no significant differences between the experiments (all *p*s > .21), but the main effect of tDCS on adverse effects ratings was highly significant, $F(1,66) = 20.79$, $p < .001$, $\eta_p^2 = 0.24$. Blinding guesses did not exceed chance level: In the first session, 57% guesses were correct, $X^2(1, N = 72) = 1.39$, $p = .24$. In the second session, 61% guesses were correct, $X^2(1, N = 71) = 3.17$, $p = .08$. Participants' mood [as quantified by the PANAS questionnaire (Watson et al., 1988)] was not significantly altered after anodal or cathodal vs. sham stimulation, *p*s > .41.

Discussion

The results of our experiments outline a polarity-specific and task-dependent elimination of interference from implicit cognitive conflicts by concurrent prefrontal cortex inhibitory tDCS. Specifically, parity as well as magnitude judgments were no longer affected by task-irrelevant, but distracting space-number associations during cathodal tDCS whereas such implicit cognitive conflicts emerged during sham and anodal tDCS. In contrast, the distracting influence of externally available visuo-spatial information in the Simon task affected task performance in all stimulation conditions (for comparable results, see: Zmigrod, Zmigrod, & Hommel, 2016).

Of note, significant numerical distance effects that indicate typical magnitude representations remained unaffected throughout experiment 2. Functionally, this result indicates that the concurrently abolished intrinsic spatial property of number – be it as maintenance in working memory or recall from parietal sites – is not required for simple comparisons of numerical magnitudes, an interpretation corroborated by the reduced SNARC in professional mathematicians (Cipora et al., 2015) and by observations of magnitude-based effects in absence of magnitude-space associations (Nuerk, Bauer, Krummenacher, Heller, & Willmes, 2005). It is further consistent with the idea that magnitude processing precedes spatial mappings in a separable step (Gevers & Santens, 2008; Gevers, Verguts, Reynvoet, Caessens, & Fias, 2006), possibly along a hierarchical frontoparietal pathway (Nieder, 2016). Therefore, these findings point towards a specific suppression of implicit dysfunctional spatial-numerical information by PFC down-regulation, but not of effective magnitude representations. In turn, our results underline the necessity of prefrontal activity for implicit conflict generation in case of the SNARC effect and thus corroborate the significant role of prefrontal activity for space-number associations.

Nevertheless, alternative physiological effects have to be considered (Nitsche et al., 2008; Tremblay et al., 2014): Instead of inducing a focal PFC activity decrease, cathodal tDCS could have down-regulated a fronto-parietal number network including prefrontal cortex and relevant parietal cortex areas, i.e., intraparietal sulcus (Eger, Sterzer, Russ, Giraud, & Kleinschmidt, 2003; Klein et al., 2014). Via PFC-parietal intercommunication, the observed stimulation effect could also partly draw on parietal representations, for instance in form of an enhanced number fact retrieval from relevant parietal sites (Dehaene et al., 2003; Smirni, Turriziani, Mangano, Cipolotti, & Oliveri, 2015; Klein, Moeller, Glauche, Weiller, & Willmes, 2013). As for the latter, cathodal stimulation has been attributed a noise filter function before (Miniussi, Harris, & Ruzzoli, 2013) that allowed more effective distinctions between target and flanker or lure stimuli (Weiss, Lavidor, O'Neil, & Adamson, 2012; Zwissler et al., 2014). Seeing the flexible emergence of SNARC also observed from different context manipulations (Bächtold, Baumüller, & Brugger, 1998; Fischer, Mills, & Shaki, 2010), slight membrane threshold modulations by tDCS might have just blocked the jittery and task-irrelevant spatial-numerical signal chain. Considering also that pure (and task-relevant) magnitude processing as indicated by the numerical distance effect necessarily recruits parietal areas, as outlined by recent rTMS and tDCS studies (Cappelletti, Barth, & Spelke, 2008; Klein et al., 2013), attributing the stimulation effect to a down-regulation of PFC efficiency seems the most parsimonious mechanism, albeit not the only one possible. In future studies, concurrent imaging methods (i.e., NIRS and/ or tES-EEG) could be used to investigate network-effect activation changes by focal stimulations, i.e., at parietal sites. By relating our results to previous behavioral studies and including further theoretical accounts, we propose attributing the stimulation effect to the neurocognitive downregulation of WM efficiency.

Functional Implications of the PFC in Number Processing

Currently, prefrontal cortex involvement in numerical cognition is integrated in corresponding neurocognitive models (Arsalidou & Taylor, 2011; Klein et al., 2014), emphasizing its relevance for arithmetic performance. For instance, in children with mathematical disabilities, increased prefrontal activation, amongst parietal and occipito-temporal cortex activation, was observed during arithmetic problem solving and traced back to hyper-connectivity of several networks, including fronto-parietal hyper-connectivity (Rosenberg-Lee et al., 2014). Also, children with mild traumatic brain injury displayed specific arithmetic difficulties associated with visual WM deficits (Van Beek, Ghesquière, Lagae, & De Smedt, 2015). Moreover, using non-invasive brain stimulation, it has been demonstrated that the administration of excitatory anodal tDCS (Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010) and transcranial random noise stimulation (tRNS) to the bilateral PFC during arithmetic training improved learning effects (Snowball et al., 2013).

While both learning paradigms and advanced arithmetic competencies thus point to prefrontal involvement in numerical cognition in general, our study highlights a critical role of prefrontal circuits in the very basics of number representation and spatial-numerical processing. Our experimental design allows for specific conclusions regarding the underlying cognitive mechanisms that produced differential effects of tDCS on SNARC and Simon conflicts. Previous studies dissociated slightly different posterior parietal processing pathways for these types of conflict (Rusconi, Turatto, & Umiltà, 2007), as well as different time courses and a lack of additivity of the two conflict effects (Mapelli et al., 2003). Yet, different regional activations can still be explained by a common dual-route architecture with abstract spatial representations on an intermediate layer (Gevers, Caessens, & Fias, 2005; Gevers & Notebaert, 2008). Functionally, it appears consistent with a framework in which prefrontal cathodal tDCS blocks the emergence, maintenance, or recall of an abstract spatial code, resulting in the observed reduction of interference with response selection processes. Nevertheless, in both tasks, suppression of distracting spatial content by a cognitive control mechanism is required to respond correctly. So, if cognitive control in general had been impaired by cathodal stimulation of the prefrontal cortex (Wolkenstein, Zeiller, Kanske, & Plewnia, 2014), task performance should have suffered in both the Simon and the SNARC task, leading to generally increased conflict effects. Here, in this respect, tDCS was ineffective, possibly undermined by compensatory processes (Pirulli, Fertonani, & Miniussi, 2014) or by the intermediate role of dorsolateral PFC (i.e., as compared to the anterior cingulate cortex; Botvinick, Cohen, & Carter, 2004) during non-emotional conflict processing (i.e., as compared to emotional processing; Plewnia et al., 2015). Similar behavioral results have been obtained from applying tDCS over medial prefrontal cortex during an Eriksen flanker conflict task, i.e., there was no modulation of executive attention from 2 mA anodal tDCS (Coffman, Trumbo, & Clark, 2012).

Do PFC Modulations of SNARC Effects Draw on Working Memory?

In order to relate our findings to working memory, it is essential to conciliate previous behavioral and theoretical results, since it is a broad set of cognitive processes involved in the prefrontal cortex including, but also exceeding WM processes (D’Esposito & Postle, 2015). Specifically, previous work repeatedly demonstrated WM maintenances to corrupt spatial-numerical activations (Herrera et al., 2008; van Dijck & Fias, 2011; van Dijck et al., 2009). Furthermore, by maintaining random number sequences during number judgment tasks, the regular left-to-right SNARC effect was replaced flexibly by the ordinal positions of the exact number sequence kept in mind (van Dijck et al., 2014; van Dijck & Fias, 2011). As these short-term representations were constructed during task execution, it was suggested that ascending order representations of target digit positions (and not magnitudes) account for the SNARC effect by drawing on WM maintenance of the existing or artificial ties between number and space. A similar elimination of regular space-number associations occurred in the presented single-task setting. In this framework, the present findings could imply separate functional mechanisms to be disentangled in future research: (1) Participants might fail to adapt to the current task-set (though this mechanism is improbable due to the correct maintenance of response-mapping), (2) the systematic association of task-set stimuli with space might have been corrupted, and/ or (3) spatial task-set information maintained in WM is blocked from transfer to task-relevant response selection. While any of these possibilities is in line with a WM account on SNARC, other prefrontal functions could also account for the observed results. Nevertheless, using tDCS, we here demonstrate and replicate that prefrontal activity is critical for distraction by implicit cognitive conflicts based on SNARC.

Consequently, the stimulation was less efficient in modulating the Simon effect, which builds on the sensory processing of externally available spatial information. Here, it should be noted that both effects require WM representations of the response mapping to occur (Ansorge & Wühr, 2004). Thus, it would be misleading to consider the observed tDCS effect a complete down-regulation of WM. Mitigating our interpretations, it was not assessed whether other established measures of WM functioning were addressed by the stimulation (but see Wager & Smith, 2003; Zaehle et al., 2011; Wolkenstein et al., 2014). Also, both tasks require spatial information processing; however, spatial information in the SNARC task is not directly available in the external stimulus. Thus, interference with a spatial response in the SNARC effect depends on the internally and automatically generated spatial-numerical code (Gevers et al., 2006) and not on external visuo-spatial information. While leaving open to further investigation how exactly the spatial-numerical tie is created by PFC and/ or communication networks, our results are also consistent with a WM account of the SNARC effect (i.e., van Dijck & Fias, 2011).

Alternatives to a WM Explanation

Revisiting conflict detection and resolution, one interesting speculation can be drawn from previous findings on the relation of conflict strength and recruitment of the PFC (Tsushima, Sasaki, & Watanabe, 2006). More precisely, subthreshold conflicting information does not seem to recruit LPFC as compared to suprathreshold information. Given that the SNARC effect was markedly weaker than the Simon effect in the present experiments (and participants were presumably also less aware of it), the conflicting spatial signals from number representations could similarly fail to recruit prefrontal control mechanisms. Such a perspective may further suggest alternative interpretations of our results that do not necessarily draw on WM and its supposed role in retrieving spatial-numerical associations. For instance, reduced prefrontal noise from cathodal tDCS could improve the detection (and the subsequent resolution) of internal conflict.

Furthermore, the mere fact that the Simon task provoked greater conflict than the SNARC task – i.e., as reflected in latency effect size – might mediate its resilience to tDCS. From this idea of a simple quantitative – and not qualitative – difference in conflict strength signals, it can also be predicted that within-task conflict strength differences should modulate stimulation efficacy. For the SNARC effect, it is known that the magnitude of conflict evoked is the higher for greater spatial distances (i.e., ‘1’ and ‘2’ are more strongly associated with ‘left’ than ‘3’ and ‘4’, and so on; Fs>8.2, ps<.01). Turning to the stimulation effects observed in our data, however, we did not detect different tDCS effects within the SNARC tasks (ps>.22), but – introducing this within-task factor to the corresponding ANOVAs – we were only able to replicate the global SNARC modulations with cathodal tDCS (Exp. 1: p=.014; Exp. 2: p=.004). This result corresponds to significant stimulation effects throughout the SNARC RT distribution, thus regardless of conflict increases with longer responses. Thus, the current data do not support a view of merely quantitative different conflict signals. Nevertheless, these mentioned accounts do provide interesting alternatives to the working memory-based explanation discussed above, to be tested in confirmatory tasks (i.e., by introducing other subthreshold conflicts, and manipulating response compatibility or conflict strength in further stimulation experiments).

Limitations

Further investigations into WM functioning are required to specify the theoretical interpretation and functional implications of our findings. By finding even the fastest SNARC trials to be modulated by tDCS, we can rule out that the stimulation effect was merely driven by prolonged responses. Yet, the rather large tDCS stimulation site (cf. Figure 2.1C) necessarily comes with a reduced focal specificity, and the observed effects therefore might partially draw on regions such as the frontal junction or (left) frontal eye field (Rusconi, Bueti, Walsh, & Butterworth, 2011). Stimulation of parietal control sites may further amend to the focal specificity of our observed effects and had been effective in the past to modulate magnitude-related processing which is not necessarily connected to spatial-numerical associations (Artemenko, Moeller, Huber, & Klein, 2015; Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013; Rusconi et al., 2007; Sarkar & Cohen Kadosh, 2016). Finally, the established active control from the Simon task and our additional analyses on the numerical distance effect paint a very clear picture of the outlined modulation's specificity.

Overall, verum stimulation triggered more intense sensations of tingling, itching, and exhaustion. Thus, it might be argued that any cognitive effect was due to a sensory experience of the stimulation (i.e., distraction). However, the polarity-specific cognitive effects were not reflected in differential reports on adverse effects in our study, and blinding guesses were not given beyond chance, which eventually underpins the neuromodulatory mechanism as outlined. In fact, anodal tDCS even seemed to pronounce SNARC (see Fig 3B), but here we would like to draw conclusions only from the significant polarity-specific effect as obtained in the between-subjects analysis. Since we reproduced SNARC effects in all sham conditions, a ceiling effect possibly restricted additional increases in spatial-numerical activations by anodal tDCS. Finally, while the causal dependence of spatial-numerical associations on prefrontal activity sharply fosters a working memory account of SNARC, the exact cognitive mechanisms need to be specified theoretically and empirically in further studies. In our experiments, the perfect correspondence between sequence position and magnitude neither favors linking the abolished SNARC to either of these possibly distinct representations, although the dissociation of SNARC and distance effects requires to consider multiple magnitude representations. For instance, our results leave open whether spatial-numerical activations are due to serial-order task-set adaptations (Abrahamse, van Dijck, Majerus, & Fias, 2014; van Dijck et al., 2014), or due to the spatial representation of number retrieved by PFC (i.e., from the angular gyrus; Göbel, Walsh, & Rushworth, 2001).

Conclusions

The task- and polarity-specific elimination of the SNARC effect by cathodal, activity decreasing tDCS to the left PFC during parity and magnitude judgment i) demonstrates PFC (network) involvement in the generation of spatial-numerical associations, ii) suggests a significant and distracting influence of PFC in implicit processing and iii) exemplifies that inhibition of dysfunctional processes by cathodal tDCS can improve task performance. These results extend our knowledge on the neural mechanisms and malleability of implicit cognitive conflicts and further expose the complex interactions between non-invasive brain stimulation and cognition. The inhibition of dysfunctional cognitive processes by cathodal tDCS may provide interesting new options for a targeted treatment of neuropsychiatric disorders.

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Post-Publication Supplementary Analysis of Order Effects

In a further exploratory analysis, I was interested in potentially different effectivities of tDCS in the first vs. the second session of the sham-controlled cross-over design. Particularly, two lines of research would indicate the interesting possibility of such an interaction between the day of testing and stimulation effectivity. (1) It was hypothesized that tDCS could be more effective in modulating cognitive processes when applied at different levels of brain excitation. For example, Dockery et al. (2009) observed that 1 mA anodal tDCS would enhance performance in the Tower of London test of planning ability specifically when administered in the third session following two previous sessions with sham and cathodal tDCS. Vice versa, cathodal tDCS would enhance performance when administered in the first session (Dockery et al., 2009). (2) Combinations of certain tasks with tDCS are often used for learning and training purposes. Thus, there is the controversial possibility of tDCS that could induce long-lasting changes in behavioral performance, which could possibly already influence a second testing session (see Chapter I and Plewnia, Ruf, & Fallgatter, 2017, for examples of longer trainings).

For these reasons, I wanted to inspect in an exploratory, post-hoc analysis whether the effects of tDCS were different for the first vs. the second session of the current study. For better comparability of tasks and inclusion of polarity-specific effects [as predicted by the study of Dockery et al. (2009)], I only considered data from experiments 1 and 3 (parity judgment task with cathodal or anodal tDCS polarity, respectively), and I entered the new between-subjects factor *stimulation-order*$_{\text{SHAM FIRST, VERUM FIRST}}$ to the main ANOVA on mean RTs.

This analysis reproduced the previously obtained result of polarity-specific modulations of SNARC effects in a significant three-way interaction between *SNARC-congruency*$_{\text{CONGRUENT,INCONGRUENT}}$, *stimulation*$_{\text{VERUM,SHAM}}$ and *polarity*$_{\text{ANODAL,CATHODAL}}$, $F(1,44) = 10.93$, $p = .002$, $\eta_p^2 = 0.19$. The four-way interaction with the additional between-subjects factor *stimulation-order*$_{\text{SHAM-FIRST,VERUM-FIRST}}$ was not significant, $F(1,44) = 1.24$, $p = .272$, $\eta_p^2 = 0.03$. However, there was another three-way interaction between *stimulation-order*$_{\text{SHAM-FIRST,VERUM-FIRST}}$, *SNARC-congruency*$_{\text{CONGRUENT,INCONGRUENT}}$, and *polarity*$_{\text{ANODAL,CATHODAL}}$, $F(1,44) = 4.95$, $p = .031$, $\eta_p^2 = 0.10$. As displayed in Figure 2.4, if tDCS was applied in the first session, the overall SNARC effects in the group receiving cathodal tDCS (0.2 ms; Exp. 1) were smaller than SNARC effects in the group receiving anodal tDCS (24.9 ms; Exp. 3; irrespective of the session itself). In contrast, if tDCS was applied in the second session, overall SNARC effects (i.e., irrespective of verum or sham session) were roughly of comparable size in the cathodal group (16.3 ms) and in the anodal group (12.6 ms).

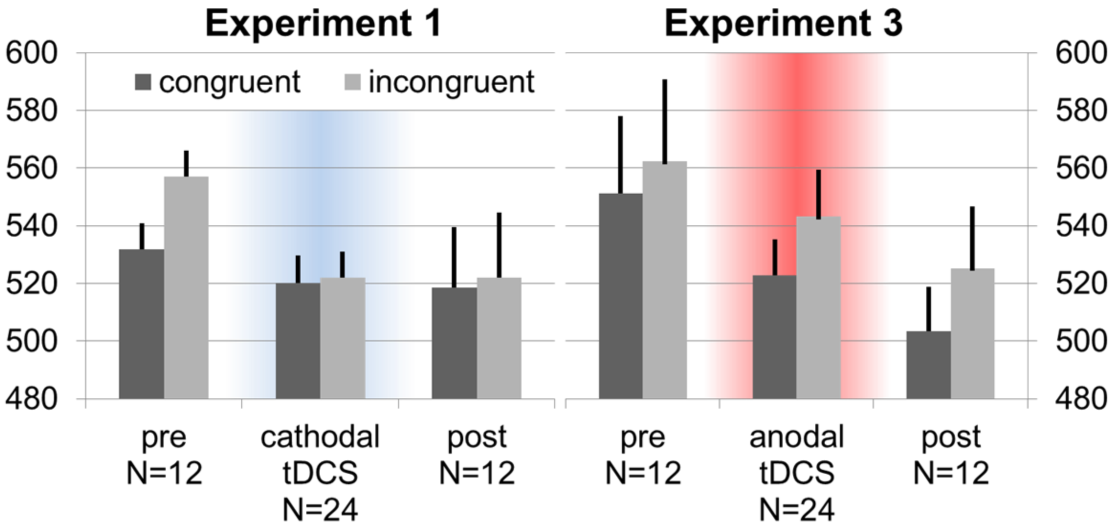

Figure 2.4. *Mean RTs in SNARC–congruent and –incongruent conditions of Experiments 1 and 3 separately shown for the session before, concurrent to, and after stimulation with tDCS. Note that each half of the data points in the cathodal / anodal tDCS column were also tested in the sham sessions pre / post tDCS and the actual study was a counterbalanced cross-over design.*

Although these post-hoc obtained results at first glance appear to reflect either state-dependency of tDCS effects (cf. Dockery et al., 2009) or even long-term stimulation effects that outlast a single session, it is important to emphasize the exploratory nature of above analysis and inherent limitations to the presented approach. Importantly, because SNARC effects in particular are rather variable at the individual level (Cipora et al., in preparation; see also the next Chapter III), it is not known whether these observations are due to the tDCS intervention or due to specific participant group characteristics. More precisely, because participants' performance was never assessed before stimulation in the group that obtained tDCS in the first session, the potential long-term state-dependent tDCS modulations of SNARC effects still need to be examined in parallel design with baseline performance assessment in future experiments. Another limitation pertains to other, unexplored variations in the four examined participant groups that could influence SNARC effects in general, such as counting habits (Fischer, 2008), or variations that could influence responses to tDCS with numerical stimuli, such as math anxiety (Sarkar, Dowker, & Cohen Kadosh, 2014). Moreover, it should be submitted to future confirmatory research whether the observed absence of a four-way interaction indeed reflects a separate stimulation mechanism than the general effect of cathodal tDCS on SNARC, such as cortical plasticity, learning, or brain-state-dependent stimulation effects.

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III. SNARC EFFECTS FOR NUMBER AND ORDER

Space in numerical and ordinal information: A common construct?

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Abstract

Space is markedly involved in numerical processing, both explicitly in instrumental learning and implicitly in mental operations on numbers. Besides action decisions, action generations, and attention, the response-related effect of numerical magnitude or ordinality on space is well documented in the Spatial-Numerical Associations of Response Codes (SNARC) effect. Here, right- over left-hand responses become relatively faster with increasing magnitude positions. However, SNARC-like behavioral signatures in non-numerical tasks with ordinal information were also observed and inspired new models integrating seemingly spatial effects of ordinal and numerical metrics. To examine this issue further, we report a comparison between numerical SNARC and ordinal SNARC-like effects to investigate group-level characteristics and individual-level deductions from generalized views, i.e., convergent validity. Participants solved order-relevant (before/after classification) and order-irrelevant tasks (font color classification) with numerical stimuli 1-5, comprising both magnitude and order information, and with weekday stimuli, comprising only ordinal information. A small correlation between magnitude- and order-related SNARCs was observed, but effects are not pronounced in order-irrelevant color judgments. On the group level, order-relevant spatial-numerical associations were best accounted for by a linear magnitude predictor, whereas the SNARC effect for weekdays was categorical. Limited by the representativeness of these tasks and analyses, results are inconsistent with a single amodal cognitive mechanism that activates space in mental processing of cardinal and ordinal information alike. A possible resolution to maintain a generalized view is proposed by discriminating different spatial activations, possibly mediated by visuospatial and verbal working memory, and by relating results to findings from embodied numerical cognition.

Introduction

Abstract concepts are often embedded into physical space: Numerical magnitudes increase to the right of a number line, weekdays are spatially organized in calendars, and the first step in a user manual is usually written either at the top or on the leftmost side. Numerical cognition research has outlined that also the mental representations of magnitude and order concepts include spatial components. As a consequence, responding spatially can be facilitated or inhibited relative to the spatial association of the current target stimulus. However, since spatial representations are available for many different stimuli, is it plausible to assume distinct domain-specific spatial associations of numerical magnitude, weekday orders, sequences, and so on? In other words, is it possible that a domain-general mechanism drives the associations between any concept and space?

Extensive research has outlined for long that mental associations with space are involved in numerical processing, as for instance reflected in the Spatial-Numerical Associations of Response Codes (SNARC) effect (Dehaene, Bossini, & Giraux, 1993; Wood, Willmes, Nuerk, & Fischer, 2008). Here, left-hand responses are faster to relatively small numerical value and right-hand responses are faster to relatively large numerical value, even if response decisions are not directly linked to numerical magnitude. The important question for our cognitive models is: Where does this association stem from? Traditionally, SNARC effects were conceptualized in the mental number line (MNL) hypothesis, describing left-to-right spatial representation of numerical magnitude. To date, although MNL is still prominent and incorporated in corresponding models of number processing (Dehaene, Piazza, Pinel, & Cohen, 2003), several lines of research propel alternative explanations. For instance, spatial-numerical associations could also stem from a general WM mechanism for binding sequential order with spatial templates (Abrahamse, van Dijck, & Fias, 2016; Guida et al., 2016), or from the principle of polarity correspondence in tasks with orthogonal stimulus dimensions (Proctor & Xiong, 2015). Particularly, we here focus on investigations into a domain-general cognitive mechanism for SNARC and aim to provide insights into the cross-validity of this mechanism for the generation of numerical SNARC and non-numerical SNARC-like effects in the ordinal weekday sequence.

Spatial Associations for Non-Numerical Sequences

Interactions with space are well documented in different paradigms for several variations of magnitude information, such as pitch volume and height (Heinemann, Pfister, & Janczyk, 2013; Lidji, Kolinsky, Lochy, & Morais, 2007; Weis, Estner, van Leeuwen, & Lachmann, 2016), time

(Ishihara, Keller, Rossetti, & Prinz, 2008; Vallesi, Binns, & Shallice, 2008), or response force (Vierck & Kiesel, 2010). Task-irrelevant quantity information was sufficient to influence response decisions in parity and comparison judgment tasks, free-choice and fair decisions (Schroeder & Pfister, 2015; Shaki & Fischer, 2014), and attention (Fischer, Castel, Dodd, & Pratt, 2003), corroborating the automaticity of spatial activations throughout a variety of cognitions and actions. From a broader view, the spatial involvement in processing abstract quantity of any type – e.g., in form of number, pitch, time, or force – is consistent with a common framework for magnitude (Bueti & Walsh, 2009; Walsh, 2003) and could originate from the recycling of available brain circuits (Dehaene & Cohen, 2007; Knops et al., 2009).

Less consistent with this framework are spatial activations from ordinal information: Whereas cardinal magnitude can continuously map onto spatial extension, ordinality describes discrete objects or sequence lists. Thus, one-way translations from ordinality to quantity are possible, but order information is not necessarily identical to spatial cues such as length or extent. Non-continuous ordinal and serial cues surround the human experience (i.e., in everyday routines such as wake-up, work-out, food preparation, brush-teeth), and being able to represent order information effectively is an important feature of cognitive processing – but is it connected to the processing of continuous cardinality?

Several studies have demonstrated SNARC-like effects with ordinal (sequential) information where objects early in a sequence facilitated left-hand responses whereas late objects were assigned to right-hand responses. Such a spatial response advantage corresponding to a position in the sequence was for instance documented in the weekday sequence (Gevers, Reynvoet, & Fias, 2004) and in months-of-the-year (Gevers, Reynvoet, & Fias, 2003). Comparable to the numerical SNARC, these effects also appeared in order-irrelevant tasks, suggesting the automaticity of a spatial activation from ordinal information, and they were also found in other tasks such as random number and letter generation (Di Bono & Zorzi, 2013). Yet, partially distinct mechanisms for numerical cardinality and non-numerical ordinality were observed as well: Specifically, in the random number and letter generation task by Di Bono & Zorzi, ordinal letter and month – but not number – sequences systematically triggered ascending order generations at fast pacing rates (Di Bono & Zorzi, 2013). Within their participants and across tasks, correlations were remarkably low between a preference for generating small numbers and early letters. This suggests potentially different mechanisms for cardinal (magnitude) and ordinal SNARC-like effects. In this respect, it is important to note that within-task correlations (split-half reliability) are fairly high (e.g., Cipora & Nuerk, 2013). Thus, low correlations are not due to high noise of the SNARC as a difference measure per se, but seem to be specific to the different SNARC-like effects and stimuli investigated.

However, correlational designs were not the only ones used to examine the relation of different SNARC-like effects. In an experimental design, it was investigated whether digits, weekdays, months, and alphabet letters similarly modulate attention allocation in peripheral cueing (Dodd, Van der Stigchel, Adil Leghari, Fung, & Kingstone, 2008). In their paradigm, the detection of a peripheral target was facilitated by corresponding number magnitude (i.e., priming of the left hemi-field by a small number) or by sequence position (i.e., priming of the left hemi-field by an early sequence position). However, the latter attentional SNARC-like shift by ordinal information was restricted to an order-relevant task, whereas attentional shifts also occurred from perceiving numbers without task-relevance. Moreover, in functional neuroimaging, and with support vector machine learning, distinct voxel sets were identified for numerical vs. ordinal judgment (Zorzi, Di Bono, & Fias, 2011). These results independently suggested (at least partially) different processing mechanisms for numerical and non-numerical sequences. It could be argued that both the dominance of numbers in attention modulation and the ease of producing random number sequences rely on the overlearned availability of the number sequence (Dehaene, 1997). Another view suggested that spatial coding itself might differ and that letters – as compared to numbers – elicit a more categorical processing naturally (Zorzi, Priftis, Meneghello, Marenzi, & Umiltá, 2006).

The Present Study

From a diagnostic point of view, suggestions of a common cognitive mechanism for the spatial association of ordinal and cardinal information include that SNARC and SNARC-like effects should constitute measures of a latent variable. Separate theories have conceptualized the latent process beyond numerical and non-numerical SNARC, i.e., in form of working memory (van Dijck, Abrahamse, Acar, Ketels, & Fias, 2014) or polarity correspondence (Proctor & Cho, 2006). Some previous work outlined candidates for such latent variables only for the numerical SNARC effect that could include inhibition capacities (Hoffmann, Pigat, & Schiltz, 2014) and spatial working memory in 2D mental rotation (Viarouge et al., 2014). To the best of our knowledge, however, there are no reports on the premise of convergent validity: If a latent variable exists, separate tests should come to the same conclusions. The same rationale should be true for SNARC: To test working memory, polarity correspondence, or any other latent construct beyond numerical and non-numerical spatial associations, SNARC tasks with different stimuli should render similar behavioral patterns in the same individuals. Thus, correlations of SNARC indices from different tasks that assume to address the same construct should demonstrate convergence.

To test this assumption of a domain-general factor underlying the cardinal SNARC and ordinal SNARC-like effects, we administered separate tasks that should elicit an ordinal weekday SNARC and a comparable numerical SNARC with matched number symbols. To account for the hypothesized increased salience of number-sequence mappings, i.e., by fast experimental learning, two different task settings were administered in randomized order and the tasks either afforded magnitude and/ or order-relevant processing (comparison task) or were irrelevant to the magnitude and order dimensions (color judgment). Besides the target stimuli, the tasks were perceptually identical. To identify a convergent validity even below recommendations, we aimed to include enough participants for detecting at least low correlations ($r > .31$) with a power of 80% and calculated a total sample size of 60 participants in a within-subjects between-tasks design.

Methods and Materials

The data of this study were collected as part of a large (neural) numerical learning project, which will be described in detail in the next chapter (Chapter IV). Following the procedures and measurements outlined here, some of the participants were assigned to groups that received different manipulations of brain activity with transcranial direct current stimulation while performing the same tasks a second time ($N = 48$), whereas others were tested exclusively for the current report ($N = 12$). No additional measurements or procedures preceded the tasks as described here.

Participants

A total of $N = 60$ right-handed participants was available for analyses (13 males, mean 23.7 ± 0.6 y, range: 18-47 y).[8] All participants gave written informed consent in order to take part in the experiment for monetary or course credit compensation. The study was conducted in

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[8] We found no substantial differences if only younger participants were analyzed. There is a small correlation with age ($r = -.07$) also reported in the meta-analysis of Wood et al. (2008), which however explains less than 0,5% of the variance and therefore does not change results substantially.

accordance with the Declaration of Helsinki and approval was obtained by the Ethical commission of University Hospital Tübingen (NO: 701/2015BO2).

Procedure and Design

Five separate tasks were completed blockwise in pseudo-randomized order. Both number symbols (1-5 except 3) and non-numerical weekdays (monday-friday except wednesday; cf. Gevers et al., 2004) were separately judged for font color and sequence position by left-hand and right-hand index finger key presses. The order-irrelevant color judgment tasks were grouped such that they always started or ended with a color-word interference Stroop task to test for automatic reading (Stroop, 1935/1992).

All tasks comprised the same perceptual appearance apart the critical stimulus material. A brief practice block (16 trials) preceded each task and instructions were re-iterated after providing brief error feedback from these practice trials. Stimulus-repetitions were omitted (Pfister, Schroeder, & Kunde, 2013; Tan & Dixon, 2011). In the color judgment tasks, participants were asked to discriminate light yellow and blue fonts by pressing one of two tagged keyboard buttons with their right-hand or left-hand index finger (inter-key distance: 11.6 cm). In the comparison tasks, they were instructed to indicate whether the target was before/smaller or after/greater than Wednesday/3 and the target-response mapping was reversed in the adjacent block. Each trial consisted of a fixation mark (# for 300ms), target presentation (2s) and a brief inter-stimulus interval (300ms). Wrong and slow responses (>2s) triggered an immediate error feedback (300ms). All items appeared equally often (20 repetitions) in the respective order-relevant and order-irrelevant tasks, but the control Stroop task was trimmed to 10 target repetitions. The tasks were implemented in PsychoPy experimental software (Peirce, 2007).

Results

Since errors were seldom in some conditions and most participants, only analyses on median latencies are reported. Outliers exceeding 3SD of design cell means (5.9%) and errors (4.6%) were discarded from the analyses. We first performed separate ANOVAs to investigate the presence of SNARC and SNARC-like patterns in the collected data, to replicate and generalize the results of Gevers et al. (2004), and to validate their account for our task. After the replication turned out to be successful in general, we proceeded with more fine-grained analyses like multiple regressions to investigate the shape of SNARC-like effects and finally with the individual differences correlation analysis.

ANOVA: SNARC and SNARC-like Effects

To outline systematic response hand advantages from magnitude or sequence position, separate 2x4 ANOVAs were conducted comprising the factors $hand_{\text{LEFT-HAND,RIGHT-HAND}}$ and $magnitude/position_{\text{1,2,4,5(NUMERICAL TASKS); OR: MONDAY,TUESDAY,THURSDAY,FRIDAY(ORDINAL TASKS)}}$. From these analyses, spatial-numerical and spatial-positional associations are observed in terms of significant two-way interactions (Tzelgov, Zohar-Shai, & Nuerk, 2013). Greenhouse-Geisser corrections are reported upon violations of sphericity.

Comparison Tasks: The numerical SNARC effect was significant, $F(2.04,177) = 4.64$, $p = .011$, $\eta p^2 = 0.07$, GG = .68 (Figure 3.1, right panel), as well as both main effects of $hand_{\text{LEFT-HAND,RIGHT-HAND}}$, $F(1,59) = 4.18$, $p = .046$, $\eta p^2 = 0.07$, and $magnitude_{1,2,4,5}$, $F(2.52, 177) = 19.76$, $p < .001$, $\eta p^2 = 0.25$, GG = .84. Respectively, the significant main effects were driven by faster right-hand responses (510 ms) than left-hand responses (520 ms; hand dominance), and by latency increases for targets close to the referent ‘3’ (‘2’: 517 ms; ‘4’: 539 ms) as opposed to targets far from the referent (‘1’: 496 ms; ‘5’: 507 ms; distance effect). Correspondingly, we also obtained significant ordinal SNARC-like effects with weekday stimuli, $F(2.40, 177) = 11.34$, $p < .001$, $\eta p^2 = 0.16$, GG = .80 (Figure 3.1, left panel), as well as significant main effects of $hand_{\text{LEFT-HAND,RIGHT-HAND}}$, $F(1,59) = 8.73$, $p = .005$, $\eta p^2 = 0.13$ (left-hand: 583 ms; right-hand: 572 ms), and $position_{\text{MONDAY,TUESDAY,THURSDAY,FRIDAY}}$, $F(3,177) = 8.96$, $p < .001$, $\eta p^2 = 0.13$ (‘Monday’: 564 ms; ‘Tuesday’: 586 ms; ‘Thursday’: 591 ms; ‘Friday’: 568 ms).

To quantify the presence of distance effects, we inspected polynomial contrasts for the significant main effects of *magnitude* and *position*. The rationale for this analysis was to capture the expected pattern of response time increases with closer proximity to the comparison referent by a quadratic function. For both sequences, we found evidence for distance effects by the quadratic trends, numbers: $F(1,59) = 41.50$, $p < .001$, $\eta p^2 = 0.41$; weekdays: $F(1,59) = 36.57$, $p < .001$, $\eta p^2 = 0.38$.

To investigate whether the effects with number and weekday stimuli were already different at the group level, we also performed another ANOVA with all data and comprising the additional repeated measures factor $item\text{-}set_{\text{WEEKDAYS,NUMBERS}}$. Here, we observed a significant three-way interaction between the factors $item\text{-}set_{\text{WEEKDAYS,NUMBERS}}$, $hand_{\text{LEFT-HAND,RIGHT-HAND}}$, and $magnitude/position_{\text{1,2,4,5(NUMERICAL TASKS); OR: MONDAY,TUESDAY,THURSDAY,FRIDAY(ORDINAL TASKS)}}$, $F(3,177) = 3.23$, $p = .024$, $\eta p^2 = 0.05$. Thus, already at the group level, SNARC and SNARC-like effects appeared to be different, although the separate ANOVAs confirm that the effects are present in both studied sequences (see Figure 3.1). In addition, ANOVA yielded a significant main effect of *item-set*$_{WEEKDAYS,NUMBERS}$, *F*(1,59) = 121.99, $p < .001$, $\eta p^2 = 0.67$, driven by faster responses to numbers (515 ms) than to weekdays (577 ms).

Color Judgment: Two assumptions are made for an emergence of SNARC and SNARC-like effects in the color judgment tasks: 1) Automatic reading of the colored words and 2) an automatic activation of spatial-numerical and spatial-positional associations. The first assumption was confirmed by a significant *Stroop*$_{CONGRUENT,INCONGRUENT}$ main effect, *F*(1,59) = 5.61, $p = .021$, $\eta p^2 = 0.09$, indicating that color word meaning systematically interfered with font color judgment. Thus, it can be assumed that participants also automatically read weekday names and number symbols. Indeed, we obtained a (marginally) significant two-way interaction of *position*$_{MONDAY,TUESDAY,THURSDAY,FRIDAY}$ and *hand*$_{LEFT\text{-}HAND,RIGHT\text{-}HAND}$ in weekday stimuli, *F*(3,177) = 2.71, $p = .047$, $\eta p^2 = 0.04$. The main effect of *position*$_{MONDAY,TUESDAY,THURSDAY,FRIDAY}$ was not significant, *F*(2.62,177) = 1.87, $p = .144$, GG = .87. However, in the other item set, number symbol *magnitude*$_{1,2,4,5}$ did not significantly interact with response *hand*$_{LEFT\text{-}HAND,RIGHT\text{-}HAND}$, *F*(3,177) = 1.57, $p = .198$, and only a main effect of *magnitude*$_{1,2,4,5}$ emerged in the numerical item set, *F*(3,177) = 3.06, $p = .030$, $\eta p^2 = 0.05$. Here, the *magnitude*$_{1,2,4,5}$ main effect appeared not to be driven by a numerical distance quadratic trend, *F*(1,59) = 2.45, $p = .123$, but rather reflected slow responses to ‚1‘ (510 ms; ‘2’: 498 ms; ‘4’: 503 ms; ‘5’: 501 ms). Again, another ANOVA with all data and the additional repeated measures factor *item-set*$_{WEEKDAYS,NUMBERS}$ was performed, but the three-way interaction effect was not significant, *F*(3,177) = 0.12, $p = .948$.

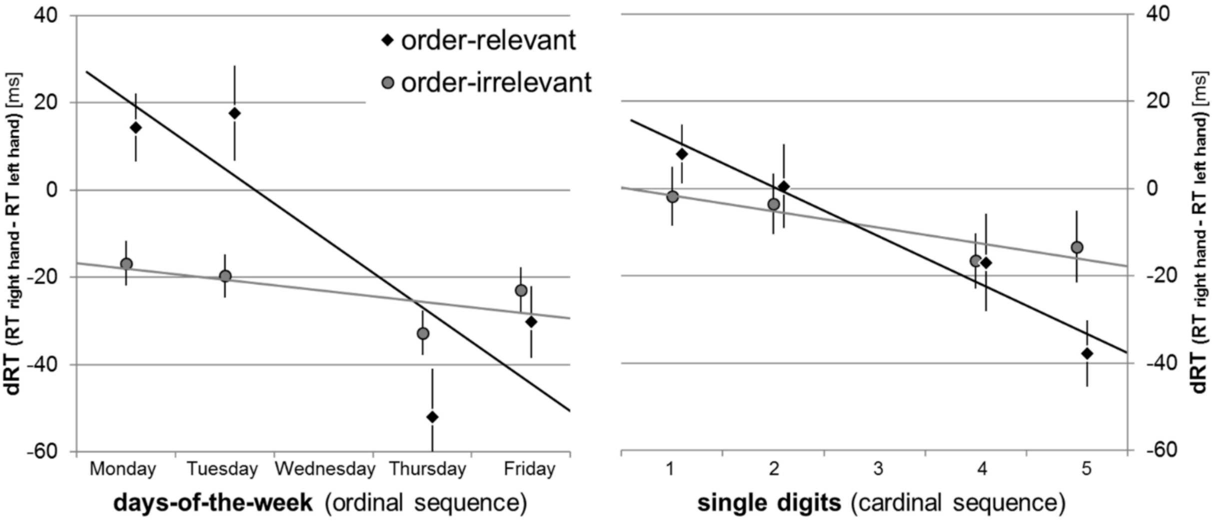

Figure 3.1. *Right-hand over left-hand response time advantage (dRT) as a function of weekday position (left panel) and numerical magnitude (right panel) in color-judgment (grey circles and line) and comparison tasks (black squares and line).*

Regression: Binary or Continuous Spatial Mappings?

Although SNARC is often quantified by linear regression, i.e., larger right-hand advantages emerge for increasing magnitudes, there are two concerns with this analysis approach and they apply specifically for magnitude/position comparison tasks (as compared to parity judgment tasks). First, longer latencies close to the comparison reference might emerge due to distance effects (the psychophysical difficulty of comparing close entities; Moyer & Landauer, 1967) and this can lead to an enhanced spatial activation (Gevers, Verguts, Reynvoet, Caessens, & Fias, 2006; Nuerk, Wood, & Willmes, 2005). Second, some theoretical accounts (i.e., polarity correspondence) offer explanations of observed SNARC effects by the (internal) declaration of binary classification poles (i.e., before or after, smaller or larger) that can correspond or interfere with a response hand polarity (i.e., dominant right hand). Hence, these arguments would predict a categorical, but not a continuous spatial mapping. To investigate whether a binary categorical or linear continuous frame of magnitude / position best accounts for SNARC and SNARC-like effects, both predictors were mean-centered and entered in a multiple regression on dRT (right hand-left hand) while controlling for mean latency, distance effects, and in case of number symbols also for number parity (e.g., MARC effect).

For the order-irrelevant color judgment tasks, neither categorical nor continuous predictors reached significance, *t*s < 1.19, *p*s > .236. Different results were obtained in the order-relevant comparison tasks. For the weekday sequence, a categorical predictor was highly significant, $\beta = -.49$, $t = 2.57$, $p = .011$, but the continuous predictor was insignificant and even reversed in direction, $\beta = +.14$, $t = 0.71$, $p = .480$. For number comparison, a regular (negative) coefficient failed significance for the continuous predictor, $\beta = -.30$, $t = 1.53$, $p = .130$, but also for the categorical predictor, $\beta = +.08$, $t = 0.41$, $p = .687$. Interestingly, stepwise regression selected the categorical predictor for the ordinality set and the continuous predictor for the cardinality set as unique coefficient for each corresponding model with high confidence (*p*s < .001). Finally, we also tested the individually extracted regression coefficients with a t-test against zero, which has been the standard method for evaluating the presence of SNARC effects (Fias, Brysbaert, Geypens, & D'Ydewalle, 1996).[9] These results mimicked the multiple regression approach: For weekdays, the categorical SNARC was significant, b = -39.0, $t(59) = 2.32$, $p = .024$, but the continuous SNARC did not differ from zero, b = 6.0, $t(59) = 0.74$, $p = .460$. For number symbols, a categorical predictor was not significant, b = 6.04, $t(59) = 0.38$, $p = .707$, and only a trend for the continuous SNARC emerged, b = -14.4, $t(59) = 1.76$, $p = .083$, most likely underestimated due to predictor redundancy implying larger error estimates. Table 3.1 summarizes these results and especially multiple (and stepwise) regression reveal the different patterns of the ordinal and cardinal SNARC effects.

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[9] Precisely, simple linear regression with the continuous magnitude predictor is the standard measure; however, it does not allow for distinguishing categorical and continuous effects (cf. Nuerk, Bauer, et al., 2005). When performing another simple linear regression, both SNARC slopes appeared significantly different from zero, ts > 3.0, ps < .005. Some disparity between simple and multiple linear regression with single-digits may emerge due to predictor redundancy implying larger error estimates.

Table 3.1. Emergence of SNARC and SNARC-like Effects in the Different Tasks and Stimulus Sets as a Function of Analysis Approach.

	order-relevant (*comparison task)*		order-irrelevant *(color judgment task)*	
	single digits	Weekdays	single digits	weekdays
ANOVA	✓	✓		(✓)
Linear	✓	✓	(✓)	(✓)
$\text{Linear}_{\text{part}}$	(✓)			
$\text{Categorical}_{\text{part}}$		✓		

Note. Results from individual regression tests resemble the repeated-measures ANOVA (see also: Pinhas, Tzelgov, & Ganor-Stern, 2012), multiple regression reveals the different nature of a cardinal and ordinal effects. ✓$p < .05$. (✓)$p < .10$.

Convergent Validity of Spatial Mappings: A Common Construct?

All analyses above already pointed out slight differences in the spatial associations of numerical and ordinal sequences. Yet, the main concern of this study is the question whether ordinal and cardinal SNARC effects emerge from a common unified process. Thus, it is important to not only analyze group-level performance, but to also explore individual differences. This can be particularly fruitful since large individual variation in SNARC has been documented before, with approximately 70% of a common Western sample exhibiting the typical SNARC effect. If the spatial associations are alike in ordinal (weekday-sequence) and cardinal item sets (small single-digits), resembling coefficients should emerge for the two different ordinality and cardinality sets. Since the evidence for SNARC in the order-irrelevant color judgment was less substantial, we focused only on the comparison tasks. Here, when we analyzed unstandardized slopes as obtained from individual linear regressions (c.f. Fias et al., 1996; Lorch & Myers, 1990), a small positive correlation was obtained, Pearson's $r(60) = .219$, $p = .092$ (see Figure 3.2). However, the small coefficient further diminished by z-standardization of regression slopes, $r(60) = .159$, $p = .226$.

Following the preceding analyses, we next sought to inspect more closely the SNARC coefficients as obtained from a categorical and continuous predictor, since they might represent the data better. In particular, a categorical weekday SNARC was thought to correlate with a continuous numerical SNARC, but this was not the case, $r(60) = -.174$, $p = .185$ (for standardized coefficients: $r(60) = -.198$, $p = .130$). After removal of possible outlier participants (with slopes deviating more than 2SD), reducing the sample size to $N = 52$, this correlation between ordinal and cardinal SNARC was still negative and insignificant, $r(52) = -.181$, $p = .200$.

Together, these analyses suggest the link between numerical and non-numerical SNARC effects to be small and – if present at all – highly susceptible of different assessments. An assumed convergent validity due to a common cognitive mechanism failed to produce a substantial correlation between spatial associations in the weekday and numerical set.

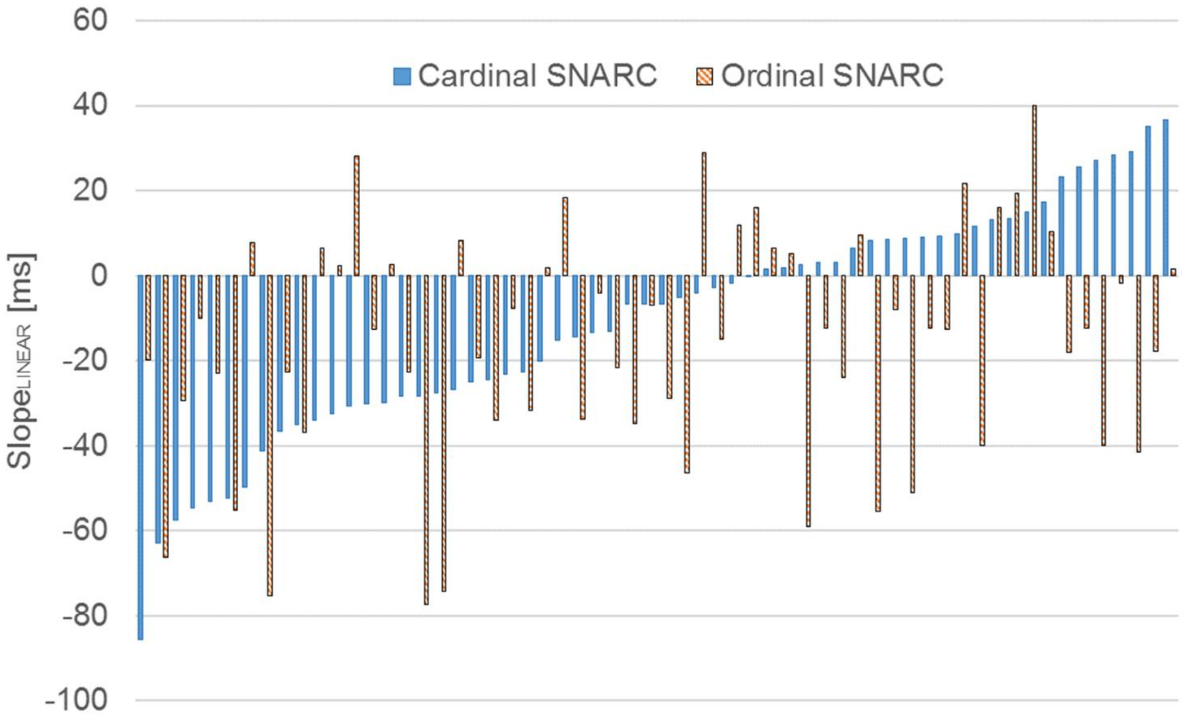

Figure 3.2. *Individual linear regression slope estimates for numerical (cardinal) and weekday sequence (ordinal) stimuli in the comparison task. Participants are sorted by magnitude of the cardinal SNARC and the adjacent striped bar displays the corresponding ordinal SNARC slope. It can be seen that there is no evidence of a systematic relation between ordinal and cardinal SNARC.*

Discussion

We investigated SNARC and SNARC-like effects based on numerical magnitude and sequence position with small-range number symbols and weekday names in order-relevant magnitude/position comparison and order-irrelevant color judgment tasks. Following generalized views, interactions with spatial responses were hypothesized to resemble in both the cardinal and the ordinal item set. However, in the presented analyses, several differences between cardinal and ordinal items were outlined and these differences cast doubt on a simple general cognitive mechanism that links cardinal and ordinal information alike with space.

Specifically, at the group level, we observed systematic advantages of spatially congruent responses in both comparison tasks – i.e., a left-hand advantage for classification of relatively small numbers and relatively early weekdays, and a right-hand advantage for classification of relatively large numbers and late weekdays. In the order-irrelevant color judgment task, this SNARC-like pattern was less substantial and we found a marginally significant ANOVA interaction only with weekday stimuli. This latter result is at odds with the view that differences in ordinal and numerical spatial associations can be attributed to a special overlearned spatial alignment of numbers. Even when taking into account successful inductions of SNARC with larger number sets in comparable color judgment tasks (Bull, Cleland, & Mitchell, 2013; Keus & Schwarz, 2005), a significant weekday SNARC in this (and other) order-irrelevant setting (see Gevers et al., 2004) still disagrees with explaining differences in numerical and non-numerical spatial activations by the increased, overlearned availability of number over weekday sequences. Finally, regarding ordinal and cardinal SNARC effects in the comparison tasks, our analyses suggest different shapes of the effects, with a categorical classification of early and late weekdays, but a linear shaped mapping of numbers onto space.

With regards to the individual differences analysis, some theoretical considerations have to be highlighted in order to relate inferences from the obtained results and we discuss limitations and recommendations for future research extensively below. This approach was chosen to understand whether a common construct lies beyond spatial associations from ordinal and cardinal sequences. If this was the case, and response hand advantages with increasing magnitude and ordinal position emerged due to a unified cognitive process susceptible to individual differences alike, the coefficients should resemble. Importantly, however, whereas some recommendations and intuition imply that high correlations should emerge between two tasks that are mediated by the same mechanism (i.e., Carlson & Herdman, 2012), there exist considerable pitfalls in interpreting correlations between RT difference effects. For instance, many other and task-unspecific factors can influence participants' performance, thus difference time parameters are additionally constrained (Miller & Ulrich, 2013). In this context, the reliabilities of comparison SNARC effects (Cipora et al., 2016; Viarouge, Hubbard, & McCandliss, 2014) are a primary requirement for the interpretation of between-task convergent validity. Further, systematic correlations with SNARC in other studies (inhibition capacities: Hoffmann, Pigat, & Schiltz, 2014; 2D mental rotation: Viarouge et al., 2014, between effectors: Hesse & Bremmer, 2016) render a fundamental utility of the individual-differences approach for this task.

In this study, we observed that the ordinal and cardinal SNARC indices were weakly correlated, but the obtained correlation vanished for standardized SNARC estimates and also especially if we extracted slope coefficients according to the best fit, categorical for ordinality and linear for numerosity. Thus, the data from this study suggest poor (if any) convergent validity for a single common construct beyond the spatial alignment of numbers and weekdays, exemplifying two cardinal and ordinal item ranges. Essentially, these findings comply with our group-level results.

Notably, in this respect, our findings also reflect the size of recently obtained correlations between spatial activations in numerical and non-numerical tasks with number and letter stimuli (i.e., Di Bono & Zorzi, 2013). An interpretation of these results' significance requires care since conclusions about the systematics of such weak links are often underpowered due to the small correlation coefficients. Thus, it may well be the case that small convergence exists between measures of ordinal and cardinal spatial associations. However, correlations of such small magnitude as observed can certainly be regarded in-exhaustive in indicating a single common cognitive mechanism. Large-scale investigations into diagnostic validity of different SNARC effects, discriminative validity, and experimental dissociations are needed to better outline the latent factors driving associations of numerical and ordinal information with space.

Different Shapes of Categorical and Linear Spatial Mappings

Interestingly, the finding of a linear SNARC effect in magnitude comparison deviates from several recent observations of a categorical effect as compared to implicit tasks such as parity judgment (Nuerk, Bauer, Krummenacher, Heller, & Willmes, 2005; Wood et al., 2008). The categorical pattern in number comparison was theoretically and computationally traced back to the latency increase for digits close to the referent (i.e., the numerical distance effect), that in turn also emphasized spatial activations in these trials and artificially produced larger hand deflections, which can ultimately result in a categorical response pattern (Gevers et al., 2006). To reconcile the finding of a linear SNARC in number comparison with the literature, it should be highlighted that previous studies usually employed larger number sets (i.e., 1-9 with referent 5) whereas our experiment targeted small numbers, mirroring the sequence of the working weekdays in Western cultures (i.e., 1-5 with referent 3). With such a small numerical frame, a presumably linear SNARC effect was obtained before in parity judgment only (Dehaene et al., 1993; Fias et al., 1996), but the authority of a numerical distance effect – despite being still relevant in the analyses – might be reduced when applied to the smaller numerical set.

Another possible explanation for this result turns up when considering recent findings from embodied numerical cognition and the role of finger-based magnitude representations. For instance, in a large cohort of primary schoolers, calculation errors frequently include the erratic assignment of full hands (i.e., 5 items; Domahs, Krinzinger, & Willmes, 2008). But also in adults, implicit hand-based magnitude representations were reported to produce increased calculation latencies when addition problems crossed the five-boundary (Klein, Moeller, Willmes, Nuerk, & Domahs, 2011). In Western groups, such sub-base-five effects had been particularly pronounced and it was concluded that finger experiences (i.e., counting habits) influence mental number representations (Domahs, Moeller, Huber, Willmes, & Nuerk, 2010). Thus, it could be argued that a linear magnitude-space mapping is more likely in tasks that lack an embodied sub-base-five border as compared to larger number ranges that utilize the referent ‘5’ and thus possibly emphasize a hand-based (categorical) magnitude reference. In contrast, the categorical mapping of weekdays (with the same number of stimuli) further indicates a different processing of these stimuli and might point to discriminative (verbal-spatial) strategies. Outlining the decisive context characteristics that determine continuous and categorical SNARC effects may inspire future research and may better characterize the exact processes involved interfering with spatial attention, response selection, and action.

Implications for a Common Framework of Mental Space Activations

At least two lines of research have accumulated considerable evidence for working memory (WM) involvement in the SNARC effect. First, in dual-task situations, susceptibility to WM load was demonstrated (Herrera, Macizo, & Semenza, 2008), and a double dissociation was driven by the susceptibility of SNARC in parity judgment to verbal WM load and the susceptibility of SNARC in magnitude judgment to spatial WM load (van Dijck, Gevers, &

Fias, 2009). This corresponds to a lack of spatial correspondences in number comparison in children with visuospatial disabilities (Bachot, Gevers, Fias, & Roeyers, 2005).

The second line of evidence for a working memory account comes from spontaneous learning of random sequences. In a seminal study, van Dijck & Fias introduced a combined learning-judgment paradigm that ascribed numbers to a new sequence position before spatial response classifications were given. Their results demonstrated that newly acquired sequence positions determined spatial associations in numerical and non-numerical stimuli, effectively countering the spatial association of numerical magnitude (van Dijck & Fias, 2011). Some studies have replicated this finding (Abrahamse, van Dijck, Majerus, & Fias, 2014), bolstering the nuisance that arbitrary sequences in general appear ordered in space (Previtali, De Hevia, & Girelli, 2010).

Since the formulation of a working memory involvement in spatial-numerical associations (van Dijck et al., 2014; van Dijck & Fias, 2011), some attempts have focused on the differentiation of verbal-spatial and visuo-spatial strategies for SNARC in specific and numerical processing in general (Georges, Schiltz, & Hoffmann, 2015; Soltanlou, Pixner, & Nuerk, 2015; van Dijck et al., 2009). One preliminary conclusion from these studies could be the availability of multiple spatial codes and a flexible attainment of those depending on task contexts, for instance in different associations of ordinalities and cardinalities with spatial directions (Patro, Nuerk, Cress, & Haman, 2014). Experimentally, this idea is supported by a reported visuo-motor directional training experience in preliterate children that modulated non-symbolic space-magnitude associations (a cardinal SNARC-like effect), but had no impact on ordinal counting directions (Patro, Fischer, Nuerk, & Cress, 2016).

This conclusion is further supported by the recent observation of co-existing SNARC and sequence positional order effects in the same tasks and participants (Huber, Klein, Moeller, & Willmes, 2016). Considering also the different notations employed in our tasks for number symbols and weekday words, it is possible that different verbal-spatial and visuo-spatial concepts were triggered by the item notations (cf. Iversen, Nuerk, Jaeger, & Willmes, 2006; Nuerk, Iversen, & Willmes, 2004), which could be accounted for by different spatial codes available even within ordinal or cardinal sequences. For instance, the assessed dominance of a categorical (e.g., verbal-spatial coding) and linear SNARC (e.g., visuospatial MNL associations) might be stimulus- or task-specific. However, our results should not be taken as compelling evidence for either theory, but rather call for empirical dissociations of different SNARC-like effects.

Limitations of the Individual-Differences Approach for the Study of Latent SNARC Processes

Although we outlined several subtle differences in the data drawn from single-digit numbers and weekday spatial associations, it is important to highlight two major limitations of our approach that limit the evidential value of the reported results. Whereas the observations from this study suggest some differences to exist between spatial associations of numbers and weekdays, the observations cannot theoretically refute the existence of a common construct.

The first limitation is the representativeness of our tasks for assessing spatial associations of single-digits and non-numerical sequences. Traditionally, spatial-numerical associations are assessed using single-digits ranging from 1-9 except 5, or ranging from 2-9, or using 1, 2, 8, and 9. In the current study, we selected number stimuli to most closely resemble the sequential structure of weekdays and thus tested performance on the digits 1-5, which also has been shown to elicit spatial-numerical associations before (Dehaene et al., 1993; Fias et al., 1996). To the best of our knowledge, critically, it is currently not known whether and to what extent SNARC effects for different ranges correlate (even if they are most likely produced by the same cognitive mechanism), but the critical observations of comparable spatial alignments were only observed at the group level in previous studies.[10] Although some range-specific differences could be expected from including the subitizing range and testing larger numerals with longer response times (size effect), from testing decades (e.g., Huber et al., 2016), and also from additional processes in multi-digit numbers (such as inhibition of a task-irrelevant decade-digit and unit-decade compatibility), individual differences analyses from different range SNARCs would be informative regarding the strength of a correlation to be expected. For instance, at least one study points to a lack of SNARC effects for unit-digits in multi-digit task settings (Zhou et al., 2008). Even more provocative, it could be the case that specific cognitive processes could exist for the same stimulus material in different ranges and this issue needs to be studied in future designs.

The second limitation is somewhat related to the first and concerns the difficulty of interpreting correlation coefficients between difference indices for which no significant benchmarks are available. For example, correlations between difference scores may diminish due to task-

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[10] I would like to thank Alessandro Guida for pointing to this alternative account.

unspecific variation and for relatively smaller effect sizes (Miller & Ulrich, 2013), which we cannot exclude for the current data sets. At its essence, these constraints indicate that a lack of correlation can also be observed if two processes have a common construct. For some rough anchoring, it might be informative to turn to results from other studies; for instance, SNARC effects for the 1-9 range assessed by hand and arm movements separately correlated with a coefficient of r = .52 (Hesse & Bremmer, 2016). In another study, the (inverse) correlation between SNARC with the angle effect in mental rotation was also relatively high (r = -.429; Viarouge, Hubbard, & McCandliss, 2014). Notably, both coefficients showcase that the interpretation of a significant link can be supported by difference score correlations that would traditionally indicate small-to-medium correlation (Cohen, 1988). Arguably, we believe that the results obtained here cast at least some doubt on the convergent validity of the assessed effects, assuming that spatial-numerical associations with different ranges are comparable across studies. Thus, we consider our results as a first skeptical hint for future research to closely inspect the diagnostic validities of different SNARC effects that are presumably driven by a shared mechanism. In addition, for future studies, we recommend to include and replicate also other domain-specific and domain-general assessments of latent variables that are assumed to drive the cognitive mapping of numbers and other variables onto space.

Conclusion

SNARC-like patterns might be the result of a more complex activation of several spatial codes that ought to bolster effective task handling. This view does not necessarily refute the involvement of a general cognitive mechanism, but rather suggests a multidimensionality of spatial coding processes (i.e., working memory, polarity correspondence). Instead of a single unifying latent concept, different manifestations of SNARC and SNARC-like behaviors might emerge from ordinality, cardinality, embodied directionality, and task characteristics such as verbal cues.

How can the human mind utilize and decipher abstract information such as numerical magnitude? Space plays a critical role in both communication and mental operations on magnitude, and our study replicates that space also intrudes ordinal representations as for the weekdays. Yet, internal spatial codes can differ substantially in their appearance and should be investigated more differentially regarding both their task-dependent emergence as well as their cognitive origin. Our study demonstrates several distinctions in the nature of spatial associations in perceptually similar tasks with the same participants, but different target stimuli.

Unifying these spatial associations under a common conceptualization should reveal middle-to-high construct validity. However, our study yielded poor construct validity. Inherent limitations of this approach are the representativeness of tasks and stimuli, the lack of studies on construct validity of SNARC effects with different number ranges, and interpretation of difference score correlation coefficients. Nevertheless, the results from our study point to the view that a single domain-general construct like a general serial-order process in working memory may account for single SNARC effects, but is not consistent with the poor construct validity of multiple SNARC effects obtained with different stimuli and tasks.

Acknowledgements

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IV. SPACE, ORDER, AND STIMULATION: A REVERSAL

Prefrontal neuromodulation reverses spatial associations of non-numerical sequences, but not numbers

The following chapter is published as:

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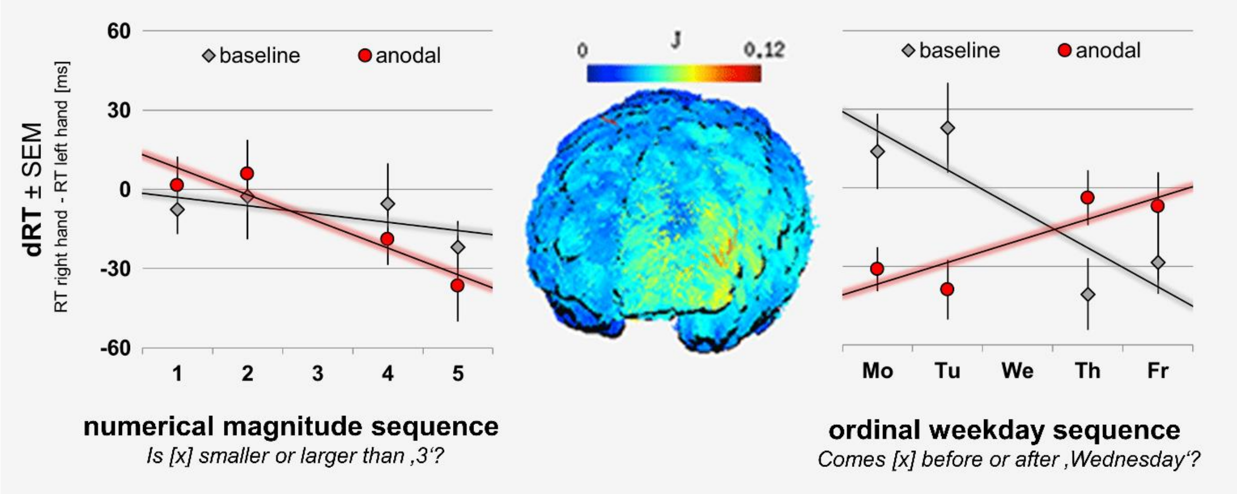
Abstract

Numerical and non-numerical sequence items interact with spatial responding, pointing towards mental representations that are grounded in space and referred to as SNARC effects (spatial-numerical association of response codes). An ongoing controversy pertains to the universal origin of different SNARC effects and whether their underpinning is a spatial arrangement of cardinal magnitude (mental number line) or a sequential arrangement of ordinal elements in working memory. Recent results from prefrontal neuromodulation with transcranial direct current stimulation (tDCS) were supportive of the unified working memory account. The current tDCS experiment was designed to empirically test the generalizability of the prefrontal modulation effects previously found for numbers in a non-numerical sequence (weekdays) and to examine predictions from the universal account. Participants performed a series of classification tasks with numerical and non-numerical sequences (1-5, Monday-Friday) before and concurrent to a prefrontal stimulation with either anodal (N = 24) or cathodal polarity (N = 24). Results show a dissociation of SNARC effects for numbers and weekdays by anodal tDCS: Spatial associations of weekdays were reversed by stimulation, when order was relevant for the task, but SNARC effects with number symbols were emphasized in the regular left-to-right direction, corroborating previous results. A control experiment showed that the polarity-dependent neuromodulation effects were absent in order-irrelevant font color classification, supporting the tDCS principle of activity-dependence. We discuss differences in linguistic markedness between temporal and magnitude-related classifications in an integrative account explaining the full pattern. We suggest that stimulation-enhanced psycholinguistic processing can evoke space-number associations whose direction is opposite to cultural visuospatial experience.

Graphical Abstract



Highlights

- Numerical and non-numerical sequences are associated with space (SNARC effect)
- Prefrontal neuromodulation dissociates spatial mapping of numbers and weekdays
- Anodal tDCS reverses spatial representation of weekday sequence, when task-relevant
- Modulations by tDCS require task-specific activation of the target concept

Introduction

Is Friday ’right’ and Monday ‘left’? Some individuals experience vivid spatial forms for non-numerical sequences such as the weekdays, and most would agree on a left-to-right arrangement, at least in Western societies reading from left-to-right. In fact, psychological experiments show that the cognitive representation of sequence includes a spatial component: In natural sequences such as numbers, months and weekdays (Dehaene, Bossini, & Giraux, 1993; Gevers, Reynvoet, & Fias, 2003, 2004), but also in just rehearsed artificial sequences of random numbers or objects (van Dijck & Fias, 2011), the primary/final items are mentally arranged to the left/right by healthy participants and corresponding left-hand and right-hand responses are relatively faster in simple classification tasks. Seeing these resembling behavioral patterns, a concise theory could assume that the same neurocognitive process underlies the tendency to project all enumerable objects mentally onto space.

The SNARC effect (spatial-numerical associations of response codes) offers a reliable and insightful testbed for exploring spatial associations and the effect was originally observed in judgments of numerical symbols. Numerous studies replicated its central finding of relatively faster left-side than right-side responding to smaller numbers, and vice versa for larger numbers (Dehaene et al., 1993; see Wood, Willmes, Nuerk, & Fischer, 2008 for a meta-analysis). Originally, the SNARC effect was understood as a long-term spatial representation of numerical magnitude resembling a mental number line (Pinel, Piazza, Bihan, & Dehaene, 2004; Restle, 1970). However, this classical account would assume that a distinct spatial representation would produce SNARC effects with non-numerical sequences such as letters or weekdays.

Notably, although SNARC and SNARC-like effects were documented for both numerical and non-numerical sequences (Dehaene et al., 1993; Fias, Brysbaert, Geypens, & D’Ydewalle, 1996; Gevers et al., 2004), sequences such as the weekdays expose a clear ordinal structure with additional cyclic component (Zamarian, Egger, & Delazer, 2007) whereas the number sequence includes mixed ordinal and cardinal magnitude features. For instance, the single-digit ‘2’ could refer to the second item in a row (ordinality), but the same digit ‘2’ could also imply twice the amount of something (cardinality). In contrast, ‘Tuesday’ only refers to the second day of the week and never implies the summed-up amount of two days. A conceptual controversy among numerical cognition researchers regards therefore the distinction between number magnitude and sequential order information (e.g., Fitousi, 2010) and their respective roles in forming spatial representations in the SNARC effect (e.g., Nathan, Shaki, Salti, & Algom, 2009). A potentially unifying account was recently promoted by experimentally disentangling the cardinal and ordinal properties of number: In a delayed working memory (WM) paradigm, participants were asked to maintain randomized number sequences (e.g., 4-1-6-8-3) and performed a SNARC task on the memorized numbers in a delay period. In this experiment (and in several follow-up studies), it turned out that spatial-numerical associations were based on the sequential order and not on the semantic magnitude information of the numbers (van Dijck, Abrahamse, Acar, Ketels, & Fias, 2014; van Dijck & Fias, 2011). This finding led to the WM account of the SNARC effect: Here, numbers are thought to elicit spontaneous adaptations of a general cognitive process to arrange the present sequence with a spatial layout at the level of WM to temporarily built an effective (spatial) mental representation (Abrahamse, van Dijck, & Fias, 2016). The important contribution of verbal WM to the SNARC effect was highlighted even before in different studies that showed reversals of SNARC effects by verbal labels positioned at physically incompatible locations (Gevers et al., 2006, 2010). Moreover, compatibility effects were observed between the parity concept and spatial responding in the MARC effect (Berch, Foley, Hill, & McDonough Ryan, 1999; Iversen, Nuerk, Jäger, & Willmes, 2006; Iversen, Nuerk, & Willmes, 2004; Nuerk, Iversen, & Willmes, 2004; Schroeder & Pfister, 2015). The assumption of the MARC effect is based on the principle of markedness: Linguistically, there is a default member in opposite pairs which is defined by semantic, distributional, or formal characteristics. If a classification involves stimulus and response features that share their markedness status, this can lead to faster performance than when one feature is marked and the other is not. This behavior can also account for the standard numerical SNARC effect because response features and verbal magnitude categorization share the marked members (small-left) or unmarked linguistic members (large-right) in compatible trials, which usually yield faster responses than incompatible trials. In less detail, the verbally mediated categorical correspondence principle is also compatible with the proposal of polarity correspondence (Proctor & Cho, 2006) and the involvement of verbal circuits for magnitude processing (Dehaene, Piazza, Pinel, & Cohen, 2003).

Regarding the underlying functional neuroanatomy, the unified theory also invites shifting the focus from the parietal regions bolstering numerical representations and operations (Cohen Kadosh & Walsh, 2009; Dehaene et al., 2003; Piazza, Pinel, Le Bihan, & Dehaene, 2007) to prefrontal cortex regions and their contributions to the processing of sequential order (Marshuetz, Smith, Jonides, DeGutis, & Chenevert, 2000; Shimamura, Janowsky, & Squire, 1990), most likely in conjunction with distributed WM systems (Baddeley, 2000; D’Esposito & Postle, 2015; Hurlstone, Hitch, & Baddeley, 2014). Furthermore, previous research identified especially frontoparietal networks for abstract quantity representations in non-human primates, possibly along a hierarchical gradient (Nieder, 2016; Tudusciuc & Nieder, 2009). Prefrontal activations were also often found in early neuroimaging studies of number processing; however, they were often interpreted as subserving only or predominantly non-numerical processes and were thus not (or less) considered in neurofunctional models (e.g., Dehaene et al., 2003). Disruption of the frontoparietal number circuits in human participants with transcranial magnetic stimulation over right frontal eye field and inferior frontal gyrus, but not over parietal regions, reduced spatial-numerical associations (Rusconi, Dervinis, Verbruggen, & Chambers, 2013). Furthermore, functional and structural connectivities between neuroanatomically distinct frontal and parietal areas corroborate verbal and non-verbal processing of numerical magnitude (Klein et al., 2016).

By administering transcranial direct current stimulation (tDCS) to the left prefrontal cortex, we recently demonstrated polarity-dependent modulations of SNARC effects in a sham-controlled setting (Schroeder, Pfister, Kunde, Nuerk, & Plewnia, 2016). Originally, this tDCS configuration was motivated by the possibility to modulate WM processes with cathodal tDCS (e.g., Wolkenstein, Zeiller, Kanske, & Plewnia, 2014; Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011), and a recent publication demonstrated the selectivity of left-hemispheric tDCS on a verbal letter n-back WM tasks and right-hemispheric tDCS on a visuospatial n-back task (Ruf, Fallgatter, & Plewnia, 2017). Similar modulations of number processing by prefrontal tDCS were also observed in number bisection and clock drawing tasks (Arshad et al., 2016). Transcranial brain stimulation with tDCS directs weak currents in the range of 1-2 mA to targeted brain regions and its effects are best defined by the current polarity, which produces predominant excitation underneath the ‘anodal’ electrode and inhibition underneath the ‘cathodal’ electrode (Nitsche & Paulus, 2000). The effects of tDCS are thought to be dependent on the current network activity (Fertonani & Miniussi, 2016), as neural structures are not entirely blocked, but resting membrane potentials are shifted and thus firing thresholds are reduced (anodal tDCS) or increased (cathodal tDCS). However, cathodal tDCS can also modulate resting-state connectivity (Keeser et al., 2011) and engagement of task-specific fronto-parietal networks in arithmetic processing (Hauser et al., 2016) and in verbal fluency (Ehlis, Haeussinger, Gastel, Fallgatter, & Plewnia, 2015). Thus, the method is ideally suited to modulate SNARC-related network activity, including left-hemispheric verbal WM (Gevers et al., 2010; van Dijck & Fias, 2011). Nevertheless, it is mandatory to highlight that the mechanisms of tDCS are not yet clearly understood and its efficacy is rather controversial

(Horvath, Forte, & Carter, 2015). In behavioral tasks, it should be further acknowledged that internal consistency and test-retest reliability for reaction time measurements can be fairly low [e.g., $r_{1/2} = .698$ for SNARC regression slopes (Cipora & Nuerk, 2013)]. Finally, behavioral effects of tDCS can be observed best when a task implies a targeted region, and stimulation effects were most pronounced for the most active task instructions (Gill, Shah-basak, & Hamilton, 2015; Zwissler et al., 2014).

In separate experiments involving parity and magnitude judgment, we recently observed a reduction of SNARC effects by cathodal tDCS to the left prefrontal cortex (Schroeder et al., 2016). However, the mere correspondence between WM-implied areas and neuromodulation results only provided suggestive evidence for a WM account of the SNARC effect, and alternative explanations such as a modulation of subthreshold conflict detection processes still required further empirical validation (Schroeder et al., 2016). Moreover, the tested single-digit stimuli could not differentiate whether the modulation of SNARC effects by prefrontal tDCS depended on numerical magnitude or sequential order information, because numbers convey simultaneous ordinal and cardinal magnitude information, as noted above. However, the unified ordinal WM account would predict comparable behavioral changes from the same manipulation of neurocognitive activity in both ordinal, non-numerical sequences as well as in cardinal, numerical sequences with magnitude information.

Thus, following up on the previously reported effects of tDCS on spatial-numerical processing (Arshad et al., 2016; Schroeder et al., 2016), the current study set out to also investigate modulations of the spatial associations of a non-numerical sequence by the identical left-hemispheric prefrontal tDCS configuration. More precisely, to address whether the same neurocognitive mechanism is involved in mentally aligning numerical and non-numerical sequences spatially, we tested two groups of healthy participants before and concurrent to anodal or cathodal tDCS in a series of classification tasks. From the previous results, we expected that the stimulation would attenuate (cathodal group) or emphasize (anodal group) the associations between space and sequence positions for a single-digit numerical sequence (1-5) and we expected the same behavior for a non-numerical weekday sequence (Monday-Friday). Thus, the design tested the presence of a generalized neurocognitive mechanism that would predict similar stimulation effects from the spontaneous arrangement of order along a spatial template.

In a separate control experiment conducted in the same participants on the same testing day, we also asked whether stimulation effects could persist even in cases where the target concept (e.g., numerical or non-numerical sequence) is only weakly activated. We therefore tested participants' performance with the same stimuli on a task variant that does not require active processing of the sequence (font color classification). In the order-irrelevant tasks, SNARC-like effects are less substantial (Gevers et al., 2003, 2004) or even abolished due to involvement of SNARC-irrelevant neural circuits in color classification (Fias, Lauwereyns, & Lammertyn, 2001). Thus, given that sequence information is here available to somewhat smaller extents, this task variant tested the possibility of subthreshold detection modulations (Schroeder et al., 2016) as opposed to the state dependency principle of tDCS (Gill et al., 2015; Zwissler et al., 2014). The subthreshold detection hypothesis would anticipate greater neuromodulation effects in the color judgment tasks in the sense that a response conflict between the spatial code extracted from numerical/ordinal information and spatial responding would become behaviorally relevant only concurrent to tDCS when capacities are enhanced, but the state dependency principle would anticipate greater neuromodulation effects in the order-relevant judgment tasks.

The main prediction, however, was that the relatively faster left-hand responses for small and early items and relatively faster right-hand responses for large and late items would assemble substantial SNARC effects in both groups and both tested sequences during the baseline measurement. Moreover, in line with a unified account of the SNARC effect, we hypothesized that this link between space and order would become less pronounced during cathodal tDCS and stronger during anodal tDCS irrespective of the tested sequence.

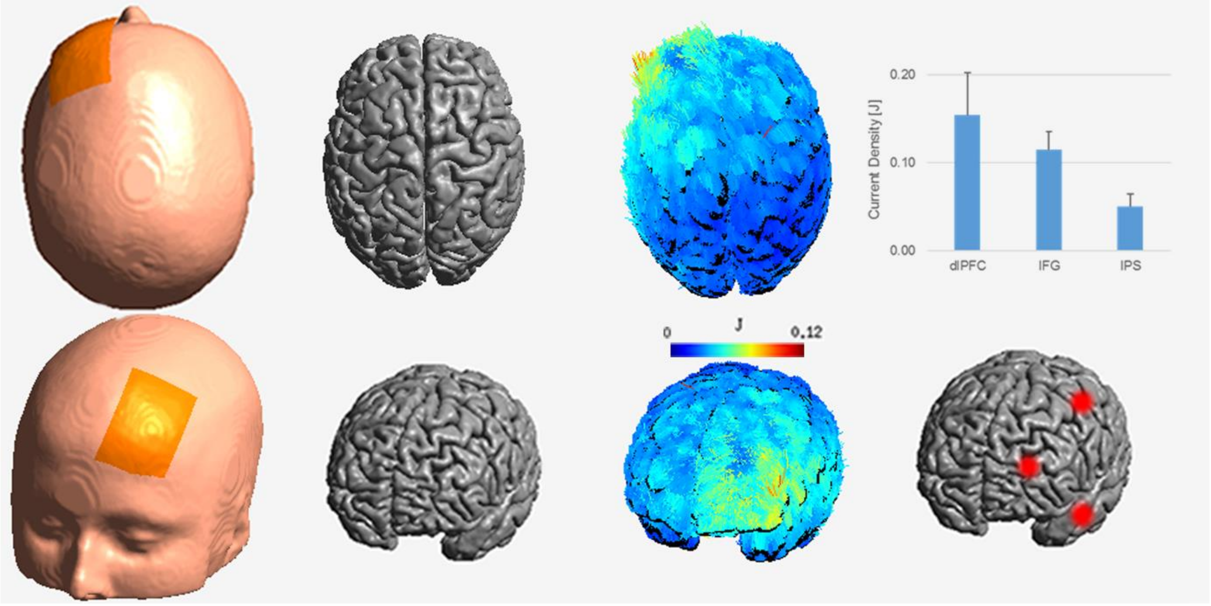


Figure 4.1. *Electric field model of the investigated tDCS configuration. The first column depicts the placement of target electrode (anode / cathode dependent on group assignment), the second and third column display the standard finite element head model and current density computations. Finally, in column 4, current density values above three regions of interest (dorsolateral prefrontal cortex [dlPFC], inferior frontal gyrus [IFG], intraparietal sulcus [IPS]) were probed and cross-validated using SIMNIBS and COMETS toolboxes (Jung, Kim, & Im, 2013; Opitz, Paulus, Will, Antunes, & Thielscher, 2015).*

Materials and Methods

Participants

Forty-eight healthy right-handed participants were tested twice, before (baseline performance) and during 1 mA tDCS (stimulation performance) either with anodal polarity (n = 24; mean age: 22.4 y, range: 18 – 30 y, 4 male) or with cathodal polarity (n = 24; mean age: 23.0 y, range: 18 – 27y, 5 male). The two groups were matched in terms of age, *p* = .463, gender, *p* = .719, handedness score, *p* = .726, years of education, *p* = .381 (mean: 16.17 y, range: 12.5 – 22.0 y), and verbal intelligence, *p* = 721 (assessed with a brief German vocabulary test; Lehrl, 2005). All participants gave written informed consent and received monetary compensation or course credits for their attendance. Ethical agreement was obtained from University Hospital Tuebingen Ethical Commision (NO: 701/2015BO2). Participants were eligible for the study if they were native German speakers without neurological or psychiatric impairment (explicitly including epilepsy, developmental disorders, as well as synesthesia and color blindness), and if they complied with safety regulation (no metallic implants, pregnancy, medication or use of recreational drugs, cardiac pacemaker, according to participant self-reports).

Procedure

Participants were randomly assigned to the anodal or cathodal tDCS group. Except for the administered stimulation polarity, all procedures for the two groups were identical. All participants completed both the order-relevant experiment as well as the order-irrelevant control experiment. After completion of the baseline performance phase, participants completed an unrelated cognitive test (beads task), rated their mood (Watson, Clark, & Tellegen, 1988) and were equipped with tDCS. A resting phase of 5 minutes after stimulation onset preceded repeated testing of SNARC and SNARC-like effects with numerical and non-numerical sequences in order-relevant comparison tasks and also in order-irrelevant classification tasks (control experiment). Participants from both groups (anodal and cathodal) completed all tasks in both experiments. The orders of experiments and tasks within experiments were counterbalanced across participants. In the order-relevant experiment, participants had to decide whether a weekday came before or after ‘Wednesday’ (ordinal sequence) or whether a number was smaller or greater than the referent ‘3’ (cardinal sequence). Two keyboard buttons (covert ‘s’ and ‘l’ on a QWERTZ-keyboard) were operated by left-hand and right-hand index finger presses and response-mappings were switched within the tasks in counterbalanced order across participants. In the control experiment, the task was to indicate font colors by left-hand or right-hand index finger key presses and ignore in separate blocks weekday names (Monday, Tuesday, Thursday, Friday), number symbols (1, 2, 4, 5), and color words in a control Stroop task (blue, green) that was included to assess automatic color-word interference and possible tDCS modulations of executive functions (Stroop, 1935). The same weekday and number stimuli appeared in both order-relevant and order-irrelevant experiments.

All single tasks were preceded by a brief training block (16 trials) and an error count emphasized correct responding. Corresponding to previous studies with weekday stimuli (Gevers et al., 2004), the experimental procedure comprised 20 target repetitions in each task, with 300ms fixation hash (#), 2 s target presentation (or until response), and 300ms error feedback (German words ‘Fehler’ [error] or ‘Bitte schneller antworten’ [please respond faster]) or a blank inter-trial interval.

transcranial Direct Current Stimulation (tDCS)

Direct current was generated by a CE-certified stimulator (DC-STIMULATOR MC, NeuroConn, Ilmenau, Germany). The active electrode (anode or cathode in the respective groups) was placed over the left PFC (F3), the return electrode was fixed to the right upper arm (Schroeder, Ehlis, Wolkenstein, Fallgatter, & Plewnia, 2015; Vandermeeren, Jamart, & Ossemann, 2010; Wolkenstein & Plewnia, 2013; Zwissler et al., 2014). Both 5 × 7 cm rubber electrodes were covered with adhesive paste (10/20 conductive EEG paste, Kappamedical, USA) and impedances were kept below 10 kΩ. 1 mA direct current was faded in with a 5 s ramp and a 5 min idle time preceded task initiation, with a stimulation duration of 25 min. Participants were told to relax during the idle time before the task and the experimenter announced the beginning of classification tasks with initiation of written instructions on the computer screen. Figure 4.1 displays a current flow model with standard conductivity values of the used electrode montage (Thielscher, Antunes, & Saturnino, 2015), which emphasizes a relatively dense field in lateral PFC, but not in parietal regions. In the stimulation phase, all tasks were completed concurrent to active tDCS. Participants rated adverse effects (Brunoni et al., 2011) as well as mood (Watson et al., 1988) after completion of the stimulation protocol. Stimulation polarity (anodal, cathodal) was randomly assigned and balanced across participants to create equally sized groups.

Data Treatment

The current data were collected as part of a larger project on the cognitive foundations of numerical and non-numerical spatial associations. Results from the baseline sessions are also reported in another paper which examines in greater detail individual differences, psychometric properties, and construct validity of different spatial associations (see Chapter III). The effects of tDCS are analysed for the first time in the current manuscript.

SNARC and SNARC-like effects are indicated by an interaction (ANOVA) of the repeated measures factors $hand_{\text{LEFT-HAND,RIGHT-HAND}}$ and *position* (which corresponds to increasing magnitudes in number stimuli: 1, 2, 4, 5; weekdays: Monday, Tuesday, Thursday, Friday), as recommended by Tzelgov, Zohar-Shai, & Nuerk (2013). The repeated measures factor $set_{\text{NUMBERS,WEEKDAYS}}$ was further introduced to differentiate numerical and non-numerical sequence representations. Polarity-dependent effects of the *stimulation* denoted the factor combination of time (baseline performance, stimulation performance) with the inter-subjects factor tDCS polarity (anodal, cathodal). For brevity, we refer to these critical two-way interactions as *SNARC* (position × hand) and *stimulation* (polarity × time).

In a second step, as recommended in SNARC research, individual regression coefficients were extracted for a quantification of SNARC effects, and for follow-up tests of its modulations by prefrontal tDCS, following the method introduced by Lorch & Myers (1990). To that end, response-hand latency differences (dRT = left hand – right hand) were regressed on the individual sequence positions (see Figure 4.2). From this procedure, a single negative coefficient signals the typical mapping of numbers and weekdays onto space: With increasing sequence position, right-hand responses become relatively faster than left-hand responses. We ran LSD simple effects interaction analyses and student's *t*-tests to isolate significant results of ANOVA on these regression coefficients.

Finally, in the order-irrelevant control experiment, we additionally report modulations in the Stroop task in terms of a repeated measures ANOVA comprising the factor $\mathit{Stroop}_{\text{COMPATIBLE,INCOMPATIBLE}}$ and the factor *stimulation* (considered as the interaction term between stimulation polarity and time, as above). Trials in the Stroop task were regarded compatible if font color and written color were identical.

We considered only correct responses for response times analyses (94.4 % of all trials) and latencies deviating more than 3.0 SDs of the corresponding cell mean were discarded as outliers (1.7 %). Greenhouse-Geisser corrected df- and *p*-values are reported upon violations of sphericity.

Results

Stimulation Adverse Effects and Mood

Common and moderate sensations of tingling and discomfort at stimulation sites were reported, but there were no significant polarity differences (*p*s > .48). Detailed adverse effect ratings from both experiments are reported in Table 4.1. Positive and negative affect were not significantly modulated by *stimulation*, *F*s(1,46) < 1, *p*s > .33.

Table 4.1. TDCS adverse effects. Adverse sensations were assessed on a 5-point Likert-like scale after each session (1=none, 5=very strong). Ratings from anodal and cathodal groups were subjected to independent samples t-tests.

	Anodal tDCS	Cathodal tDCS	
Adverse Sensation	*M (SD)*	*M (SD)*	*p*
Tingling at the site of the electrode	2.79 (1.18)	3.00 (1.18)	.54
Tingling elsewhere	1.29 (0.69)	1.33 (0.56)	.82
Exhaustion	1.71 (0.91)	1.67 (0.87)	.87
Itching	2.13 (1.33)	2.08 (1.14)	.91
Headache	1.21 (0.51)	1.33 (0.70)	.48
Nausea	1.00 (-)	1.00 (-)	-

Order-Relevant Magnitude Classification Tasks

ANOVA

In the order-relevant comparison tasks, the anticipated two-way interaction between *hand* and *position* – indicating the presence of *SNARC* effects – was significant, $F(2.14,138) = 10.55$, $p < .001$, $\eta p^2 = 0.19$. The main effect of *time* was significant $F(1,46) = 24.73$, $p < .001$, $\eta p^2 = 0.35$, and mean responses were faster during anodal or cathodal tDCS (523 ms) than in the preceding baseline session (543 ms), but this was irrespective of stimulation polarity as rated by the absence of significance in the *time* × *polarity* interaction, $F(1,46) < 0.01$, $p = .950$. In line with general effects of word length and familiarity (e.g., Gernsbacher, 1984), we observed generally faster responses to numerical symbols (502 ms) than to letter strings (563 ms) in a significant main effect of *set*, $F(1,46) = 242.55$, $p < .001$, $\eta p^2 = 0.84$. This observation is in line with previous within-participant designs that also found much faster responses (42 ms – 87 ms) for Arabic number symbols (Nuerk et al., 2004; Nuerk, Wood, & Willmes, 2005).

Most importantly, a five-way interaction of *set* with hand × position (henceforth: *SNARC*) and with time × polarity (henceforth: *stimulation*) was significant, $F(2.27,138) = 5.66$, $p = .003$, $\eta p^2 = 0.11$. This result points to differential modulations of spatial associations in weekday and number sequences by prefrontal tDCS. To more precisely interpret the effect of tDCS, we next quantified the obtained SNARC effects by linear regressions for the different tasks and stimulation conditions.

Since response hand differences are aggregated in SNARC slopes, we also checked in the ANOVA whether there was a more basic modulation of *hand* by tDCS. At least one study suggested such modulations to result from tDCS over sensorimotor cortex (Minarik et al., 2016). In our results, a significant *hand* main effect signaled faster right-hand (526 ms) than left-hand key presses (540 ms), $F(1,46) = 30.73$, $p < .001$, $\eta p^2 = 0.40$, as expected for a right-handed population. The interaction term for *hand* with *stimulation* was not significant, $F(1,46) < 1$, $p = .707$, and there were also no significantly faster responses in general from *tDCS*, $F(1,46) < 1$ $p = .950$, as expected from our electrode placement and current flow model (cf. Figure 4.1). We reasoned not to consider generally modulated response speed meaningful with our data and resumed with the analyses of different SNARC modulations.

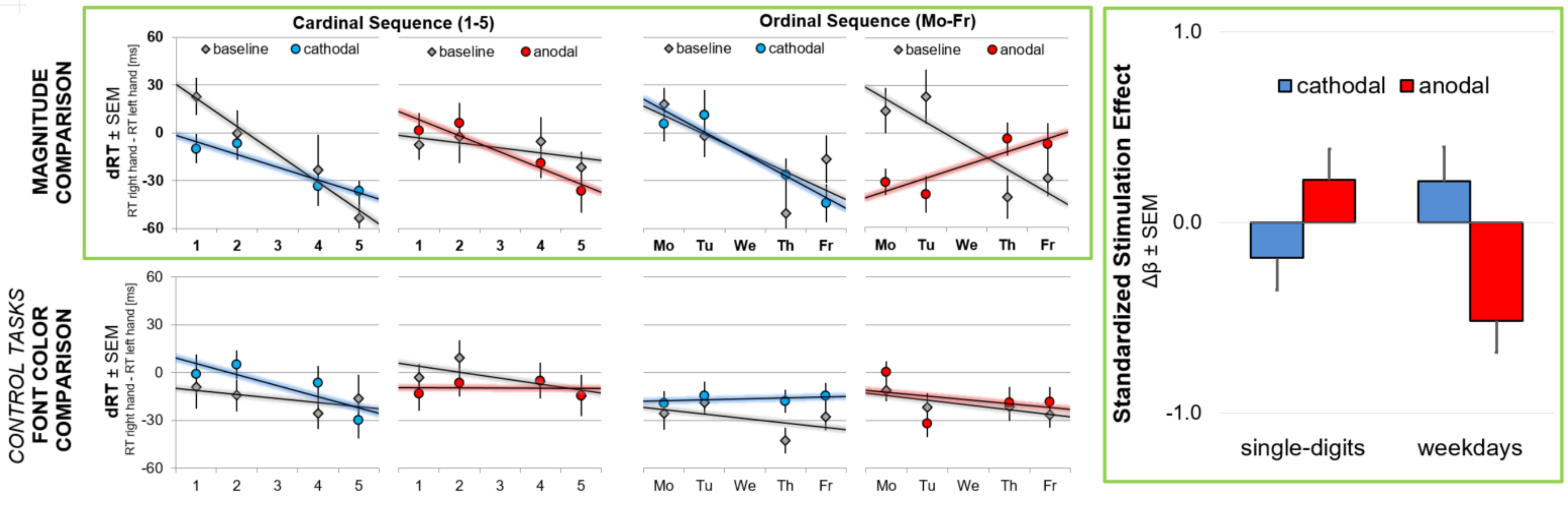


Figure 4.2. *Behavioral results in order-relevant (top row) and order-irrelevant (bottom row) behavioral tasks and stimulation effects. Separate graphs for each task and group depict response hand latency differences (right hand – left hand) as a function of position in the sequence. Gray lines and bars indicate baseline performance, blue and red lines and bars refer to performance during cathodal and anodal tDCS, respectively. Standardized stimulation effects based on extracted ß regression coefficients for the order-relevant magnitude comparison task are summarized in the right panel.*

Table 4.2. Spatial Association Indices. Unstandardized b regression coefficients indicate response hand advantage increases (SNARC and SNARC-like effects) with single position/magnitude increments in the corresponding sequence (dRT/position[ms]), whereas standardized β coefficients correct for individual variance. All regression coefficients were individually extracted and the resulting group-level mean was tested with one-sample t-tests against zero (Fias et al., 1996).

		ORDER-RELEVANT TASK							
		baseline / sham				**stimulation**			
sequence	**polarity**	b	*p*	β	*p*	b	*p*	β	*p*
numbers (1-5)	anodal	-3.130	.519	-.016	.907	-10.125	.047	-.239	.087
	cathodal	-17.545	.011	-.414	.003	-7.976	.023	-.228	.057
weekdays (Mo-Fr)	anodal	-14.841	.015	-.220	.120	+8.296	.056	+.296	.026
	cathodal	-11.770	.022	-.205	.109	-13.689	.010	-.420	.002

		CONTROL EXPERIMENT (ORDER-IRRELEVANT TASK)							
		baseline / sham				**stimulation**			
sequence	**polarity**	b	*p*	β	*p*	b	*p*	β	*p*
numbers (1-5)	anodal	-3.782	.350	-.080	.499	-0.067	.985	-.066	.660
	cathodal	-2.562	.295	-.129	.285	-6.950	.110	-.273	.025
weekdays (Mo-Fr)	anodal	-3.017	.123	-.151	.199	-2.446	.284	-.047	.677
	cathodal	-2.826	.229	-.119	.286	+0.540	.821	+.043	.737

Regression Coefficient Analyses: Quantification of SNARC Effects and Their Modulations by Prefrontal tDCS

Mean response hand differences as a function of sequence position for all experimental conditions are displayed in Figure 4.2 (top row). The unstandardized and standardized regression coefficients resulting from linear regression for both stimulation conditions are reported in Table 4.2 including test statistics. To quantify the observed polarity- and stimulus-dependent stimulation effects, coefficients of the order-relevant SNARC tasks were submitted to a repeated measures ANOVA comprising the factors *set* and *stimulation*, as above, followed up by simple effects analyses for significant interaction terms.

The analysis revealed a different tDCS modulation of SNARC effects for numbers and weekdays, as indicated by a significant interaction term between *set* × *stimulation*, $F(1,46) = 14.01$, $p < .001$, $\eta p^2 = 0.23$. Thus, this analysis based on extracted regression coefficients reproduced the previously obtained dissociative result. For the baseline session only, the main effect of *set* was not significant, $F(1,47) = 0.37$, $p = .544$, suggesting that the SNARC regression slopes for numerical and non-numerical stimuli were comparable in terms of their intensity. For numbers, interaction analyses revealed that a difference between SNARC slopes was significant already during the baseline session, $F(1,46) = 4.69$, $p = .036$, $\eta p^2 = 0.09$. However, the difference between groups vanished for the stimulation session, $F(1,46) < 1$, $p = .952$, most likely due to the attenuation of numerical SNARC effects by cathodal tDCS and amplification of numerical SNARC effects by anodal tDCS (Figure 4.2), as observed before in sham-controlled experiments (cf. Schroeder et al., 2016). In contrast to the sham-controlled results, the direct comparisons of SNARC slopes before and concurrent to tDCS were not significant for the cathodal group, $t(23) = 1.23$, $p = .230$, or for the anodal group, $t(23) = 1.19$, $p = .248$. In all conditions, negative signed coefficients implied left-to-right oriented mental number representations during both cathodal and anodal stimulation (see Table 4.2).

For the ordinal weekday sequence, the pattern of results was essentially reversed (Figure 4.2): No differences were detected during the baseline session, $F(1,46) < 1$, $p = .932$. However, a clear and highly significant group difference emerged for the stimulation session, $F(1,46) = 16.74$, $p < .001$, $\eta p^2 = 0.27$, driven by a reversal of SNARC directionality during anodal tDCS. In this case, a positive signed coefficient emerged during anodal stimulation, indicative of a reversed right-to-left representation of the weekday order, and opposite in directionality as compared to both baseline performance within the same participants,

$t(23) = 3.54$, $p = .002$, d = 0.95, and as also compared to stimulation performance in the cathodal tDCS group, $t(46) = 3.43$, $p < .001$, d = 0.99.

Error Rates

In total, participants made relatively few errors (5.6 %). When we analyzed error rates with ANOVA, the SNARC effect was not significant, $F(2.81,138) = 1.98$, $p = .124$. The interaction terms of SNARC × *set* and SNARC × *stimulation* were not significant as well, *p*s > .60.

Control Experiment: Order-Irrelevant Font Color Classification Tasks

ANOVA

Mean response hand differences as a function of sequence position for all experimental conditions are displayed in Figure 4.2 (bottom row). In the color judgment tasks, weekday order and number magnitude information was less active, because the task required only a classification of the stimulus font color. Nevertheless, a trend for an overall SNARC effect was detected, $F(2.67,138) = 2.26$, $p = .092$, $\eta p^2 = 0.05$. In striking contrast to the main results from the order-relevant classifications, there was no further modulation of SNARC by *stimulation* nor by *set*, all *p*s > .200. Also, the previously significant interaction between *SNARC*, *set*, and *stimulation* did not approach significance in the order-irrelevant color judgment task, $F(2.51,138) < 1$, $p = .599$.

Also in these tasks, we observed generally faster responses to numerical symbols (462 ms) than to letter strings (506 ms) in a significant main effect of *set*, $F(1,46) = 115.89$, $p < .001$, $\eta p^2 = 0.72$. The main effect of *time* was not significant in the order-irrelevant tasks, $F(1,46) < 0.01$, $p = .967$. In particular, there was no *time* × *polarity* interaction, $F(1,46) = 0.18$, $p = .676$.

Error Rates

The *SNARC* effect was not significant, $F(2.20,138) = 1.09$, $p = .346$. The interaction terms of *SNARC* with *set* and *stimulation* were not significant as well, *p*s > .54.

Stroop Control Task

The Stroop task was included as a control measure for both automatic reading in color judgment and modulation of executive functions by tDCS. RTs were submitted to ANOVA comprising the factors *Stroop*$_{\text{COMPATIBLE,INCOMPATIBLE}}$ and *stimulation* as reported above. There was no significant interaction of *Stroop* × *stimulation*, $F(1,46) < 1$, $p = .879$, and a main effect of *Stroop* signaled reliable color-word interference from automatic reading, $F(1,46) = 17.63$, $p < .001$, $\eta p^2 = 0.28$. This manipulation check indicates i) that the significant findings from order-relevant classifications are not accounted for by a general modulation of executive functions as captured by Stroop (e.g., inhibition), and ii) that different stimulation effects between the two experiments are not due to a lack of automaticity in the color judgment task.

Comparison of Stimulation Effects on Order-Relevant and Order-Irrelevant Classification Tasks

A final ANOVA was performed including all experimental factors to resolve whether the different results from the two experimental *tasks* (order-relevant comparison vs. order-irrelevant color classification) were statistically significant. Overall, the analysis again detected significant *SNARC* effects, $F(2.03,138) = 13.37$, $p < .001$, $\eta p^2 = 0.23$. Critically, the anticipated six-way interaction of *task, set, stimulation* (polarity × time) and *SNARC* (position × hand) was significant, $F(2.44,138) = 6.30$, $p = .001$, $\eta p^2 = 0.12$, corroborating the orthogonal and polarity-specific stimulation effects for the two tasks and sequence sets. This result substantiates our previous observation of different modulations in the order-relevant tasks, but no systematic modulations in the order-irrelevant color judgment tasks. In addition, we also obtained an interaction of *SNARC* with *task*, $F(2.44,138) = 3.52$, $p = .025$, $\eta p^2 = 0.07$, in line with the observation that SNARC effect sizes were relatively larger in the order-relevant tasks ($\eta p^2 = 0.19$ as compared to $\eta p^2 = 0.05$), as also reported in previous research (Fias et al., 2001; Gevers et al., 2003). Thus, a modulation of spatial associations by prefrontal tDCS was not only dependent on the stimulation polarity and the currently employed sequence set, but also on the task-induced activation of the sequence.

Discussion

In the current study, the neuromodulatory effect of transcranial direct current stimulation (tDCS) was employed to investigate a prefrontal circuit linking space with numerical and non-numerical sequence information. Participants compared number magnitude and weekday positions in a baseline session without stimulation followed by another session paralleled by either anodal or cathodal tDCS. We hypothesized to observe similar modulations of spatial associations (SNARC effects) in both of the tested sequences from the recent proposal of a unified WM mechanism, that was thought to generally pair sequence information with a spatial template to build up effective mental representations in space (Abrahamse et al., 2016; van Dijck & Fias, 2011).

However, the results clearly demonstrated dissociative effects of the prefrontal stimulation in task- and polarity-dependent structure: Whereas spatial-numerical associations maintained a rightwards direction with increased prefrontal activity, the spatial alignment of weekdays reversed to a leftwards direction with anodal, excitability increasing stimulation. More precisely, during anodal tDCS, participants accomplished relatively faster right-hand than left-hand responses for the primary weekdays (Monday, Tuesday), and vice versa for the later weekdays (Thursday, Friday), whereas the mental alignment of numbers tended to follow a left-to-right directional alignment, with different intensities, in all remaining conditions. Thus, we observed a neurobehavioral dissociation of number and weekday spatial associations during anodal tDCS in the same participants.

Before drawing inferences on the underlying theories, some aspects need to be highlighted. First, the polarity-specific stimulation effects on spatial-numerical associations in the current data were additionally pronounced due to group differences in the baseline session. Specifically, in the anodal tDCS group, the SNARC effect for numbers was not significant before stimulation, but only concurrent to anodal tDCS (see Table 4.2). Thus, although results are suggestive of reductions of numerical SNARC effects by cathodal tDCS and amplifications thereof by anodal tDCS, as observed before (Schroeder et al., 2016), the current results alone provide insufficient evidence of this behavior due to the a priori group differences and lack of significance in within-group comparison tests. In contrast, both groups exhibited comparable spatial associations of the weekday sequence in the baseline measurements, but stimulation effects in the ordinal sequence were effectively orthogonal and statistically significant for both within-group and between-group comparisons.

Stimulation effects emerged only for the order-relevant comparison tasks, but not in a control experiment testing the effects of font color classification. Moreover, color-word interference was present in all stimulation conditions which suggests automatic reading at least for words; we did not implement a specific test for automatic number magnitude extraction (Dehaene et al., 1993; Henik & Tzelgov, 1982). This demonstration of task selectivity is in line with reduced

SNARC effects in order-irrelevant tasks (Gevers et al., 2003, 2004) that do not necessarily overlap with number-related neural activations (Fias et al., 2001). Thus, the additional result underlines the notion that tDCS modulations of behavior are dependent on task-related activations (i.e., state-dependency principle of transcranial brain stimulation; Gill et al., 2015; Silvanto & Pascual-Leone, 2008; Zwissler et al., 2014). In contrast, however, results from the order-irrelevant task do not permit to nullify the possibility of subthreshold conflict detection modulations by tDCS, but rather suggest that such effects are negligible in the current set of tasks as compared to the modulating effects of stimuli and instruction. Regarding clinical applications of tDCS, the results highlight how the selection of stimuli and tasks (beyond configuration and individualization of stimulation parameters) can invert the outcome of a stimulation. Consideration and further examination of this complex interaction between stimulation, task, and individual could render targeted stimulation treatments for neuropsychiatric conditions and possibly for deficits in numerical processing more effective. However, at the moment we would like to handle such interpretation with great care, especially since the SNARC effect is not consistently linked to arithmetic achievement and performance (Cipora & Nuerk, 2013; Cipora, Patro, & Nuerk, 2015). Because tDCS is still a relatively novel and controversial technique, it remains mandatory to investigate its basic principles and also challenge the reliability of seemingly solid findings. For example, in an influential quantitative review, evaluation of single-session tDCS effects on cognitive effects revealed no significant stimulation effects (Horvath et al., 2015). We believe that this result in generally emphasizes the need for more precision and careful implementation of tDCS mechanisms in the research field.

The malleability of SNARC by prefrontal neuromodulation complements previous studies (Arshad et al., 2016; Schroeder et al., 2016), but the results challenge the unified conception of spatial representations. Given the apparent incompatibility with the WM account (Abrahamse et al., 2016; van Dijck & Fias, 2011), it is important to point out that the obtained tDCS dissociation appears to be consistent with evidence from neuropsychological patient studies. For instance, prefrontal damage could alter the representation of physical and mental number lines differentially (Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005). But also for reproduction of a non-numerical verbal list, frontal lobe lesions across different patient groups appeared related to disproportionate deficits for organizing ordered information, even despite normal item memory in some groups (Shimamura et al., 1990). Interestingly, neglect patients (after right parietal lesion) usually demonstrate a rightward bias when bisecting physical lines (thus the exact midpoint is actually more to the left than the declared bisection), but also numeric intervals, which is consistent with their visuo-spatial deficit. In contrast, the same neglect patients exhibited an opposite leftward bias for bisections of non-numerical intervals such as months (Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006) and also the weekday sequence (Zamarian et al., 2007). Theoretically, in number line bisection tasks, the cyclic nature of non-numerical sequences such as weekdays and months could drive this reversal in patients' representational space exploration, comparable to results from imagining numbers on a clockface (Vuilleumier, Ortigue, & Brugger, 2004). However, Zorzi et al. (2006) also found that neglect patients' bias was independent of interval length and thus argued for a categorical verbal-spatial process. In the following, we motivate one possible explanation for the observed reversal by drawing on linguistic markedness principles (MARC effect) as one of multiple spatial codes that can compete for different directionalities observed in SNARC effects. In this framework, the biasing effect of left-hemispheric anodal tDCS towards markedness correspondence accounts for the observed reversal of the spatial association of the weekday sequence.

Towards a Linguistic Processing Account: SNARC Becomes MARC

Further empirical evidence supports the involvement of verbal-spatial coding in the SNARC effect. For instance, spatial-numerical associations can be obtained without involvement of a physically lateralized response by asking participants to respond verbally to centrally presented numbers by naming spatial labels (e.g., by saying 'left' and 'right' for odd and even digits; Gevers et al., 2010). Such verbal-spatial labels furthermore determined the direction of spatial-numerical associations when they were configured contrarily to a physical lateralization (e.g., the left display side was labelled as 'right') (Gevers et al., 2010; Gevers, Verguts, Reynvoet, Caessens, & Fias, 2006). Similar SNARC effects from verbal-spatial codes were already documented to replace the physical shaping of visual spatial-numerical information in experiments with 10-year-old children (Imbo, Brauwer, Fias, & Gevers, 2012). Moreover, regular SNARC effects were observed in neglect patients who, paradoxically, also showed impaired number bisection performance (Priftis, Zorzi, Meneghello, Marenzi, & Umiltà, 2006; Zorzi et al., 2006). This result also supports the hypothesis of (auxiliary) verbal-spatial coding that enables spatial representations with otherwise impaired system.

In principle, the availability of a verbal-spatial code is consistent with the dual-coding theory of mental representations (Paivio, 1986) and also more specifically with the triple-code model of magnitude representation, which proposes that numerical representations also include left-hemispheric verbal codes among (visuo-)spatial and non-symbolic analogue magnitude codes (Dehaene et al., 2003). In line with these multiple codes, we can inspect in more depth why anodal tDCS could have induced a bias towards a verbal-spatial code, which could have produced the observed reversal in the weekday sequence by drawing on linguistic markedness.

More precisely, regarding the verbal codes for non-numerical sequence representations, it is mandatory which categorical relation is being mapped by means of the task instruction.

For instance, smaller/larger and earlier/later judgments in numerical and non-numerical sequences might draw on different linguistic categorical dimensions. From a linguistic perspective, this precise verbal distinction is highly relevant because it determines the linguistic markedness of the categorical dimension, that is: the positive, unmarked (+polar) and negative, marked (-polar) endpoints of the linguistic continuum (Jakobson, 1984; Lakens, 2012). Linguistically, the marked form of complementary terms is determined either by formal, distributional, or semantic characteristics. For instance, the marked endpoint of a dimension may include a pre- or suffix (formal), have less frequent use cases (distributional), or its meaning is more specific (semantic; Lyons, 1977). Psycholinguistically, across many different domains, classification responses are faster when linguistic markedness poles are identical across the continuums implied in a task, including number, time, and space (Clark, 1969; Lakens, 2012; Proctor & Cho, 2006). For instance, by requiring left-hand and right-hand responses in typical SNARC tasks, a second, spatial dimension is superimposed on classifications of numerical magnitude or sequential order. The spatial dimension similarly involves a default, unmarked ('right') and linguistically marked ('left') feature polarity (Zimmer, 1964), which could possibly be body-specific for right-handers, in addition (Casasanto, 2009). Furthermore, 'large' is the semantically unmarked form of the verbal magnitude dimension because of its syntactic distribution and default occurrence in the neutral question form (e.g., how large is something; Jakobson, 1984; Lehrer, 2008). Thus, faster responses should emerge for aligning large numbers with right-hand responses, as typically evidenced by the SNARC effect. This complex linguistically motivated behavior was termed MARC effect and it becomes prototypically apparent in parity judgment tasks, where a correspondence between even and un-even (i.e., odd) digits with right-hand and left-hand responses can be observed (Berch et al., 1999; Nuerk et al., 2004).

Regarding judgments on the sequential continuum, critically, the ‚before – after' dichotomy is lexically different from the 'larger – smaller' classification (Clark, 1969). According to linguistic markedness principles, temporal propositions such as ‘earlier’ and ‘later’ both deviate from the unmarked standard moment in time (‘now’), yet judgments on ‘earlier’ are easier (and faster) than judgments on ‘later’ (Handel, DeSoto, & London, 1968). Moreover, the principle of temporal iconicity predicts ‘earlier’ to be coordinated lexically first (Renner, 2014), comparable to the lexically unmarked member of complementary adjective pairs. Also following Greenberg’s criteria of lexical marking, it can be concluded that ‘early’ is the unmarked positive polarity (Clark, 1973; Greenberg, 2005). This becomes apparent in frequency of before-after, first-later, and primary-finally constellations in usual sentence constructions (Landsberg, 1995). As a result, and most critical for the results obtained with sequential stimuli in the present study, the preferred linguistic processing of ‘before’ and ‘large’ over ‘after’ and ‘small’ would qualitatively predict different orientations of correspondence effects with spatial response dimensions (e.g., SNARC effects). More precisely, both ‘large’ and ‘before’ would constitute the positive form as opposed to ‘small’ and ‘after’ (Clark, 1973), and markedness correspondence would thus actually predict opposed stimulus-response compatibility effects (Nuerk et al., 2004) for numerical magnitude and temporal relation judgments as observed in the current study during anodal, but not cathodal tDCS.

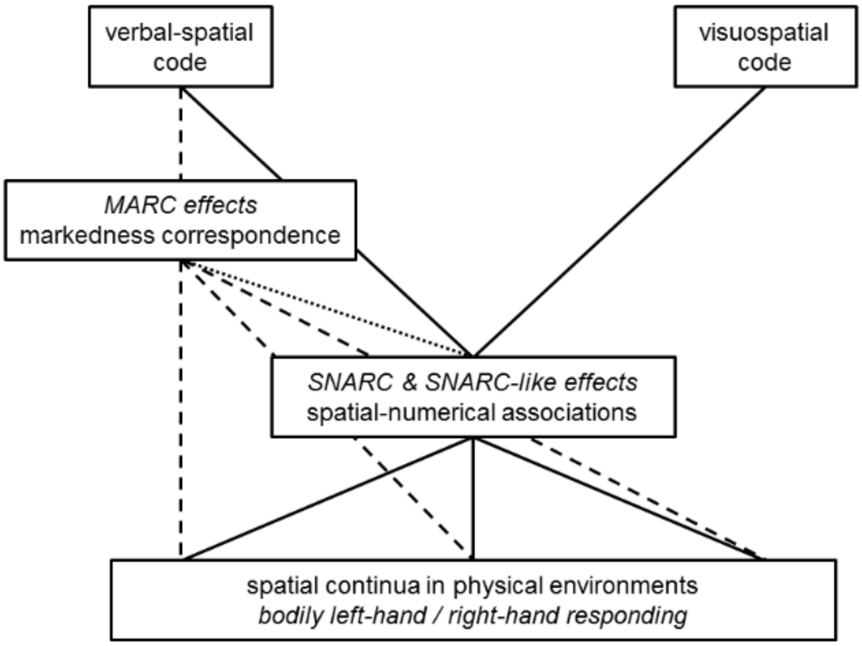


Figure 4.3. *Contribution of verbal-spatial and visuospatial codes to spatial-numerical associations. By route of markedness correspondence (MARC effects), conflicting verbal-*

spatial or visuospatial codes may either determine the direction of SNARC and SNARC-like effects. Spatial continua in the physical environment (e.g., left-hand and right-hand responses) can produce SNARC effects due to either correspondence with a visuospatial code or with a verbal-spatial code. In contrast, markedness correspondence is limited to the correspondence with verbal-spatial codes. Interactions between SNARC and MARC effects can be possible. Behavioral effects can emerge due to both codes that sometimes produce identical behavior in the case of SNARC effects for numbers in Western cultures, but certain manipulations such as the stimulation with anodal tDCS when judging ordinal stimuli may produce different outcomes due to switched prevalence of one kind of cognitive processing.

Note that this is only one possible (yet rather exhaustive) explanation for the observed reversal, but that the verbal markedness correspondence alone does not account for regular left-to-right orientations during baseline performance. Instead, different explanations may account for the emergence of a linguistically incompatible mapping without tDCS: For instance, cultural practices (e.g., reading habits) or certain trainings can produce different directions of spatial associations (Göbel, Shaki, & Fischer, 2011; Notebaert, Gevers, Verguts, & Fias, 2006). Similarly, continuous sensorimotor interactions with sequence stimuli in predefined manner can shape a mental representation thereof (Fischer, 2012). Already in children, space-number associations are malleable by brief directional training procedures (Patro, Fischer, Nuerk, & Cress, 2015), and spatial correspondences are additionally utilized by metaphorical thinking, since only selected spatial schemas produce behaviorally relevant effects (Dolscheid & Casasanto, 2015). In any case, the mapping of weekdays prior to tDCS is not accounted for by the markedness correspondence principle, but rather by any of the described mapping effects.

The possibility of multiple spatial codes for numerical representations, however, was already acknowledged in early theories (Dehaene et al., 2003) and has been – in lesser detail – previously proposed accounting for parity effects (e.g. Iversen et al., 2006, Figure 3, pp. 735-736). The current paper generalizes this account to magnitude, sequences, and any marked entity. Additionally, we provide a neurofunctional test of this account allowing for integration in neurocognitive models of number processing.

Marked SNARC Effects in Other Domains

The presented elaboration of contrary spatial associations from linguistic processes in different tasks and sequences is also consistent with other previous empirical results not directly related to above results, thereby suggesting generalizability of the account. For example, the asymmetrical exploration of numerical and non-numerical spatial representations in neglect (Zamarian et al., 2007; Zorzi et al., 2006) can be accounted for by considering contrarily oriented spatial representations from linguistic markedness correspondence (and when the regular code that arranges weekdays from left-to-right is presumably not available). More precisely, leftward shifts by left-spatial neglect patients in some ordinal, but never in numerical sequences could result from compensatory verbal-spatial processing and correspondence between verbal spatial labels and ordinal properties, if a visuospatial simulation in neglected space is not available or impaired. Furthermore, the vivid spatial representation of months in a single-case synesthesia report switched for different modality presentations: For instance, the written word ‘January’ was aligned to the left whereas its auditory presentation was aligned to the right (Jarick, Dixon, Stewart, Maxwell, & Smilek, 2009). This result is highly consistent with our account if the dominance of verbal-spatial codes is activated by verbal auditory presentation and activation of visuospatial codes is enhanced by visual presentation. But also the original speculations are compatible with our integrative account if her month series learning as a child was indeed facilitated by mapping ‘January’ to the right, as it was reported (Jarick et al., 2009).

Finally, when ascending and descending number and letter sequences were judged, only numbers (with consistent markedness) were spatially coordinated along with the direction instruction (Cheung & Lourenco, 2016). Likewise, linguistic markedness could also contribute to the reversal of SNARC effects in *earlier* vs. *later* numerical judgments on imagined clockfaces (Bächtold, Baumüller, & Brugger, 1998; Vuilleumier et al., 2004).

Neurophysiologically, it appears as if the prefrontal stimulation administered here induced a switch from the default dominance of a visuospatial code (with left-to-right orientation of magnitude and ordinal position) to the verbal network. Here, a consistent linguistic markededness correspondence of magnitude (small – large) with spatial codes (left – right) exists in number, but an opposite MARC effect in the weekday-sequence (late – early) reverses SNARC effects with non-numerical items. Thus, tDCS may have increased verbal-spatial coding by either drawing on prefrontal (Miller & Cohen, 2001) or inferior frontal structures (Costafreda et al., 2006), as also confirmed by our electric field modelling (cf. Figure 1). However, future research is required to empirically validate the assumed neurophysiological effects of tDCS, which are best qualified by modulation of a verbal-numerical left hemispheric network, possibly including superior fasciculus longitudinalis III (Klein et al., 2016). Cross-cortical effects from prefrontal neuromodulation on parietal activity patterns could underlie the switch from a dominant SNARC to a MARC effect, but concurrent imaging is necessary to verify the precise neurophysiological network effects of tDCS.

Alternative Accounts

The presented hybrid model of two or more (competing) codes involved in the generation of spatial associations (Figure 3) can fully account for the current empirical observations, but it is mandatory to highlight that this model is only one plausible explanation out of many other possibilities.[11] Most importantly, it may be possible that different cognitive processes underlie the SNARC effect for weekdays and numbers, or that SNARC effects for numbers arise from a different underlying prefrontal mechanism (e.g., WM account) than the SNARC effects for weekdays (e.g., verbal-spatial processes). Actually, our results point to multiple (verbal and visuo-spatial) processes underlying the SNARC effect (see Iversen et al., 2006, for similar suggestions in deaf participants), which may differ for numbers and other orders and whose weight might differ depending on stimuli and stimulation. Since the direction of stimulation effects would be identical for a WM account and a linguistic markedness account for numbers, pinpointing this matter requires additional experimental evidence in future studies.

Conceptually, although other explanations are possible, the linguistic markedness correspondence principle can be used to test precise predictions on the theory in the future. For example, the observed effects of reversal should be also observed in other non-numerical ordinal sequences (e.g., Gevers et al., 2003), but not for numerical stimuli in another notation, and future research will bring about corresponding tests of this model. Moreover, although the outlined principle is in general agreement with a polarity correspondence account (Proctor & Cho, 2006), the specifications of linguistic markedness have the advantage of directionality here; i.e., they can transparently explain why and when a positive or negative polarity is assigned.

Moreover, it needs to be acknowledged that number stimuli necessarily bring about a whole series of different (linguistic) features that discriminate them from other stimuli, such as the consistent length of syllables (e.g., one syllable and four characters for all number words *1-5*,

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[11] I would like to thank one anonymous reviewer for pointing out this limitation of our interpretation.

but 2-3 syllables and 6-10 characters for all weekday names in the German language), the frequency with which numbers are used in ubiquitous situations, but also the extraordinary ancient origin of simple counting words (1-5) across different languages (Pagel & Meade, 2018). Future research may investigate in more detail how these potentially isolated linguistic characteristics come together in forming psychologically meaningful spatial associations.

Finally, it is important to note that the current markedness account is not principally incompatible with an augmented WM account, but the linguistic markedness correspondence account can provide a well-defined description of its verbally mediated compartments. For instance, recent amendments to the WM account of the SNARC effect specified the possibility of multiple spatial codes that could even co-exist in parallel (Abrahamse et al., 2016; Ginsburg & Gevers, 2015) and spatial-numerical processing may be biased towards verbal or visual coding mechanisms by context-guided task instructions (Georges, Schiltz, & Hoffmann, 2014). Indeed, in a recent study, both sequence position and numerical magnitude were demonstrated to produce different associations with space during maintenance of a random number sequence (Huber, Klein, Moeller, & Willmes, 2016). These recent results suggest multiple spatial coding mechanisms, highly consistent with our proposed multiple-coding framework involving linguistic processes.

In sum, we believe that the verbal-spatial markedness account may be surprising at first and the account may certainly not be the only possible explanation for the data, but upon a closer look at the literature, it is actually astonishingly consistent with the current results, previous patient studies, with previous postulates of multiple spatial codes, and also with recent results suggesting an augmented WM account allowing for visuospatial and verbal-spatial associations.

Conclusion

By administration of transcranial direct current stimulation (tDCS), we demonstrate that increasing left-hemispheric prefrontal activity can reverse the mental alignment of the weekday sequence, but not the mental number line. Moreover, polarity-dependent stimulation effects are activity-dependent and only observed in order-relevant comparison tasks, but not in font color classification. The observed reversal of SNARC effects with weekday stimuli can also be accounted for by a generalized markedness account for number and sequences, suggesting opposed correspondence between the linguistic markedness of spatial dimension with *large-small* and *before-after* (MARC effect). Alternatively, the observed dissociation could imply different underlying prefrontal mechanisms for SNARC effects obtained in different stimuli. Furthermore, the current data provide a basis for the neurofunctional implementation of markedness correspondence. Switching to consistently MARC-driven spatial representations was related to the enhancement of prefrontal and left-hemispheric processing by anodal tDCS, which is in line with current number processing networks ideas where connectivity between parietal and frontal areas are crucially considered (Klein et al., 2016).

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V. REPLICATING THE MARKEDNESS MODEL

The following chapter is published as:

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Abstract

In societies with left-to-right reading direction, left-side vs. right-side behavioral decisions are faster for relatively small vs. large number magnitudes, and vice versa, a phenomenon termed Spatial-Numerical Associations of Response Codes (SNARC) effect. But also for non-numerical sequential items, SNARC-like effects were observed, suggesting a common neurocognitive mechanism based on the ordinal structures of both numbers and sequences. Modulation of prefrontal networks that are involved in providing spatial associations during cognitive behavior can contribute to elaborate their neuropsychological theoretical foundations. With transcranial direct current stimulation (tDCS) directed to the left prefrontal cortex, we recently showed that i) cathodal tDCS can block the emergence of spatial-numerical associations and that ii) anodal tDCS can reverse spatial associations of sequential order, most likely based on markedness correspondence. Two conceptual replication attempts of the latter reversal of space-order associations are presented in the current sham-controlled experiment, using either weekdays (Monday-Friday) or month names (January-December) as stimuli in the temporal order classification task. In addition, to control for possible influences of notation, number stimuli were presented as written German names (One-Five). We report on a successful modulation of spatial-numerical associations of response codes (SNARC) effects with month stimuli induced by anodal tDCS, but failed to observe the same reversal of SNARC effects for weekday stimuli. The former stimulation effect was orthogonal to the small anodal tDCS effect on written number words, which replicates the dissociation of SNARC effects for numbers vs. non-numerical sequences. Moreover, this result reinforces the hypothesis that the ordinal item and task structure was the source of dissociation (as opposed to verbal presentation). We suggest that the diverging results can be explained by the markedness correspondence account of spatial associations in a multiple coding framework. Left-hemispheric prefrontal excitation from anodal tDCS renders verbal markedness relatively more dominant, but this effect is not absolute. We discuss task contagion, study design, and individual differences in performance measures or tDCS response as possible contributors to systematic variation of the weights of multiple coding parameters for spatial-numerical associations.

Introduction

Spatial associations can accompany seemingly abstract verbal concepts in highly intuitive ways. For instance, most individuals (in Western societies) tend to arrange their calendar schedules in left-to-right and top-to-bottom manner, and they tend to arrange numbers on physical layouts (such as computer keyboards) in a certain spatial direction (e.g., a left-to-right number line). Since the spatial dimension is immediately available in the human experience as the playground for physical action, it appears plausible that also verbal and symbolic-cognitive processes can mentally project onto space. Even more theoretically, it had been argued that sensorimotor interactions with the environment shape the understanding of increasingly abstract concepts such as sequential order or numerical magnitude in various theories of embodied cognition (Barsalou, 1999; Fischer, 2012; Santiago, Román, & Ouellet, 2011), child development and space-number acquisition (Patro, Nuerk, & Cress, 2016), theories of magnitude (Bueti & Walsh, 2009; Walsh, 2003), or grounded cognition of serial order in working memory (Abrahamse, van Dijck, & Fias, 2017; Hurlstone, Hitch, & Baddeley, 2014). The empirical behaviour in experimental studies showcases the fascinating capacity of human agents to simulate and involve the spatial dimension also for concepts that are not directly physically available. But how do spatial associations emerge within the neurocognitive processing loop?

Theoretical Background

A good proxy measure for spatial associations of symbolic information is available in the Spatial-Numerical Association of Response Codes (SNARC) effect, which is evident in cognitive performance during very simple two-choice reaction tasks. When healthy participants classify features of sequential or numerical stimuli by key presses on the left- or right-hand side, the central finding of the SNARC effect consists in relatively faster left-hand over right-hand responses for small over large magnitudes (and initial over posterior sequence positions), and vice versa (Dehaene, Bossini, & Giraux, 1993; Gevers, Reynvoet, & Fias, 2003; van Dijck & Fias, 2011; Wood, Willmes, Nuerk, & Fischer, 2008). Regarding the neurocognitive processes beyond the SNARC effect, several theoretical positions are currently available in the literature and the exact mechanisms may be more multifaceted than initially declared, including the context of mental number representations in long-term memory (Hubbard, Piazza, Pinel, & Dehaene, 2005), polarity correspondence (Proctor & Cho, 2006), working memory and / or spatial attention (Abrahamse, van Dijck, & Fias, 2016; Ginsburg, van Dijck, Previtali, Fias, & Gevers, 2014; van Dijck & Fias, 2011).

Regarding the underlying functional neuroanatomy, studies in numerical cognition have increasingly acknowledged the role of prefrontal-parietal circuits in intracortical recordings (Nieder, 2016; Nieder & Dehaene, 2009) or diffusion-tensor-imaging of white matter connectivity in human cortex (Klein et al., 2016). Thus, prefrontal regions appear to complement the established role of parietal regions in number representation (Dehaene, Piazza, Pinel, & Cohen, 2003) and spatial-numerical associations (Cutini, Scarpa, Scatturin, Dell'Acqua, & Zorzi, 2014). These recent results dovetail with theoretical accounts of the SNARC effects that predict prefrontal involvement in the form of verbal working memory. Using subthreshold neuromodulation of brain activity in prefrontal areas concurrent to respective tasks, studies with transcranial direct current stimulation (tDCS) can investigate and causally bolster these supposed linkages between prefrontal networks and subtle activation of implicit spatial associations of numbers and non-numerical sequences.

Previous Evidence

By testing the effect of left-hemispheric prefrontal tDCS on SNARC effects, we recently observed that inhibitory cathodal tDCS specifically blocked the generation of spatial associations in case of numerical symbols, but the stimulation did not affect performance when visuospatial distraction was directly available in the spatial displacement of stimuli (Schroeder, Pfister, Kunde, Nuerk, & Plewnia, 2016). Precisely, in three sham-controlled cross-over experiments with either 1 mA anodal or cathodal tDCS, healthy participants were asked to classify centrally presented numbers. The task included left-hand or right-hand classifications according to features that were irrelevant to the spatial dimension, namely: number parity or magnitude. During a sham tDCS condition (which elicits comparable sensations, but no changes in brain activity), we obtained relatively faster response times for the congruent combinations of small (large) numbers and left-side (right-side) responding than for the incongruent combinations (e.g., small number and right-side responding), but this SNARC effect for single digits (1-9, without 5) was specifically abolished during another session of concurrent 1 mA cathodal tDCS (target cathode: left PFC, return anode: extracephalic placement on right upper arm). The effect of cathodal tDCS on SNARC effects was reproduced in two different paradigms (parity judgment and magnitude judgment, Schroeder et al., 2016, experiments 1 and 2), but there were no general performance modulations in a control task, and polarity-specificity could be substantiated by a descriptive increase in SNARC effects during a separate experiment with excitatory anodal tDCS (Schroeder et al., 2016, experiment 3).

In a follow-up study, we investigated whether stimulation effects were specific for numbers or whether the polarity-specific tDCS effects would generalize to non-numerical sequence items. Having established a valid sham-control for modulations of spatial associations of numbers in the first study, we now tested different SNARC effects in a more economic parallel design with two groups of participants who performed baseline assessments (without tDCS) immediately followed by 1 mA anodal or cathodal tDCS applied concurrent to a second assessment of task performance (Schroeder et al., 2017). The cardinal number sequence included number symbols 1, 2, 4, and 5, and the ordinal non-numerical sequence included written weekday names Monday, Tuesday, Thursday, and Friday (in German). In separate tasks, participants classified whether a number was smaller/greater than 3, and whether a weekday name came before/after Wednesday, by means of a left-side or right-side button press in congruent and incongruent blocks of trials. In line with the literature (Gevers, Reynvoet, & Fias, 2004), we observed left-to-right oriented SNARC effects during the baseline condition in the order-relevant magnitude judgment tasks for both sets of stimuli, with some variations across participant groups. The tDCS results, however, showed polarity-dependent dissociations of the directional arrangement (spatial associations) of the numerical vs. non-numerical stimuli. Specifically, in this previous study, participants displayed the reverse orientation for a SNARC effect for weekday stimuli (that is, Monday and Tuesday were faster responded to with their right hands, while Thursday and Friday were responded faster to with their left hands) when stimulated with anodal tDCS, but not with cathodal tDCS. For the group stimulated with anodal tDCS, we thus observed a striking reversal of the spatial association of a non-numerical sequence in the same two-choice reaction time testing paradigm, highlighting a dissociation between numerical and non-numerical sequential (weekday) spatial associations (Schroeder et al., 2017).

However, weekdays are only one instance of non-numerical sequential stimuli. To conclude that the diverging stimulation results hold for non-numerical sequential stimuli in general, and not only specifically for weekdays, a conceptual replication with at least one other non-numerical sequence was required.

A Multiple Coding Framework of SNARC-like Effects

Theoretically, the obtained dissociation between SNARC effects for numbers and sequential stimuli (weekdays) was highly relevant and inconsistent with the view that spatial associations might be based on sequential order in general (van Dijck & Fias, 2011; Abrahamse et al., 2016). In a multiple-coding framework, we thus suggested that different mechanisms may all provoke spatial associations. We predicted at least three such codes:

(i) Spatial organisation of numbers on a directed spatial mental number line,

(ii) Sequential organisation of items in verbal working memory

(iii) Markedness congruency.

Disruption or alteration of one dominant code by tDCS may lead to a greater influence of other codes contributing to the SNARC effect. Dependent on task, stimuli and culture, these codes may all facilitate space-number or space-sequence associations in the same direction or sometimes also in opposite directions.

The account that multiple spatial associations may exist was recently put forward for codes (i) and (ii) in a study that showed spatial associations for both the numerical value of a number, but also its sequential position in a randomized working memory sequence (Huber, Klein, Moeller, & Willmes, 2016). Earlier suggestions of different possible routes based on Arabic digits vs. language system were inspired by studies in German deaf signers' spatial-numerical and parity-space associations (e.g., Iversen, Nuerk, Jäger, & Willmes, 2006, Figure 3, corresponding to codes (i) and (iii)). Interestingly, the dominant activation of either routes was suggested to depend on stimulus attributes, e.g., lexical access modes for printed number words or sign language symbols for deaf signers.

As Abrahamse et al. argued (2016, p.6), the result of co-existing space-number and space-sequence associations (Huber et al., 2016) could be also explained by influx from long-term memory for heavily overlearned number magnitude associations from the Western participants' previous life experience. Such magnitude associations may have been pronounced in the Huber study particularly because a within-subject manipulation of number range could have drawn attention to number magnitude information. However, this same mechanism hardly accounts for reversed spatial associations of weekdays during anodal tDCS (Schroeder et al., 2017), because retrieval of weekday spatial associations from long-term memory should also yield a left-to-right oriented SNARC effect in Western participants, but not a reversed one.

The diverging results from tDCS experiments allow to pinpoint theoretical claims in this regard: For example, if tasks were based on the same type of cognitive mechanism, stimulation should affect behavioral results in the same way. More specifically, activity-enhancing anodal PFC stimulation (most likely augmenting working memory; Ruf, Fallgatter, & Plewnia, 2017) should lead to an increase of sequential ordering of information. Vice versa, a decrease should only be observed if the influence of working memory is decreased by cathodal stimulation. Finally, definitely no stimulation should lead to a reversal of the SNARC effect. There is just no concept in the working memory account that predicts a reversal within the same people in a Western culture. In our view, one must assume an additional code responsible for such reversals to account for such data.

Because the third code in our model has seen less attention so far, we elaborate this one in a little bit more detail. The predictions of markedness correspondence specify the emergence of a reversed SNARC effect for *right-before* and *left-after* associations in the weekday task based on the linguistic markedness property of feature polarities (Berch, Foley, Hill, & Ryan, 1999; Iversen, Nuerk, & Willmes, 2004; Iversen et al., 2006; Nuerk, Iversen, & Willmes, 2004; see also: Lakens, 2012; Proctor & Cho, 2006, for conceptually similar theoretical accounts). Generally, this proposed mechanism draws on structural asymmetries in orthogonal verbal concepts such as utilized in SNARC tasks. For example, the *large* polarity can be considered the default endpoint of the magnitude dimension, whereas *small* constitutes its marked opposite category. The definition of marked vs. unmarked polarities can be reflected in default language usage, based on formal marking by a pre- or suffix (e.g., *male* vs. *female, efficient* vs. *inefficient*), distributional marking by usage restriction (e.g., *large* vs. *small;* large being more frequent), or specificity in semantic marking (e.g., *dog* vs. *bitch*, because the dog category can include both male and female dogs; therefore dog being unmarked). It should be noted, however, that the linguistic markedness concept has its theoretical barriers as well within linguistics (Haspelmath, 2006) and markedness-based effects on cognitive processing may be also found in non-linguistic stimuli as well (Proctor & Cho, 2006). Psychologically, the mere presence of marked features alone can lead to longer responses (e.g., H. H. Clark, 1969), as exemplified by lengthened responses to *odd* as compared to *even* (Hines, 1990).

The concepts of structural symmetry and polarity correspondence moreover posit that response selection in classification tasks should be faster when the markedness or polarities of stimulus and response alternatives are matched, which was found to be true for a series of effects (Proctor & Cho, 2006, Proctor & Xiong, 2015). One remarkable example for such correspondence effects is the association between parity status and spatial responding in a direction consistent with the linguistic marking of *left* and *odd* feature polarities (Berch, Foley, Hill, & Ryan, 1999; Nuerk, Iversen, & Willmes, 2004), at least for right-handers (Huber et al., 2014). Based on this concept, interestingly, also the regular *left-small* and *right-large* associations between space and numerical magnitude in the default SNARC effect for numbers can be explained (e.g., Schroeder & Pfister, 2015), because *small* and *left* are considered to be marked. Yet, it is important that the markedness code alone cannot explain all SNARC results. Another coding mechanism must be dominant for left-to-right oriented SNARC effects of non-numerical sequences in order classification tasks, because *after* and *left* polarities are considered to be marked and their combinations should facilitate responding (as in Bächtold, Baumüller, & Brugger., 1998, experiment 2, with before-after judgments of numerical stimuli), which is, however, not the case under usual circumstances and without concurrent tDCS (Gevers et al., 2003, 2004, Schroeder et al., 2017).

The suggestion of an activated dominant route among several possible cognitive processing alternatives can be substantiated by additional previous results. For example, space-number associations were found to be resilient to modulations of spatial response polarity by keyboard eccentricity (Santiago & Lakens, 2015). Another interesting example was found in selective number magnitude associations with “left” vs. “right” vocal responding, and parity associations with “good” vs. “bad” vocal responding, but not vice versa, which constrained the validity of a general polarity account (e.g., exclusively (iii); Leth-Steensen & Citta, 2016; see also Fischer, Moeller, Class, Huber, & Nuerk, 2016, for vocal space-number associations in children). Further advancing this recent result of selective associations, another independent tDCS study showed reduced parity-space (but not magnitude-space) modulations from 1.5 mA cathodal tDCS over the parietal cortex (returned at supraorbital location; Di Rosa et al., 2017). While polarizing entirely different networks than the prefrontal-extracephalic configuration used in our studies, their dissociation results from tDCS converge to the notion that numerical SNARC effects may preserve based on alternative codes (such as (i) or (ii)) during neuromodulation, whereas other effects that depend much more on markedness-based processing (e.g., parity-space associations, (iii)) would deteriorate.

Apparently, flexible switching between spatial association mechanisms by the active anodal tDCS condition in our previous study (Schroeder et al., 2017) would have produced the observed dissociation by rendering the markedness process (iii) most dominant during left-hemispheric prefrontal excitation by anodal tDCS. The presented multiple code framework is also consistent with previous dissociations of spatial associations for numerical and non-numerical sequences in some observations of hemispheric neglect (Zamarian, Egger, & Delazer, 2007; Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006), that showed different (reversed) error patterns for bisections of non-numerical as opposed to numerical sequences.

Moreover, the multiple-coding account dovetailed with orthogonally oriented spatial associations for auditory and verbal presentations of month names in a case of sequence-space synaesthesia (Jarick, Dixon, Stewart, Maxwell, & Smilek, 2009). In sum, we believe the multiple code framework can account for a multitude of SNARC-like effects with and without tDCS stimulation.

Aim of the Study and Hypotheses

In contrast to the stable and replicated effect of cathodal tDCS (Schroeder et al., 2016), the overall effect of anodal tDCS was less clear. For instance, although the reversal of spatial associations of weekday stimuli during anodal tDCS was theoretically meaningful and statistically clear-cut in our previous analysis (Schroeder et al., 2017), results were based on a single tDCS study in parallel design without sham control condition. Thus, in the current study, we set out to challenge the robustness of our previous finding and to test the generalizability to another set of sequential stimuli. Moreover, by testing month stimuli as another non-numerical sequence, we also tested the presented multiple-coding framework which would predict dissociations between number and month stimuli by anodal tDCS, unlike potential unifying accounts.

The full publication of such replication attempts is particularly important in the domain of tDCS to transparently address the contemporary scepticism among researchers and practitioners. Specifically, the conception of the neuromodulation technology is rather reserved and some recent articles have sparked doubt on its potential effects in quantitative review (Horvath, Forte, & Carter, 2015) or have outlined large variability in physiological measures of motor cortex excitability modulations (Strube et al., 2016). Due to publication biases, it is possible that an even larger number of negative results had not been reported on, but underlying reasons remain elusive. For instance, we found in our previous results that the efficacy of modulation depended on the level of cognitive activity induced by a task (Zwissler et al., 2014) or on the timing of stimulation in a first, second, or third session of repeated task performance (Dockery, Hueckel-Weng, Birbaumer, & Plewnia, 2009). Moreover, if a task classification rule incorporated a stimulus dimension not necessarily recruiting the respective (prefrontal) network (Fias, Lauwereyns, & Lammertyn, 2001), stimulation was not effective (Schroeder et al., 2017). These findings line up with the general theoretical premise of state dependency of transcranial brain stimulation (Fertonani & Miniussi, 2016; Silvanto & Pascual-Leone, 2008).

The aim of the current study was therefore threefold. First, following the striking reversal of the weekday sequence spatial associations, we sought to replicate the reversal of a non-numerical ordinal sequence with anodal tDCS in a sham-controlled design. Our primary outcome was defined as differences in the unstandardized regression coefficients capturing the SNARC effects (Fias et al., 1996; see Data Treatment in the next section) between sham and anodal tDCS condition, which should resemble the observed difference between baseline and anodal tDCS in the same parameter in our previous study (Schroeder et al., 2017, p. 43, paired *t*-test on unstandardized regression coefficients). We decided to change the experimental design in order to establish a valid sham-control that elicits comparable sensations and thus to control for any motivation-related changes (although it has to be noted that we could not observe significantly different sensations between anodal and cathodal tDCS before). In the present study, participants were tested on separate days with a minimum wash-out period of 48 h to circumvent any possible long-term neuroplastic (after-) effects of the stimulation. Second, to explore whether the observed directionality switching was directed by the verbal presentation format of weekday stimuli (which is somewhat related to the theoretical markedness correspondence account), we now also presented single-digits in their verbal, i.e. written, form (i.e., German word “eins” for “1”, and so on). Finally, we included another non-numerical sequence task with month names to examine the generalizability of our original results. With the same month names used in the new task (albeit in Dutch language), previous experiments demonstrated a spatial mapping from left-to-right akin to the SNARC effect for numbers (Gevers et al., 2003). Thus, the third experiment on month names was specifically designed to conceptually replicate our finding with another non-numerical sequence and to test the predictions of the presented multiple-coding account. Previously, we had suggested that the dissociative tDCS effect in weekdays was driven by the markedness features of their ordinal item structure (i.e., as weekdays constitute a non-numerical sequence). If these conclusions hold, similar effects should be obtained with other non-numerical sequences as well, i.e., also with month names. We hypothesized that 1 mA anodal tDCS would reverse the spatial associations of both weekdays and month names, but that stimulation would rather yield a small enhancement in opposite direction of regular left-to-right SNARC effects for numbers.

Methods

Participants

Based on a-priori power calculation, healthy volunteers (N=24, mean age: 21.8 y, range: 18-26 y, 5 males) were recruited from the general and student population. All participants attended a sham and a stimulation session with 1 mA anodal tDCS, in counterbalanced order (mean inter-session interval: 5.1 d, range: 2-9 d). This study was carried out in accordance with the recommendations of University Hospital Tuebingen Ethical Commision with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the University Hospital Tuebingen Ethical Commision (Number of approval: 701/2015BO2). Eligibility for the study was assessed by self-reports collected prior to the first experimental session. Right-handed volunteers (according to the questionnaire by Oldfield, 1971) were eligible for participation if they were native German speakers without neurological or psychiatric impairments and if they fulfilled tDCS safety requirements (no metallic implants, cardiac pacemaker, pregnancy, medication, or use of recreational drugs). Participation was compensated with money or student credits. The experiments were performed in Tübingen between June-November 2016.

Anodal transcranial Direct Current Stimulation (tDCS)

The study followed a sham-controlled cross-over design. Transcranial direct current stimulation (tDCS) was administered in either active anodal or sham configuration on separate testing days in counterbalanced order across all participants. Direct current was generated by a CE-certified stimulator (neuroConn GmbH, Illmenau, Germany). Sham stimulation was realized by fading out the direct current after only 40 seconds of stimulation, yet participants started the first task in both conditions always after 5 minutes following the tDCS fade-in. In contrast, active anodal tDCS was administered continuously at 1 mA intensity for a total duration of 25 minutes (‘online’ to the task). In contrast to offline tDCS effects (i.e., behavioral effects are assessed after the termination of stimulation), online tDCS effects can be linked directly to resting membrane threshold changes in cortical excitability as opposed to longer-lasting neuroplastic responses. A minimum wash-out period of 48 h was imposed between sessions. The target anode (5 × 7 cm) was fixed over F3, the return cathode (5 × 7 cm) was fixed over the right upper arm. Impedances were below 10 kΩ. Participants rated adverse effects (Brunoni et al., 2011) after completion of the stimulation protocol.

This specific anodal tDCS protocol was motivated by our previous observation that the reversal of SNARC effects for non-numerical ordinal words was induced by 1 mA anodal, but not by 1 mA cathodal tDCS over the left PFC with extracephalic return electrode. In contrast to the previous study, the cross-over study design was implemented here to establish a valid sham control.

Tasks and Stimuli

Participants completed all three experimental tasks during both sessions either following a 4:20 min stimulation-free rest phase in the sham session or concurrent to the anodal tDCS following 5 minutes of at-rest stimulation. All tasks were completed online in the active anodal tDCS session.

Since we observed significant modulations of spatial associations exclusively during the most active tasks with explicit comparison instructions (Schroeder et al., 2017), the testing sessions in this study included only the order-relevant magnitude comparisons in all three stimulus set variants.

The tasks closely followed previous order-relevant implementations (Gevers et al., 2003; Gevers, Reynvoet, & Fias, 2004). In all three tasks, participants had to repeatedly classify stimuli by following a response-mapping rule and by operating two keyboard buttons with their right-hand and left-hand index finger (covert ‘s’ and ‘l’ on a QWERTZ-keyboard). Stimuli included a numerical sequence in German verbal notation (‘eins’, ‘zwei’, ‘vier’, ‘fünf’; English translation: ‘one’, ‘two’, ‘four’, ‘five’, respectively), the weekday sequence (‘Montag’, ‘Dienstag’, ‘Donnerstag’, ‘Freitag’; English translation: ‘Monday’, ‘Tuesday’, ‘Thursday’, ‘Friday’, respectively), and the month series (‘Januar’, ‘Februar’, ‘März’, ‘April’, ‘September’, ‘Oktober’, ‘November’, ‘Dezember’; English translation: ‘January’, ‘February’, ‘March’, ‘April’, ‘September’, ‘October’, ‘November’, ‘December’, respectively). The task instruction was to classify whether a number was smaller or larger than ‘drei’ (three), whether a weekday was before or after ‘Mittwoch’ (Wednesday), and whether a month was before or after ‘Juli’ (July).

Response assignments to the classification decisions (e.g., right = large or right = before) were alternated within the tasks in counterbalanced order across participants. Thus, participants always solved two blocks with “compatible” and “incompatible” response assignments (e.g., a left-hand assignment to small numbers / early positions would be considered to be compatible following the standard results of relatively faster responses in this block as compared to the opposite right-hand assignment).

All single tasks were preceded by a brief training block (16 trials) and an error count emphasized correct responding. The experimental procedure comprised 40 target repetitions in each task, with 300ms fixation hash (#), 2s target presentation (or until response), and 300ms error feedback (German words ‘Fehler’ [error] or ‘Bitte schneller antworten’ [please respond faster]) or a blank inter-trial interval. Figure 1 displays a schematic of a trial. Note that consequently, because the month task included twice as many stimuli as both other tasks, experimental blocks took longer for this task. There was the possibility to take self-paced breaks between tasks and blocks.

The order of the three experimental tasks (number words, weekdays, months) was balanced across participants in a Latin Square Design, resulting in three conditions (WMN, MNW, NWM). Half of all participants started each task with the incongruent response mapping.

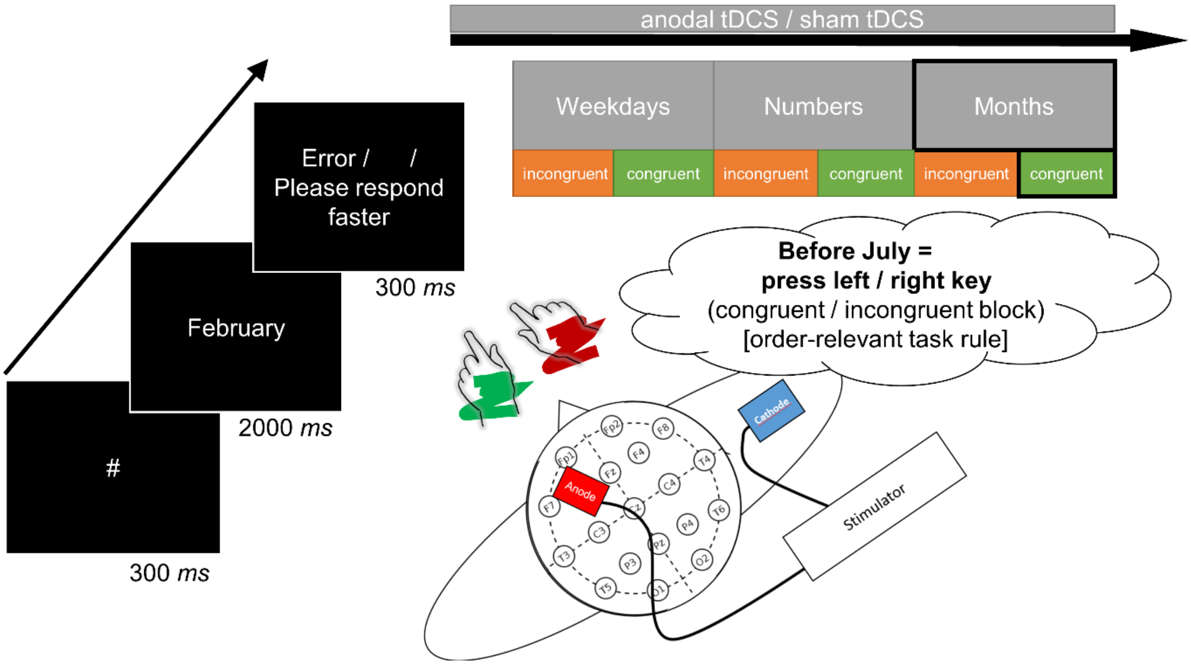

__Figure 1.__ The structure of a single trial as exemplified by judgment of the month name ‘February’ (left-side). The correct response in the respective incongruent or congruent task block was determined by the order-relevant task rule based on sequential position in the month sequence (before/after). In this case, the congruent block would afford a left-hand response for classification of “earlier” whereas the incongruent block would afford a right-hand response for classification of “earlier”. Congruent and incongruent blocks (in counterbalanced order

across participants) were presented sequentially for all three sets of stimuli (upper-side). The target anode was placed over F3 and the return cathode over the right upper arm to avoid polarization of another brain area (lower-side). All tasks were initiated and terminated concurrent to anodal tDCS in the verum session (online stimulation).

A Priori Power Calculation

A power calculation was performed to estimate sample size based on the previously observed reversal effect (Schroeder et al., 2017) using the program MorePower 601 (Campbell & Thompson, 2012). In our previous experiment, the observed effect size of anodal tDCS on weekday stimuli in the within-group comparison was d = 0.95. Assuming this effect size, the sample size for a replication (at $\alpha = .05$ and a priori power of $1 - ß = .99$) was calculated to require N = 24 participants (dependent samples *t*-test of unstandardized regression coefficients).

Data Treatment and Statistical Analyses

Only correct trials were considered for analyses of response times (RTs, 95.4 %). Additional post-error trials (3.6 %, to reject systematic RT variation in post-error slowing; Notebaert et al., 2009) as well as stimulus-repetition trials (17.9 %) were rejected from analyses (SNARC effects are reduced in stimulus repetition trials due to episodic memory; Pfister, Schroeder, & Kunde, 2013; Tan & Dixon, 2011). Next, response latencies that deviated more than 3.0 SD from the respective cell mean (computed separately for each target-response combination) were rejected (1.0 %). These criteria left 73.0 % of all trials available for subsequent analysis. The rationale of this data treatment was to reject trials that included systematic RT variation due to other known cognitive effects. Following a reviewer's comment, and acknowledging the fact that different analysis strategies could in principle yield different outcomes (Silberzahn et al., 2017), we also demonstrate in the supplementary materials (SA1) that the main results did not change substantially in an alternative analysis based on correct mean RT without further trial rejection.

We used unstandardized regression coefficient analyses[12] to extract the relative advantage of right-hand over left-hand responses with increasing numerical magnitude or sequence position, as it is usually implemented to quantify SNARC effects (Fias, Brysbaert, Geypens, & D'Ydewalle, 1996; Lorch & Myers, 1990) for numerical and non-numerical sequence stimuli (Gevers et al., 2003, 2004). The computation involves several steps: First, RT right-hand – left-hand differences are determined separately for each participant, stimulation condition, task set, and target stimulus combination from median RTs. Next, RT hand differences are predicted by numerical magnitude (1-5) or sequence position bins (numerically coded as 1-5). A negative regression coefficient (tested with one sample t-tests against zero) indicates the typical behavioral pattern of SNARC effects, that is: Participants give relatively faster left-hand than right-hand responses to small / early stimuli and participants give relatively faster right-hand than left-hand responses to large / late stimuli. The resulting regression coefficients were submitted to separate paired-samples t-tests for each task (number, weekdays, months) to outline the effect of anodal tDCS.

Results

Adverse Sensations of tDCS

Adverse effect ratings for both sham and active anodal tDCS are summarized in Table 5.1. Participants reported slightly more "tingling elsewhere" ($t(23) = 2.01$, $p = .057$), but all values were relatively close to the lower boundary of the self-report scale (see Table 5.1).

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[12] In further explorative analyses, we also modeled SNARC effects in terms of standardized regression weights and categorical compatibility effects. Results from these procedures essentially reproduced the reported results: There were significant differences between SNARC effects for month stimuli during sham vs. anodal tDCS, but not for number and weekday stimuli. For full transparency, all values and tests are reported in the Supplementary Tables ST1 and ST2. A table reporting RTs and error rates for all target-response combinations is provided in ST3.

Table 5.1. TDCS adverse effects. *Adverse sensations were assessed on a 5-point Likert-like scale after each session (1=none, 5=extensive). Ratings following anodal tDCS and sham tDCS were subjected to paired t-tests.*

	Anodal tDCS	Sham tDCS	
Adverse Sensation	*M (SD)*	*M (SD)*	*p*
Tingling at the site of the electrode	2.00 (0.78)	2.17 (0.87)	.26
Tingling elsewhere	1.29 (0.55)	1.08 (0.28)	.06
Exhaustion	1.61 (1.03)	1.87 (0.97)	.31
Itching	1.65 (0.64)	1.65 (0.88)	.99
Headache	1.22 (0.67)	1.26 (0.62)	.81
Nausea	1.00 (-)	1.00 (-)	-

Stimulation Effects

One-to-Five Number Words

SNARC effects with negative-signed coefficients were significantly different from zero for the performance during anodal tDCS (b = −6.74 ms/bin; *t*(23) = −2.28, *p* = .032), but not during the sham tDCS condition (b = −4.16 ms/bin; *t*(23) = −0.88, *p* = .386). The difference in SNARC effects was not significant (*t*(23) = −0.53, *p* = .533).

Monday-to-Friday Sequence Words

SNARC effects with negative-signed coefficients tended to be different from zero for the performance during anodal tDCS (b = −8.77 ms/bin; *t*(23) = −1.99, *p* = .057), but not during the sham tDCS condition (b = −3.09 ms/bin; *t*(23) = −0.75, *p* = .462). The difference in SNARC effects was not significant (*t*(23) = −0.75, *p* = .460).

January-to-December Sequence Words

A reversed / abolished SNARC effect with positive-signed coefficient was not significant during the anodal tDCS condition (b = +4.22 ms/bin; *t*(23) = 1.40, *p* = .175). The SNARC effect for the same month stimuli was negative-signed during the sham condition (b = −7.45 ms/bin;

t(23) = −2.00, *p* = .057). In direct comparison of the two stimulation conditions, the effect of anodal tDCS was significant (*t*(23) = 2.68, *p* = .013, *d* = 0.55).

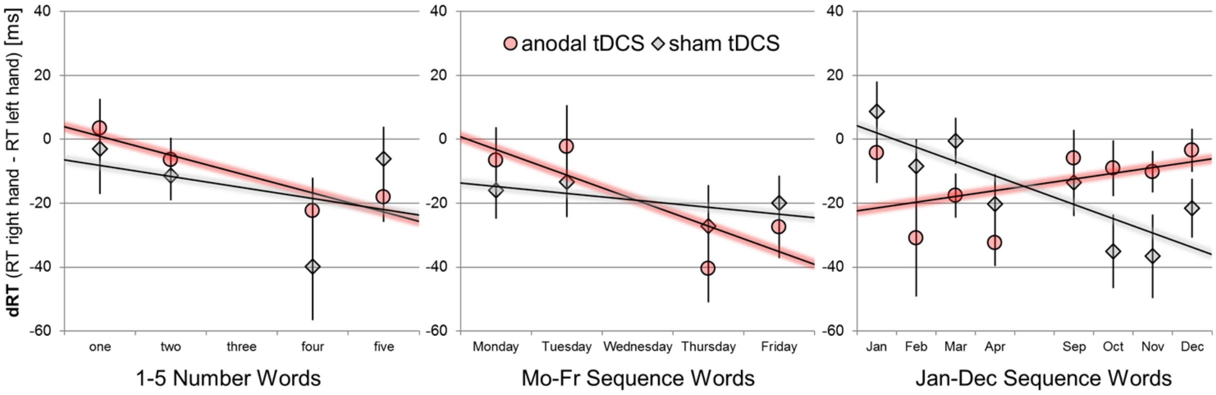

Figure 5.1. *Mean response hand differences (dRT = RT right-hand – RT left-hand) as a function of sequence position / numerical magnitude for the number stimuli, weekday stimuli, and month names. Performance during sham tDCS is indicated by gray diamonds, performance during anodal tDCS by red circles. Error bars indicate standard errors of the mean. Negative-signed linear regression lines indicate regular SNARC-like spatial associations. Note that only four predictor variables for magnitude / order position were used in all statistical analyses and thus consecutive month names were aggregated (e.g., Jan+Feb = position 1), unlike shown in the graph.*

Post-hoc Power Analysis

Overall, the results of the current study corroborate our hypotheses. With number words as target stimuli in a magnitude comparison task, we observed a descriptive increase in the regular left-to-right SNARC effect with anodal tDCS, but, in line with our previous studies, this presumable modulation effect was relatively small and not substantiated by statistically significant differences (Schroeder et al., 2016, 2017). With weekday stimuli, we could not detect the previously observed reversal of spatial associations in the sham-controlled design, and the direction of a possible effect was descriptively reversed. With month stimuli, we observed a significant effect of anodal tDCS, conceptually replicating the recent result of anodal tDCS on non-numerical spatial associations (Schroeder et al., 2017). However, the effect size of this modulation was reduced to approximately half of the effect size in the original observation (within-subject test of reversal relative to baseline performance: d = 0.95). For the paired samples t-test and the effect size observed here (d = 0.55), the current sample size of N = 24 resulted in a post-hoc power of 1 – ß = .73.

Replication of Dissociation between Numerical and Non-Numerical Sequence

An important observation of our previous study (Schroeder et al., 2017) was the dissociation between the numerical and non-numerical sequence by anodal tDCS. This observation is in conflict with the proposal of a unified WM account of the SNARC effect (Abrahamse, van Dijck, & Fias, 2016; van Dijck & Fias, 2011). Thus, we particularly tested the dissociation between the spatial associations of number and month sequences by anodal tDCS in the current data. The resulting clear interaction ($F(1,23) = 9.19$, $p = .006$, $\eta_p^2 = 0.29$) was in line with our previous observation (Schroeder et al., 2017). In more detail, the interaction effect was substantiated by a significant difference in SNARC effects for number and month stimuli during anodal tDCS ($F(1,23) = 5.81$, $p = .024$, $\eta_p^2 = 0.20$), due to a negative coefficient for numbers and a positive one for months (see above), but the difference was not significant during sham tDCS ($F(1,23) = 0.50$, $p = .486$).

Joining Data from Previous Studies

To address the shortcoming of reduced power due to smaller effects than anticipated, we decided to resubmit the previously obtained regression coefficients from earlier data sets to joint analyses. The respective experiments and their main findings are fully reported in Schroeder et al. (2016; S16) and Schroeder et al. (2017; S17). Here, we re-analysed only those datasets which were collected during the exact same anodal tDCS configuration and the respective sham or baseline control conditions.

Effect of Anodal tDCS on Spatial Associations of Number Stimuli

Data from three experiments yielded a total N = 72 (drawn from the current study, from S16, and S17). Regression coefficient analyses were run as described above and pseudo magnitude-bins (1, 2, 4, and 5) were assigned for the larger number range (1-9, S16). Coefficients were submitted to a mixed ANOVA with the repeated-measures factor *tDCS* (anodal vs. sham / baseline stimulation) and with the between-subjects factor *experiment* [1-5 (S17), eins-fünf (current study), 1-9 (S16)].

The main effect of *tDCS* was barely significant in this analysis ($F(1,69) = 2.82$, $p = .098$, $\eta_p^2 = 0.04$). There was no interaction with the between-subjects factor *experiment* ($F(1,67) = 0.24$, $p = .784$), and SNARC coefficients tended to be larger for the extended number range (1-9) in S16, possibly due to the assignment to pseudo magnitude-bins when extracting coefficients, due to individual differences, or due to the nature of the parity judgment task (see Figure 5.2; $F(1,69) = 2.66$, $p = .077$, $\eta_p^2 = 0.07$). Interestingly, this pattern also resembled the steeper SNARC slopes in the present experiment for the month series during sham tDCS, comprising an extended range of stimuli as compared to the employed weekday and number series.

For a directed paired-samples *t*-test (one-tailed) with data from all participants of the three studies, the effect of anodal tDCS was significant ($t(72) = 1.70$, $p = .047$), but the standardized effect size estimate was small ($d = 0.21$). Even for this least conservative test, the post-hoc power to detect the stimulation effect in the aggregated sample was insufficient ($1 – ß = .53$).

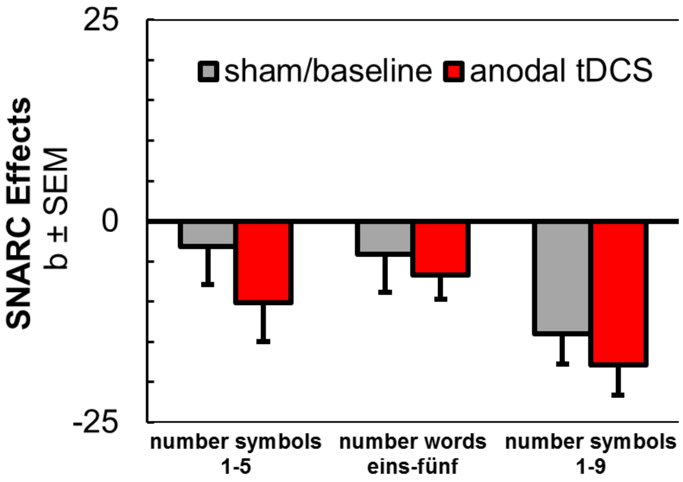

Figure 5.2. *Aggregated results from anodal tDCS during SNARC tasks with number symbols 1-5 (Schroeder, Nuerk, & Plewnia, 2017), number words (current study), and number symbols 1-9 (Schroeder, Pfister, Kunde, Nuerk, & Plewnia, 2016).*

Effect of Anodal tDCS on the Spatial Associations of Non-Numerical Sequences

Data from three experiments (drawn from the current two experiments and from Schroeder et al., 2017) yielded a total N = 72.[13] The main effect of *tDCS* was significant ($F(1,69) = 7.18$, $p = .009$, $\eta_p^2 = 0.09$). However, the stimulation effect was further qualified by a significant two-way interaction with the between-subjects factor *experiment*, which statistically confirmed the different results for weekday stimuli in the two studies ($F(2,69) = 5.33$, $p = .007$, $\eta_p^2 = 0.13$). Independent samples *t*-tests showed that SNARC effects for weekday sequence words tended to be somewhat larger during sham tDCS in our previous study (b = -14.84 ms/bin) than in the current study (b = -3.09 ms/bin; $t(42.04) = 1.68$, $p = .101$), but not larger than in the month sequence (b = -7.45 ms/bin; $t(39.74) = 1.09$, $p = .282$). The reversed SNARC effect during anodal tDCS in the previous study (b = +8.30 ms/bin) was significantly different from the result collected during stimulation in the current experiment (b = -8.77 ms/bin; $t(46) = 2.83$, $p = .007$), but not different from the reversed / abolished SNARC effect for month stimuli during anodal tDCS (b = +4.22 ms/bin, $t(26) = 0.80$, $p = .429$). Thus, the results corroborate a potential effect of the most prevailing experimental differences between the two studies, i.e., the study design (parallel vs. cross-over design), the presence of different control tasks (colour judgment tasks or testing of month stimuli with more sequential positions), but also the individual differences in the inclination of SNARC effects already during the sham / baseline session.

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[13] Repeated testing of the same participants with different sequences were treated as separate groups of participants in this analysis. Because we did not observe substantial construct validity between spatial associations in different sequences in a larger study (Chapter III), we believe that in this case the benefits of easier presentation would outweigh the consequence of overestimated error variance.

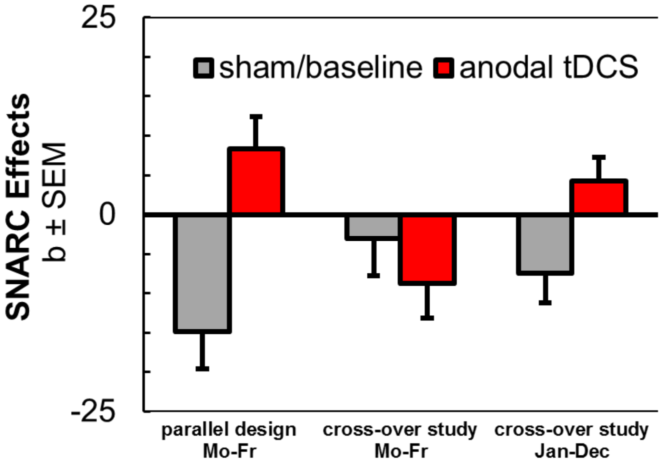

Figure 5.3. *Aggregated results from anodal tDCS during non-numerical SNARC-like tasks with weekday stimuli in parallel design (Schroeder et al., 2017), in cross-over design (current study), and with month stimuli in cross-over design (current study).*

Discussion

The purpose of the current experiments was to extend on the possibility of switching between spatial associations by concurrent administration of prefrontal anodal tDCS. Three series of stimuli were used in simple classification tasks that usually elicit spatial associations in the SNARC effects for number symbols (German words eins-fünf), weekdays (Montag-Freitag) and month names (Januar-Dezember). In line with our predictions, we observed a small and non-significant increase[14] in spatial-numerical associations for number symbols from anodal tDCS. Including more empirical data from our previous experiments (Schroeder et al., 2016, 2017), we here report for the first time that anodal tDCS can significantly enhance spatial-numerical associations (e.g., the regular SNARC effect) in left-to-right direction, but the effect is only evident in the least conservative test and with small effect size (d = 0.21). This systematic effect was always descriptively available in our earlier studies and a modulating effect of notation or number range appeared negligible in our analysis (see Figure 5.2).

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[14] Alternatively, this effect may also reflect an induction of regular SNARC effects for numbers by anodal tDCS, since the SNARC effect for numbers was not significantly different from zero during the sham condition (but see also Supplementary Analysis 2 for Bayes Factors). We wish to thank Reviewer 3 for pointing to this possibility.

Most importantly, however, we could partially replicate our previous observation of a reversal of spatial associations of a non-numerical sequence by anodal tDCS (Schroeder et al., 2017). In line with our original hypotheses, tDCS successfully modulated spatial associations of a non-numerical sequence in another series of stimuli (month sequence). During anodal stimulation, participants produced relatively faster responses with their left hands to months in the second half of the year, but they showed relatively faster responses with their right hands to months in the first half of the year, which was opposed to their behavioral performance during sham tDCS. With these stimuli, we reproduced the tDCS dissociation between spatial associations of a numerical and a non-numerical sequence, further challenging potentially unifying theoretical accounts. However, the conceptual replication of the reversal of the weekday sequence by anodal tDCS was not successful in the sham-controlled cross-over design and descriptively even opposite to our previous result (see Figure 5.3).

It should be noted that the positively signed SNARC coefficient for month stimuli during anodal tDCS was not significantly different from zero. Thus, the coefficient test could not secure the implication that this spatial association was reversed and it remains possible that anodal tDCS instead abolished the SNARC effect in the current study.

Three reasons could potentially account for the diverging results of weekdays in this study as compared to the reversal effects for weekdays in our previous study and month in the current study: (1) The stimulation effect is not true (Type I error of two observed reversals), (2) the second experiment of our current study was underpowered (Type II error of current result), or (3) other systematic reasons rendered the tDCS procedure ineffective in the case of weekday stimuli in the current study. We discuss each of these issues separately.

Type I Error: False Positives in Previous Results?

In recent years, it has come to public awareness that Type I error rates (false positives) are particularly pronounced in psychological research under the umbrella of reproducibility crisis (Open Science Collaboration, 2015), supported by publication biases, questionable research practices, and other factors that lead researchers to publish and report only on successful (“significant”) manipulations in their studies (Nosek et al., 2015). Relative to the impact of the current research topic, and also the controversy around tDCS effects on cognition, it seems reasonable to assume that some publications on the efficacy of tDCS could include Type I errors. False positives rates can inflate with inclusion of more measurement factors or tasks, which is particularly critical when only positive procedures are reported on.

Over the current set of studies, we believe that the pattern of results and especially the successful partial replication in the month sequence does not point towards a false positive in the original results (Schroeder et al., 2017). Actually, in series of experiments, the probability that one replication would not work is statistically plausible and hinges on the power of the test. For a simplified example, given a power of 73 % (i.e., the power to detect the effect of anodal tDCS on the month series in the current experiment), the chance for 3 out of 3 experiments to turn positive is relatively low (0.733 = 38 %). In contrast, the probability to obtain 2 out of 3 significant results (i.e., as it was the case here) would be even slightly higher (43 %), although this example assumes the case that the effect is actually true (see Francis, 2012 for discussion of this too-good-to-be-true approach).

Type II Error: Lack of Power for Conceptual Replication in Current Results?

Following up on the observed power of .73 (related to the reversal of spatial associations for the month sequence) it could be plausible that a tDCS effect was simply not observed in the weekday sequence due to a Type II error. Actually, running low-powered studies has a long tradition in clinical psychology and estimates were below 50% chance to detect a medium-sized effect (i.e., d = .5 or larger), but power was acknowledged only in most seldom cases (Sedlmeier & Gigerenzer, 1989). Importantly, the failure to detect an effect in null hypothesis significance testing does not provide evidence for absence of the effect in the first place.

On this occasion, it is revealing to notice that effect sizes diverged tremendously between studies. A priori sample size estimation initially suggested sufficient power with the included sample size, but the post-hoc power analysis deviated from the a priori sample size estimation due to the diminished effect size. Although it is acknowledged that initial discoveries of psychological effects may report larger effect sizes than replications (with a standardized mean difference of .21, Open Science Collaboration, 2015, p. 5), the reduction in effect size in the present case may have been also supported by other systematic differences between studies.

Systematic Reasons for Partial Failure of Replication

However, while power issues could in principle account for our results pattern, there are also reasonable alternative accounts suggesting that the obtained results are due to systematic underlying differences between our previous study and the current results. For example, the facts that other stimuli and control tasks were tested in different study designs (i.e., parallel vs. cross-over design) could play into the obtained results. Although all stimuli comprised sequence items, the month series includes a larger number of items than both number and weekday sequences, which could have influenced also the mapping of the relatively smaller item sets onto spatial templates. Actually, our joined analysis showed larger SNARC effects for extended number ranges, which dovetails with the differences in SNARC effects for different stimuli of the present study during the sham condition (showing the largest effect in the extended month range).

Next, since the markedness correspondence account attests different possible strategies to produce spatial associations from verbal markedness, but also from other mechanisms such as visuospatial simulation or serial-order processing, it may be possible that detachment from a previous task set (e.g., classification of month stimuli) to perform on a new, yet comparable task (e.g., classification of weekday stimuli) involved a subtle switch in the spatial association strategy used to allow for more effective task set representations. Thus, we speculate that the presence of different tasks in the same session could lead to contagion to another spatial association mechanism in changing item sets.

Furthermore, the possibility of individual differences could be relevant for both the modulation with tDCS and also for the effect inclined by our tasks. Regarding the SNARC effect, variation is remarkable in general and only ~70 % of the general population present regular spatial-numerical associations (Wood, Nuerk, & Willmes, 2006). We also noted that different inclinations of SNARC effects for weekdays during sham / baseline were present in the current study and the previous study, which could suggest a lack of modulation effects due to the lack of sham effects in the present sample (see Figure 5.3). Specifically, the SNARC effect in the sham tDCS condition trended towards being negative only in the month order classification task, but not in the numerical magnitude or weekday order classification tasks. Moreover, there is also noticeable variability in the responses to tDCS, already when motor cortex stimulations and physiological measurements are performed (Strube et al., 2016; Wiethoff, Hamada, & Rothwell, 2014), which could result in different effectivities as also captured by the effect size of the tDCS modulation in the month task.

In any case, all presented possibilities remain post-hoc hypotheses generated from the data and thus they need to be submitted to respective confirmatory testing in the future, since they also raise potential relevance to the systematic investigation of tDCS effects in general.

Towards an Extended Multiple-Coding Framework of Space-Metric Associations

We assume that spatial associations can result from different mechanisms and we propose several verbal and non-verbal simulation processes (see Figure 5.4). In this multiple-coding framework, anodal tDCS of left-hemispheric prefrontal circuits could facilitate the processing of verbal markedness, render correspondence effects between early-right and late-left classifications task-relevant, and thus result in the observed reversal of SNARC effects for the ordinal sequence (Schroeder et al., 2017). For the numerical sequence, the same mechanism would enhance correspondence effects between large-right and small-left task-relevant and thus result in the regular left-right direction of the SNARC effect (Schroeder & Pfister, 2015). However, in this theoretical model, it is possible that also other verbally mediated strategies (such as working memory mechanisms of sequential order) or visuospatial simulations produce spatial associations that are resistant to a certain stimulation, especially considering the possibilities of individual differences or task contagion. Such a multiple-coding framework also agrees with the inconsistent outcomes for non-numerical stimuli, as it was actually observed in the weekday stimuli in the present study.

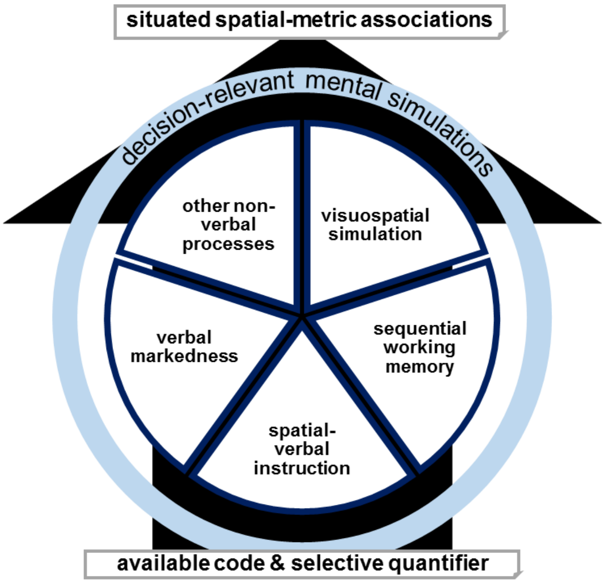

Figure 5.4. *The availability and selectivity of a quantifier decides for the dominant involvement or combination of verbal markedness, spatial-verbal instruction, sequential working memory, visuospatial simulation, or other non-verbal processes in determining situated spatial-metric associations. Decision-relevant mental simulations in either form result in behavioral effects. Targeted tDCS (or another manipulation) can modulate either code and thereby also influence the dominance of the remaining simulations. For example, targeted activating tDCS augments*

a specific code or codes dependent on the topography of stimulation and the corresponding network.

For a conceptualization of the neurocognitive processes involved in mentally aligning (properties of) objects with physical space, the results collected here basically reiterate the connotations drawn from the previous dissociation of spatial associations of number and sequence (Schroeder et al., 2017). Further support for the different coding strategies comes also from a recent dissociation of parity-space and number-space associations during tDCS over left and right parietal cortices, where only the former were modulated by cathodal tDCS (Di Rosa et al., 2017). Complementary to these results, the current study underscores that the spatial alignments of both numerical and non-numerical sequences are guided by prefrontal activity, albeit with orthogonal responses to tDCS polarities. Furthermore, the data highlight a critical dissociation between numbers and months, which opposes a unified theoretical account and provokes a multiple-coding framework.

The systematic reasons outlined above can be easily arranged along the proposed model by emphasizing the flexible and situated nature of a spatial association multiple coding framework. For example, findings from a principle component analysis showed that the SNARC effects in the parity judgment and magnitude classification tasks were placed in two separate components, suggesting unrelated spatial coding mechanisms depending on the task (van Dijck, Gevers, Lafosse, & Fias, 2012). Moreover, the spatial coding processes underlying spatial associations of numerical magnitudes were found to change depending on task instructions (Georges, Schiltz, & Hoffmann, 2015). In general, considerable heterogeneity across stimulus, task and participant attributes was documented in a meta-analysis (Wood, Willmes, Nuerk, & Fischer, 2008). More, the replicated dissociation between SNARC effects for number and order information is in line with the taxonomy proposed to disentangle the multitude of mechanisms involved in spatial associations (Cipora, Hohol, et al., 2015; Cipora, Patro, et al., 2015; Patro et al., 2014). Interestingly, in right-to-left reading native Hebrew participants, reversed SNARC effects akin to the month-performance during anodal tDCS were previously obtained for sequential stimuli (but not when the magnitude dimension was emphasized in the task instruction; Shaki & Gevers, 2011). However, also in native Hebrew participants, a regular left-to-right SNARC effect for numbers was finally observed when parity-space response mappings were tested on separate days (Zohar-Shai, Tzelgov, Karni, & Rubinsten, 2017). At large, this result could imply mutual interactions between markedness-based codes (parity-space association) and the active coding strategy for spatial-metric associations. Moreover, the findings by Zohar-Shai et al. (2017) also reiterate the crucial influence of seemingly trivial task design parameters, i.e., counterbalanced key assignments.

By drawing on the linguistic structure of the sequence comparison task, a relatively plausible (and testable) account was proposed by first assuming that multiple mechanisms can be dominant when generating spatial association for any concept. Loosely, this proposal also reflects the earliest models of numerical magnitude representations (e.g., the triple-code model) that assumed a verbal, visual spatial, and analogue representation (Dehaene, Piazza, Pinel, & Cohen, 2003) and also by the traditional dual-code assumption for mental representations in general (Paivio, 1986). In greater detail, the markedness property describes the formal requirements for identification of the default member of verbal opposite pair (Nuerk et al., 2004; Proctor & Cho, 2006). A general compatibility effect then consists in better task performance in cases where either default or non-default members are present in both dimensions of a task.

Direct Current Polarity Asymmetry of tDCS Effects in the Cognitive Domain

The combined results also demonstrate the asymmetry of polarity-specific tDCS effects in the cognitive domain (Jacobson, Koslowsky, & Lavidor, 2012): For numerical stimuli, we found that the effect size for anodal stimulation was low (d = 0.2), and the effect turned significant only for the least conservative test across all available data from N = 72 healthy participants. Here it should be noted that the three included studies used different number ranges and classification tasks (1-9 in parity judgment or 1-5 in magnitude comparison tasks) and number notations (1-5 or ‘eins’-‘fünf’, magnitude comparison tasks). The mechanisms beyond producing spatial associations for these different number stimuli and tasks are likely to differ (Georges, Hoffmann, & Schiltz, 2017). The results of our joint analysis can only suggest that the systematic interactions of these range- and task-effects are (at best) only marginally pronounced in modulating the effect of anodal tDCS on spatial-numerical associations and they are thus less decisive given the statistically non-significant interaction effects. By analysing data drawn from three experiments, the current result shows that anodal tDCS of the left prefrontal cortex can increase the inclination of SNARC effects for numerical stimuli, but the effect size of this stimulation effect is small.

In contrast, the effect of cathodal tDCS on numerical stimuli was relatively effective in previous observations (d = 0.5; Schroeder et al., 2016). This pattern of results is remarkably opposite to the typical observation that cathodal tDCS was less effective for modulating cognition

(Jacobson et al., 2012; Pirulli, Fertonani, & Miniussi, 2014). Furthermore, DC polarity-specific effects appeared rather linear and symmetric at physiological level in motor cortex studies showing excitability changes (Nitsche & Paulus, 2000; Priori, Berardelli, Rona, Accornero, & Manfredi, 1998) and also in in vitro studies (e.g., Bikson et al., 2004). The observed patterns suggest that polarity asymmetries are more likely in cognitive tasks and that they can also render the cathodal stimulation more effective than the anodal stimulation (Schroeder & Plewnia, 2016). However, the sources of polarity asymmetry and other non-linear effects of tDCS such as current intensity and individual differences (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013; Benwell, Learmonth, Miniussi, Harvey, & Thut, 2015) are currently unknown and must be scrutinized systematically in future research. Finally, the results nicely illustrate that there is no binary outcome of tDCS, but that rather different mechanisms are available for producing spatial associations which makes the stimulation more efficacious in certain cases.

Limitations and Future Directions

The conclusions of this study must be accompanied by some caveats as some further limitations exist. First, given the non-significant positive coefficient in the month sequence during anodal tDCS, it is not clear whether anodal tDCS reverses or abolishes spatial associations of non-numerical ordinal sequences generally. We believe that a reversal better describes the mechanism due to the markedness correspondence account, the significantly positive coefficient in our previous study, the positive sign of the coefficient in this study, and the dissociation with numerical symbols.[15] In future research, it may prove fruitful to study larger stimulus ranges (e.g., longer ranges of sequence (months, letters) during anodal tDCS or single-digit numbers (1-9) during cathodal tDCS).

Secondly, as stimulus attributes and ranges may affect SNARC results, future study designs should ensure that different stimulus ranges in within-subject (within-session) experiments comprise the same numbers of items. This was not the case for the present experiments with different weekday, number, and month name ranges. Given that switching between number

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[15] In principle, to draw conclusions from insignificant hypothesis test results, Bayesian analyses can be performed. For the reversed SNARC effect with month stimuli during anodal tDCS, we obtained BF = 1.155. Thus, the posterior probability of the null hypothesis was 46.4 % (and the complimentary probability for the alternative hypothesis 53.6 %). Thus, also the Bayesian result presents nothing but anecdotal evidence in the direction of the alternative hypothesis (reversal), on which no strong conclusions can be based on. See SA2 in the supplementary materials for more details on this approach.

ranges may induce different cognitive strategies (Abrahamse et al, 2016, Huber et al., 2016), such manipulations may be studied with care.

Discrepancies in the present results may have been influenced as well by the results during the sham condition. Unlike other reports, we did not observe significantly negative SNARC effects for numbers (and for weekdays) with the 1-5 range without any stimulation (e.g., Dehaene et al., 1993, Fias et al., 1996). It should be acknowledged as well that internal consistency and reliability of the SNARC effect can be medium to low (Cipora & Wood, 2017, for simulations; Cipora & Nuerk, 2013; Georges, Hoffmann, & Schiltz, 2016; Viarouge, Hubbard, & McCandliss, 2014; for estimates of reliability from .27 - .70), which may also influence differences between two tDCS conditions.

Several interesting tDCS parameters have not been explored with the present cognitive effects (see Schroeder et al., 2017, for a review of different tDCS parameters in stimulation studies). It is currently unknown whether changes in DC intensity or electrode configuration (such as a bilateral vs. extracephalic return electrode configuration) would lead to comparable stimulation outcomes. Moreover, there are no definite data on right-hemispheric tDCS. Also here, the data of Di Rosa et al. (2017) are interesting, because they show dissociations between parity-space and number-space associations in a parietal-supraorbital configuration, independent of cortical hemisphere. However, a possible effect of laterality was not significant in their study and the electrode configuration targeted entirely different areas than the prefrontal-extracephalic configuration used in the current and in our previous studies.

In sum, we view our study as a starting point, which shows at least that the neurocognitive mechanisms underlying the SNARC seem to be not as simple as often assumed. However, because these mechanisms and the codes involved may depend on task, stimuli, participants, and stimulation parameter, we wish to acknowledge that much more research is needed to explore the generality and specificities of associations of space and different cardinal or ordinal metrics.

Summary

We report mixed evidence for switching between spatial associations from prefrontal anodal tDCS and document positive and negative results within the same group of participants with different non-numerical stimuli. A conceptual replication demonstrates the possibility to modulate spatial associations of a non-numerical sequence (month names) by administration of anodal tDCS to the left prefrontal cortex. In another sequence of weekdays, the manipulation was not successful. The mixed evidence is best accounted for by unexplored systematic variations in study design, individual differences, or task contagion. Results are compatible with the previously proposed model of markedness correspondence (Schroeder et al., 2017) which accounts for the observed switching between stimulus-response compatibility effects due to markedness processing of target stimuli during anodal tDCS of the left prefrontal cortex. In the proposed multiple-coding framework, spatial-metric associations can result from various verbal and non-verbal simulations whose parameters may be selectively malleable by different tDCS configurations.

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Supplementary Materials

Supplementary Table 5.S1. Regression coefficients of spatial associations. Unstandardized b regression coefficients indicate response hand advantage increases (SNARC and SNARC-like effects) with single position/magnitude increments in the corresponding sequence (dRT/position[ms]), whereas standardized β coefficients correct for individual variance. Pseudo-position bins (1-5) were assigned to all sequences. For the month series, consecutive month names were aggregated to single position bins (e.g., January + February = position "1"). All regression coefficients were individually extracted and the resulting group-level mean was tested with one-sample t-tests against zero (cf. Fias, Brysbaert, Geypens, & D'Ydewalle, 1996).

	sham				**anodal tDCS**				***t*-test**		***t*-test beta**	
sequence	b	*p*	β	*p*	b	*p*	β	*p*	*t*	*p*	*t*	*p*
numbers ('one'-'five')	-4.157	.386	-.029	.817	-6.740	.032	-.280	.025	0.53	.533	1.61	.120
weekdays (Mo-Fr)	-3.087	.462	-.263	.049	-8.746	.058	-.204	.089	0.75	.460	0.31	.762
months (Jan-Dec)	-7.445	.057	-.190	.135	+4.217	.175	+.069	.458	2.68	.013	2.20	.038

Supplementary Table 5.S2. Compatibility Effects (CEs). CEs were computed by calculating the RT difference between SNARC congruent and SNARC-incongruent trials, defined as trial combinations of left + small / early, right + large / late (SNARC-congruent), and vice versa.

	sham		**anodal tDCS**		***t*-test**	
sequence	CE [ms]	*p*	CE [ms]	*p*	*t*	*p*
numbers (‘one’-‘five’)	12.6	.179	18.6	.003	0.53	.514
weekdays (Mo-Fr)	15.1	.012	16.7	.059	0.75	.891
months (Jan-Dec)	10.3	.126	-4.5	.403	2.68	.047

Supplementary Table ST3. Median response times (RTs) and error rates for all target-response combinations in the three tasks and two stimulation conditions.

	sham				**anodal tDCS**			
sequence	RT left [ms]	RT right [ms]	Error left [%]	Error right [%]	RT left [ms]	RT right [ms]	Error left [%]	Error right [%]
numbers ('one'-'five')								
One	484	480	6.3	3.3	477	481	2.9	1.6
Two	509	499	6.2	7.1	503	499	5.7	5.4
Four	539	499	9.5	10.4	534	510	12.0	7.7
Five	502	493	3.8	2.1	507	487	2.7	4.7
weekdays (Mo-Fr)								
Monday	512	499	3.9	6.5	520	515	4.4	6.0
Tuesday	538	523	10.5	6.1	543	543	9.2	6.0
Thursday	545	515	5.3	6.9	554	513	5.9	6.2
Friday	515	494	7.4	7.3	529	501	5.0	9.6
months (Jan-Dec)								
January	494	503	7.6	5.8	512	508	6.4	6.5
February	531	524	10.3	10.2	550	518	9.6	7.5
March	486	483	3.3	5.8	503	484	3.3	4.8
April	520	515	2.9	5.9	520	515	4.8	3.4
September	503	488	4.5	4.4	515	509	2.9	2.6
October	527	491	4.6	5.7	511	503	4.8	5.8
November	524	486	3.1	5.5	517	509	5.2	2.2
December	500	477	3.5	3.5	498	495	2.9	2.4

Supplementary Analysis SA1. Alternative analysis of main findings without data preprocessing.

Based on a reviewers concern with our data preprocessing strategy, we also submitted directly aggregated data from correct mean RTs to our main analyses. More precisely, the following preprocessing steps were skipped in this type of analysis: All but error trials were considered for RT analysis, including stimulus repetitions, trials following errors, and no outliers were rejected. Globally, this strategy led to considerably smaller percentage of trial rejection (4.6 %)

than the more conservative strategy presented in the paper (26.5 %). In this supplementary analysis here, mean correct RTs were aggregated for each stimulus, upon which we calculated dRTs (left-hand – right-hand RT) and then fitted regression coefficients based on the numerical magnitude or sequential position predictor, as described in the main methods section.

The results from this procedure were as follows:

1. Number words. SNARC effects with negative-signed coefficients were significantly different from zero for the performance during anodal tDCS (b = −11.93 ms/bin; *t*(23) = −3.67, *p* = .001), but not during the sham tDCS condition (b = −6.24 ms/bin; *t*(23) = −1.57, *p* = .131). The difference in SNARC effects was not significant (*t*(23) = −1.44, *p* = .163).

2. Monday-to-Friday Sequence Words. SNARC effects with negative-signed coefficients were significantly different from zero for the performance during anodal tDCS (b = −9.74 ms/bin; *t*(23) = −3.07, *p* = .005) and also during the sham tDCS condition (b = −8.09 ms/bin; *t*(23) = −2.41, *p* = .024). The difference in SNARC effects was not significant (*t*(23) = −0.35, *p* = .732).

3. January-to-December Sequence Words. A reversed SNARC effect with positive-signed coefficient was not significant during the anodal tDCS condition (b = +3.05 ms/bin; *t*(23) = 0.91, *p* = .373). The SNARC effect for the same month stimuli was negative-signed during the sham condition (b = −7.45 ms/bin; *t*(23) = −1.71, *p* = .102). In direct comparison of the two stimulation conditions, the effect of anodal tDCS was significant (*t*(23) = 2.49, *p* = .020, *d* = 0.51).

At large, the obtained results from the alternative analysis corroborate our main conclusions and, again, we could not find significant stimulation effects for number and weekday stimuli, but only for month stimuli. Nevertheless, we decided to present this analysis as well, because we agree with the issue that data preprocessing can offer opportunities for questionable research practices (Simmons, Nelson, & Simonsohn, 2011; Gelman & Loken, 2014) and should be transparently addressed, particularly in the case that controversial effects are investigated. Our main conclusions are thus corroborated by alternative data preprocessing strategies as well.

Supplementary References

Gelman, A., & Loken, E. "The Statistical Crisis in Science Data-dependent analysis—a “garden of forking paths”—explains why many statistically significant comparisons don't hold up." *American Scientist* 102.6 (2014), 460.

Simmons, J. P., Nelson, L. D., & Simonsohn, U. (2011). False-positive psychology: Undisclosed flexibility in data collection and analysis allows presenting anything as significant. *Psychological science*, *22*(11), 1359-1366.

Supplementary Analysis SA2. Bayes Analyses for Inconclusive Null Results

In frequentist statistics, null results can never allow researchers to reject the alternative hypothesis. To overcome this shortcoming, Bayesian statistics allow to quantify the evidence favouring either null or alternative hypothesis. In the current results, two major concerns were not sufficiently addressed by merging data from previous studies: 1) There was no significant SNARC effect for number words during sham tDCS and 2) the significant tDCS modulation of SNARC effect for month words did not lead to a significantly reversed effect. Both observed results are not compatible with previous literature on notation-independent SNARC effects (Nuerk et al., 2004; Nuerk, Wood, & Willmes, 2005) and with the effects of anodal tDCS on non-numerical sequences (Schroeder, Nuerk, & Plewnia, 2017). Thus, we analysed these data also in a Bayesian framework with the open-source software JASP (JASP Team, 2016). The respective analyses yielded Bayes Factors (BF), which can be used to rate the evidence favouring the alternative hypothesis (BF > 1) or the null hypothesis (BF < 1) and compute posterior probabilities. Jeffreys (1961) proposed a BF below 3 (above 1/3) presents anecdotal evidence, 3-10 (1/3-1/10) presents moderate evidence, 10-30 (1/10-1/30) presents strong evidence, and so on, for H1(H0).

For the SNARC effect with number words during sham tDCS, we obtained BF = 0.305. Thus, according to Masson (2011), the posterior probability of the null hypothesis was 76.6 %. Thus, the Bayesian result can only be rated as anecdotal/moderate evidence for the null hypothesis.

For the reversed SNARC effect with month stimuli during anodal tDCS, we obtained BF = 1.155. Thus, the posterior probability of the null hypothesis was 46.4 % (and the complimentary probability for the alternative hypothesis was 53.6 %). Here, also the Bayesian result presents nothing but anecdotal evidence in the direction of the alternative hypothesis.

Supplementary References

JASP Team. (2016). JASP (Version 0.7.5.5).

Jeffreys, H. (1961). *Theory of probability* (3rd edn). Oxford, UK: Oxford University Press.

Masson, M. E. J. (2011). A tutorial on a practical Bayesian alternative to null-hypothesis significance testing. *Behavior Research Methods, 43*, 679–690. http://doi.org/10.3758/s13428-010-0049-5

Nuerk, H.-C., Iversen, W., & Willmes, K. (2004). Notational modulation of the SNARC and the MARC (linguistic markedness of response codes) effect. *The Quarterly Journal of Experimental Psychology*, *57*(5), 835–63. http://doi.org/10.1080/02724980343000512

Nuerk, H.-C., Wood, G., & Willmes, K. (2005). The universal SNARC effect: the association between number magnitude and space is amodal. *Experimental Psychology*, *52*(3), 187–94. http://doi.org/10.1027/1618-3169.52.3.187

Schroeder, P. A., Nuerk, H.-C., & Plewnia, C. (2017). Prefrontal neuromodulation reverses spatial associations of non-numerical sequences, but not numbers. *Biological Psychology*, *128*(February), 39–49. http://doi.org/10.1016/j.biopsycho.2017.07.008

VI. A GENERALIZABLE THEORY: TESTING IAT SALIENCE ASYMMETRIES

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Schroeder, P.A., Nuerk, H.-C., Plewnia, C. Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2018). Reduction of Implicit Cognitive Bias with Cathodal tDCS to the Left Prefrontal Cortex. *Cognitive, Affective, & Behavioral Neuroscience*, 18(2), 263-272. doi:10.3758/s13415-018-0567-7

Abstract

Implicit associations can interfere with cognitive operations and behavioural decisions without direct intention. Enhancement of neural activity with anodal transcranial direct current stimulation (tDCS) was proposed to reduce implicit associations by means of improved cognitive control. However, the notion of a direct inhibition of implicit associations by cathodal tDCS has not yet been addressed. Here, we introduce a cathodal tDCS configuration with extracephalic return electrode to reduce implicit associations. Based on previous studies on implicit spatial-numerical associations, we generalize the stimulation rationale by demonstrating efficacy in the standardized implicit association task (IAT). In this double-classification task, insect vs. flower pictures and negative vs. positive words are mapped together onto two shared response keys with crossed response assignments in separate blocks. Responses were relatively faster when insect + negative and flower + positive stimuli required the same answer (IAT effect). Most critically, the IAT effect was reduced during 1 mA prefrontal cathodal tDCS as compared to sham stimulation. Results are consistent with the proposed stimulation rationale, with our previous observations, and complementary to previous attempts to modulate IAT effects with (medial) prefrontal anodal tDCS configurations. Limited by the validity of the IAT in general, results suggest transferability to other implicit biases.

Introduction

Human behaviour does not always reflect goal-directed deliberate choice. Instead, and particularly in demanding situations with little cognitive resources, spontaneous decisions can be based on implicit associations. The emergence of implicit associations is often neither consciously intended, directly perceived, nor convergent to explicit self-reports (Greenwald et al., 1998). Nevertheless, indirect measurements of implicit associations can predict related behaviours incremental to explicit self-report measures (Greenwald et al., 2009). For example, addictive and obesogenic behaviours are informed by implicit processes which are thus taken to moderate maladaptive choices in the long run (De Houwer, 2002; Wiers et al., 2002; Huijding et al., 2005; Hofmann et al., 2007), although the diagnostic criteria (validity and reliability) and underlying mechanisms of different measurements are still controversial (Fiedler et al., 2006). Implicit associations were also shown in critical (anti-) social behaviours such as stereotyping, paedophilia, or psychopathology (Greenwald et al., 1998 Exp. 3; Gray et al., 2005; Roefs et al., 2011; Gawronski & De Houwer, 2014). Due to the covert and indirect nature of these biases, however, it is hard to detect or change implicit associations that potentially compromise a more deliberate cognitive processing.

External modulation of prefrontal cortical areas by application of transcranial direct current stimulation (tDCS) was already proposed and investigated as a possibility to change implicit associations in healthy and patient populations (see Table 6.1). In tDCS, a weak direct current is sent through brain tissue between two electrode pads. Resting membrane potentials are slightly modulated with strongest effects in dense electric fields under the pad electrodes dependent on the current inward or outward direction (Nitsche & Paulus, 2000). The rationale of previous studies on implicit associations was to enhance higher-order regulation processes (e.g., cognitive control) by increasing firing rates in prefrontal areas, in accordance with neuroimaging correlates (Chee et al., 2000) and active interference of PFC activity with transcranial magnetic stimulation (Cattaneo et al., 2011; Crescentini et al., 2014). Anodal tDCS of the medial PFC led to smaller IAT effects in a study testing racial biases (Sellaro et al., 2015), but stimulation effects on implicit alcohol associations were not pronounced for a more lateral dlPFC configuration in a group of hazardous drinkers (den Uyl et al., 2015). In one earlier study, Gladwin and colleagues (2012) even observed increased implicit associations from anodal tDCS, opposed to their predictions. In fact, failures of the stimulation may be linked to the claims that tDCS was generally ineffective (Horvath et al., 2015) or at least that some configurations produce smaller effects than others in the cognitive domain (Jacobson et al., 2012). Alternatively, it may be possible that another tDCS configuration could be more effective, especially seeing the variety of possible protocols (e.g., Schroeder, Dresler, et al., 2017). Counterintuitively, but complementary to above neuroimaging results, it may be even possible that prefrontal networks were also involved in the activation of implicit associations. Then, the inhibition of prefrontal activity should reduce the IAT effect.

With cathodal tDCS, firing probabilities are reduced due to hyperpolarisation and increased resting membrane thresholds (Nitsche & Paulus, 2000; Nitsche et al., 2003). In working memory tasks, 1 mA cathodal tDCS of the left dlPFC reduced behavioural performance (Zaehle et al., 2011; Wolkenstein et al., 2014). From the previous IAT studies, it remained possible that a reduction of prefrontal activity may actually prove beneficial, as it was already shown for creative tool use (Chrysikou et al., 2013) and other behaviours (Schroeder & Plewnia, 2016). Actually, in previous studies on numerical cognition, we demonstrated that implicit spatial-numerical associations can be reduced specifically by 1 mA cathodal tDCS (Schroeder et al., 2016; Schroeder, Nuerk, et al., 2017). However, although implicit spatial-numerical associations are also present in other double-classification tasks (Fischer & Shaki, 2016), the generalizability of cathodal tDCS effects to different assessment procedures and implicit association effects could not be granted without further empirical evidence.

In the current study, we utilized the prominent assessment procedure in the Implicit Association Task (IAT), a standardized response time (RT) paradigm and influential research tool in social, clinical, and cognitive psychology (De Houwer et al., 2004; Roefs et al., 2011; Gawronski & De Houwer, 2014). In the IAT, participants categorize pictures of insects and flowers together with negative and positive words. Target classifications (insects vs. flowers) and attribute classifications (negative vs. positive words) are assigned to only two shared response keys, but target and attribute stimuli are presented intermixed in the two critical test blocks. The assumption is that RTs are faster in the congruent block than in the incongruent block, because targets and attributes are associated implicitly, share a common feature such as salience or familiarity, or because they allow for recoding (e.g., both insects and negatives are simply classified as negative) (Greenwald et al., 1998; Mierke & Klauer, 2001; Rothermund & Wentura, 2004; De Houwer et al., 2005; Meissner & Rothermund, 2013; Hilgard et al., 2015). Regardless of these potential mechanisms, the relative association strength (IAT effect) is inferred from performance (RT) differences in these two test blocks. Healthy participants were tested twice in the task concurrent to 1 mA cathodal tDCS or to a sham stimulation.

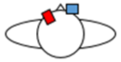
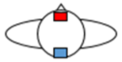
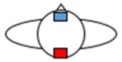
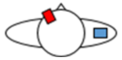
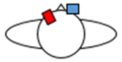
Because our previous studies tested implicit spatial associations of numbers and documented efficacy of 1 mA cathodal tDCS to the left prefrontal cortex (Schroeder et al., 2016, 2017), our hypothesis was that cathodal tDCS to the left prefrontal cortex would also reduce non-spatial implicit associations in the IAT effect. Theoretically, we expected a reduction of associations particularly due to the general polarity correspondence principle (Proctor & Cho, 2006), which explicitly predicts a shared cognitive process underlying both IAT effects and spatial-numerical associations. Furthermore, the polarity correspondence principle lines up with the notion of markedness and/ or salience asymmetries in respective stimulus associations of the two effects (Nuerk et al., 2004; Rothermund & Wentura, 2004). Thus, the current study was a direct test of the generalizability of this theoretical stimulation effect.

Method

Participants

The study followed a sham-controlled cross-over design and participants were tested in two tDCS configurations (sham vs. active cathodal tDCS) on separate days (more than two days apart). A-priori power analysis determined a required sample size of N = 23 participants to replicate the previously obtained stimulation effect on implicit spatial-numerical associations in a crossover design (effect size f = 0.639; Schroeder et al., 2016, Exp. 1) with a power of $1 - \beta = 0.8$ and error rate of $\alpha = 0.05$. To counterbalance the orders of stimulation and IAT blocks across the sample, N = 24 healthy volunteers were recruited (mean age = 24.3 y, SD = 4.7 y, range: 19-37 y; 3 male). All participants were right-handed (Oldfield, 1971) and native German-speakers. Participants confirmed that they did not take any medication with CNS-acting drugs, had no previous or current neurological or psychiatric impairments, and two of them were low-frequency smokers (less than 3 cigarettes / day; remaining participants were non-smokers). All participants provided written informed consent and the study was approved by the Ethical Commission of the Medical Faculty University Tuebingen (ID of approval: 030/2017BO2).

Table 6.1. Previous tDCS configurations for modulation of implicit associations. In the first row, red and blue rectangles refer to anode and cathode placements on head and shoulder positions in the respective studies.

						
Target-Return Electrodes	F3-SO	Fpz – Oz	Fpz – Oz	F3 – Xc	F3 – Xc	F3 – SO IFG[1] – SO
Polarity-Intensity	Anodal 1 mA	Anodal 1 mA	Cathodal 1 mA	Anodal 1 mA	Cathodal 1 mA	Anodal 1 mA (offline protocol)
Task	Insect-Flower IAT	Ingroup-Outgroup IAT	Ingroup-Outgroup IAT	Space-Number SNARC	Space-Number SNARC	Alcohol IAT, Affective IAT
Result	▼ Increased Bias	▲ Reduced Bias	ø	ø	▲ Reduced Bias	▲ / ø DLPFC Alcohol: Reduced Bias in attribute trials
Authors	Gladwin, den Uyl, & Wiers, 2012	Sellaro et al., 2015	Sellaro et al., 2015	Schroeder et al., 2016, 2017	Schroeder et al., 2016, 2017	den Uyl, Gladwin, & Wiers, 2015

Note. Xc = extracephalic location, [1] IFG = electrode positioning refers to location on the crossing of F3, Cz, Fz, and T3.

Cathodal transcranial Direct Current Stimulation (tDCS)

Direct current was generated by a CE-certified device (NeuroConn, Illmenau, Germany). An intensity of 1 mA was administered for 25 minutes, including a 5-minute pre-task idle time during which participants were told to relax. During the first minutes of stimulation, adverse sensations are most pronounced, thus the sham stimulation was realized by administering the same stimulation for a duration of 40 s and fading out subsequently. The 5-min idle time was adhered in both sham and cathodal tDCS sessions. As a consequence, the IAT procedure was started and completed either entirely during stimulation (active cathodal tDCS configuration) or entirely without active stimulation (sham tDCS configuration). Direct current was initiated and terminated with a linear 5 s ramp.

The target cathode rubber electrode (5 × 7 cm) was diagonally centred over F3 (left PFC; the position was ensured by tape measurements according to the international 10-20 system of electrode placement). The return anode rubber electrode (5 × 7 cm) was fixed over the right upper arm. This extracephalic return electrode placement avoids concurrent modulation of another brain region and thus delivers targeted modulation dependent on target cathode polarity (Wolkenstein et al., 2014; Schroeder et al., 2016). Both electrodes were buttered with a low-resistance EEG paste and additionally fixed with a bathing cap (target electrode) or adhesive tape (return electrode). Impedances were controlled to be below 10 kΩ prior to starting the sham or active stimulation.

IAT procedure

Participants performed the insect-flower evaluative IAT (Greenwald et al., 1998; Greenwald et al., 2009). The traditional double-classification procedure consists of a sequence of 7 blocks (see Table 6.2) that subsequently introduced the bimanual classifications of 10 *negative* vs. *positive* German words (taken from Rothermund & Wentura, 2004) and of 10 *insect* vs. *flower* pictures (taken from Hussey, 2017) in two practice blocks (1 & 2, respectively). Participants were asked to classify words as positive or negative (block 1) and pictures as depicting insects or flowers (block 2) by pressing one out of two keyboard keys with their left-hand (‘e’) or right-hand (‘i’) index fingers, corresponding to the positions of respective word and picture labels that were shown in the display. In the following combined test blocks (3 & 4), attribute words and target pictures appeared in randomized order. The response positions of *negative* / *positive* target labels adjacent to the *insect* / *flower* attribute labels on the left-side / right-side of the screen were determined by chance, such that these two test blocks were congruent for some participants (e.g., *insects* + *negative* and *flowers* + *positive* stimuli were classified by the same *left* and *right* key presses). For the other participants, these first test blocks (3 & 4) were presented in the incongruent response label constellation (e.g., *flowers* + *negative* and *insects* + *positive*). The positions of target labels were then reversed in the next practice block (5) and test blocks (6 & 7), such that performance during both congruent and incongruent block types was collected from all participants.

Participants were tested individually and seated at a comfortable distance (~ 60 cm from the experimentation computer). The experiment was implemented in PsychoPy (Peirce, 2007) based on a previous Open Source software of the IAT in Belgian language (Hussey, 2017). Classification labels (German words “Negativ”, “Positiv”, “Insekten”, and “Blumen”) were presented continuously on the respective sides in the top field of the computer screen. The background colour was black. Attribute labels and stimulus words were written in light green colour, whereas target labels were written in white colour, to maximize discrimination as separate categories (Nosek et al., 2007). In each trial, the classification stimulus (picture or word) appeared in the centre of the screen until a response was given with the left-hand (E-key) or right-hand index finger (I-key) on a standard QWERTZ-keyboard, corresponding to the left-side and right-side label positions. After the correct response was given, a blank inter-trial interval was shown for 400 ms and then the next trial was started. Wrong responses had to be corrected by another key press.

The current task variant closely followed the recommendations outlined in Nosek et al. (2007), with the following adjustments. The order of compatible vs. incompatible critical blocks was counterbalanced across participants in our design. Due to human error, the counterbalancing list assigned 2 fewer participants starting with compatible blocks to the sham stimulation in the first block. When these participants were removed in a separate analysis such that the combination was fully balanced, the reported stimulation results were stable. To improve reliability of the task, and to collect more data in each of the conditions, the number of trials was doubled in both congruent and incongruent blocks. Table 6.2 provides a summary of the resulting numbers of repetitions in each block. As was argued before, this manipulation could lead to generally somewhat diminished IAT effects (Greenwald et al., 2003), rendering our current procedure relatively conservative.

Table 6.2. Trial numbers for each block type in the current experiment.

	Block Type	**Stimuli assigned to left-hand key**	**Stimuli assigned to right-hand key**	**Number of trials**
1	Attribute practice	Negative	Positive	20
2	Target practice	Insect	Flower	20
3	Test (congruent block)	Insect + Negative	Flower + Positive	40
4	Test (congruent block)	Insect + Negative	Flower + Positive	80
5	Target reversed practice	Flower	Insect	40
6	Test (incongruent block)	Flower + Negative	Insect + Positive	40
7	Test (incongruent block)	Flower + Negative	Insect + Positive	80

Note. The order of IAT-compatible (*insect* + *negative* vs. *flower* + *positive*) and IAT-incompatible mappings (*flower* + *negative* vs. *insect* + *positive*) in the test blocks 3 & 4 and blocks 6 & 7, respectively, was counterbalanced across participants in the current study. Precisely, only half of participants completed the blocks in the displayed order, the other half of participants completed the target practice and combined test blocks in the reversed order (i.e., starting with the target reversed practice in block 2). As was argued in Greenwald et al. (1998; see also: Nosek et al., 2002), the initial confrontation of IAT-incompatible double classifications can reduce the IAT effect (possible also due to involvement of cognitive control processes), and this was statistically confirmed in our data by larger IAT scores for the group of participants that received the compatible condition first (D-IAT = 0.63, SE = 0.07) as compared to the group that received the incompatible condition first (D-IAT = 0.31, SE = 0.7; $F(1,22) = 12.31$, $p = .002$, $\eta p^2 = .36$). However, entering this additional factor to the ANOVA on the stimulation effect did not produce a significant two-way interaction ($F(1,22) = 0.20$, $p = .62$), suggesting that the order of presentation did not modulate the stimulation effect in the present results.

Statistical Analyses

Response times (RTs) and error rates were submitted as dependent variables to separate ANOVAs comprising the repeated measures factors $IAT_{CONGRUENT,INCONGRUENT}$ × *Trial-*

$Type_{TARGET,ATTRIBUTE} \times stimulation_{CATHODAL,SHAM}$. The hypothesized outcome (stimulation effect) was the two-way interaction between *IAT* block and *stimulation* condition. Follow-up *t*-tests were performed to outline changes between cathodal tDCS and sham tDCS (paired *t*-test) in IAT effects (i.e., the RT difference between congruent and incongruent blocks) and to test the significance of IAT effects during both sessions individual (one-sample *t*-test against zero).

Finally, we also computed the standardized D-IAT scores for the two stimulation conditions following the algorithm proposed by Greenwald (2002) and tested the reduction of D-IAT by cathodal tDCS directly. The D-IAT composite index of the IAT effect is basically a standardized difference measure of performance in the incongruent vs. congruent test blocks of the tasks, divided by the pooled standard deviation. Moreover, the algorithm specifies outlier correction and extreme-value treatments [i.e., exclusion criteria for participants based on fast RTs (k=0 were excluded), exclusion of long trials (> 10 s), penalty for wrong responses (use of correction RT), no transformation of the resulting block mean RTs]. The formula for computing the D-IAT score was:

$$\text{D-IAT}=\text{M}\left(\frac{\text{RT}_{\text{B6}} - \text{RT}_{\text{B3}}}{\text{SD}_{\text{B6, B3}}}, \frac{\text{RT}_{\text{B7}} - \text{RT}_{\text{B4}}}{\text{SD}_{\text{B7, B4}}}\right)$$

For participants who performed blocks in reversed order (i.e., starting with the incongruent blocks in B3 and B4), the respective positions of B6 & B3, and B7 & B4, were switched in above formula (such that a positive D-IAT score would always reflect associations between *insect* + *negative* and *flower* + *positive* categories).

Results

RTs

Mean RTs for all block types, trial types, and stimulation conditions are shown in Figure 6.1. Classification decisions were faster in the congruent IAT blocks (667 *ms*) than in the incongruent IAT blocks (793 *ms*), giving rise to a significant main effect of $IAT_{CONGRUENT,INCONGRUENT}$ in ANOVA, $F(1,23) = 63.51$, $p < .001$, $\eta p^2 = .73$. Target trials (containing insect vs. flower pictures; 663 *ms*) were faster answered to than attribute trials (negative vs. positive words; 798 *ms*) in the main effect of $Trial\text{-}Type_{TARGET,ATTRIBUTE,}$ $F(1,23) = 128.84$, $p < .001$, $\eta p^2 = .85$. The main effect of $stimulation_{CATHODAL,SHAM}$ was not significant, $F(1,23) < 1$, $p = .435$.

Most importantly, there was a significant two-way interaction between *stimulation*$_{CATHODAL,SHAM}$ and *IAT*$_{CONGRUENT,INCONGRUENT}$, *F*(1,23) = 7.68, *p* = .011, ηp² = .25. The RT difference between congruent and incongruent trials (IAT effect) was significantly reduced during cathodal tDCS as compared to sham tDCS, *t*(23) = 2.77, *p* = .011, d = 0.61. Nevertheless, IAT effects significantly differed from zero during both sham tDCS (153 *ms*), *t*(23) = 8.57, *p*<.001, as well as during cathodal tDCS (98 *ms*), *t*(23) = 5.04, *p*<.001. The stimulation effect was not further qualified by a three-way interaction with *Trial-Type*$_{TARGET,ATTRIBUTE}$, *F*(1,23) = 2.39, *p* = .136.

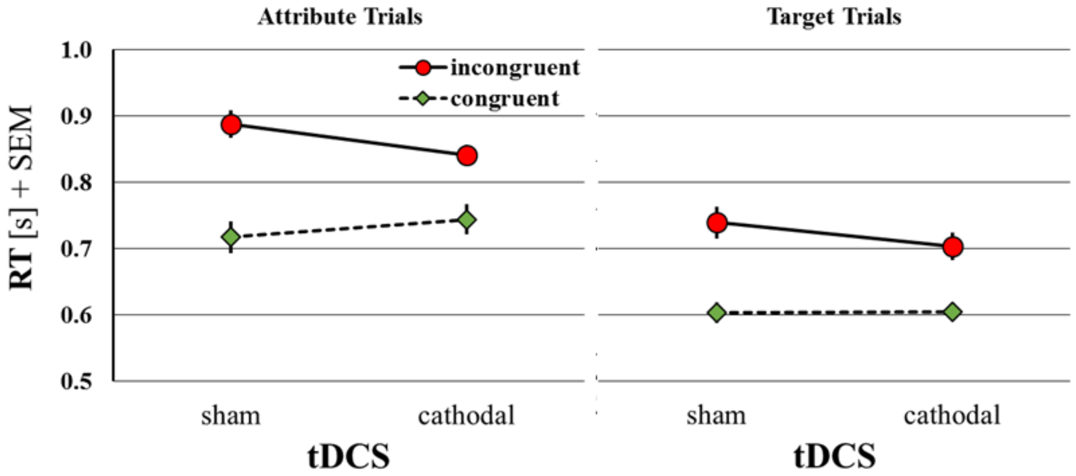


Figure 6.1. *Mean response times during sham tDCS and active cathodal tDCS as a function of IAT block type (incongruent vs. congruent). Left and right columns show data separately for attribute trials (positive vs. negative words) and relatively faster target trials (insect vs. flower pictures). Error bars reflect standard errors of the mean.*

Accuracy Rates

More accurate responses were given in the congruent IAT blocks (94.0 %) than in the incongruent IAT blocks (92.7 %), but the main effect of *IAT*$_{CONGRUENT,INCONGRUENT}$ in ANOVA was much less substantial than in RTs and not statistically significant, *F*(1,23) = 2.98, *p* = .098, ηp² = .12. Performance appeared to be more accurate in target trials (94.3 %) than in attribute trials (92.4 %), but the respective main effect of *Trial-Type*$_{TARGET,ATTRIBUTE}$ was not statistically significant either, *F*(1,23) = 3.69, *p* = .067, ηp² = .14. There was no main effect of *stimulation*$_{CATHODAL,SHAM}$ *F*(1,23) < 1, *p* = .922, and no significant two-way interaction between

$stimulation_{CATHODAL,SHAM}$ and $IAT_{CONGRUENT,INCONGRUENT}$, $F(1,23) < 1$, $p = .727$, nor were there further significant interaction terms, Fs < 1.71, ps > .205.

D-IAT Score

Finally, we also computed the composite D-IAT scores for the two sham and cathodal tDCS sessions by applying the improved scoring algorithm (Greenwald et al., 2003). In brief, the D-IAT score is a standardized RT difference measure (considering both test blocks and pooled RT standard deviations; see methods section).

There was a significant difference between the sham session and cathodal tDCS session in the hypothesized direction, $t(23) = 1.95$, $p_{\text{one-tailed}} = .032$, d = 0.39 (Figure 6.2). Complementary to the previous observation in RTs, implicit associations were more pronounced in the sham session (D-IAT = 0.53, SE = 0.05) than in the session concurrent to cathodal tDCS (D-IAT = 0.42, SE = 0.07; the D-IAT score technically ranges between -2 and 2).

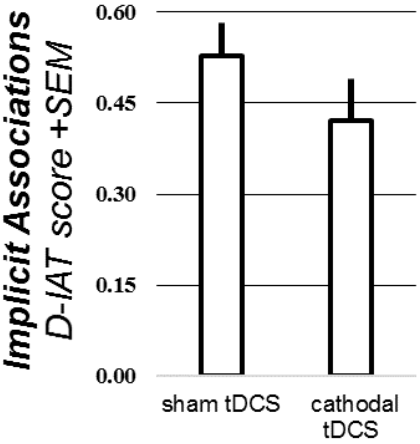


Figure 6.2. *Mean D-IAT effect during sham tDCS and cathodal tDCS. Composite scores (D-IAT) were obtained from applying the improved scoring algorithm by Greenwald et al. (2003). Error bars reflect standard errors of the mean.*

Adverse Sensations of tDCS

Adverse sensations were assessed by a questionnaire after both sham and active tDCS sessions, consisting of 7 items on a 5-point Likert scale (Brunoni et al., 2011). Participants reported more intense tingling after active cathodal tDCS (M = 2.79, SE = 0.23) than after sham tDCS (M =

2.29, SE = 0.16), *t*(23) = 2.22, *p* = .037, d = 0.45. The remaining comparisons were not significant and all values are reported in Supplementary Table 6.1.

Blinding

Participants were asked immediately after sham and active cathodal tDCS whether they had received a sham stimulation (with comparable sensations, but without modulations of cognitive processing). 15/24 participants correctly guessed the tDCS session and 15/24 (partially different) participants correctly guessed the sham session. Data were submitted to a chi-square test, $\chi^2(1) = 3.00$, $p = .083$. Although participants tended to guess correctly, results did not corroborate a significant link between guesses and sham stimulation, thus blinding was successful. We also explicitly asked whether the stimulation had improved their task performance on a 1-5 Likert scale (ranging from “not at all” to “tremendously”), but there was no explicit perception of any behavioural changes neither after anodal tDCS (*M* = 1.22, *SD* = 0.42) nor after sham tDCS (*M* = 1.17, SD = 0.39; *p* = .747).

Discussion

We tested the general capability of inhibitory, cathodal tDCS to reduce implicit associations in the insect-flower IAT. As expected by the literature, participants were consistently faster when flowers and positive words (insects and negative words) were evaluated by the same response (congruent block), as compared to the condition that paired flowers and negative words (insects and positive words) to the same response (incongruent block; IAT effect). Stimulation of the left PFC by cathodal tDCS was utilized to hyperpolarise resting membrane potentials and thus potentially reduce cortical activity in this area. As anticipated, a significant reduction of IAT effects was observed specifically in response times, and the stimulation effect was also reflected in the standardized D-IAT score.

The current results are complimentary to the previous tDCS studies that explored the effectivity of activity-enhancing anodal tDCS on cognitive control processes and IAT regulation (Gladwin et al., 2012; Sellaro et al., 2015; den Uyl et al., 2015). In contrast to these previous studies, we here explored whether it was possible to reduce implicit associations directly with the cathodal, inhibitory tDCS polarity over the left PFC. Specifically, we predicted that 1 mA activity-reducing cathodal tDCS would reduce the IAT effect, as observed before with spatial-numerical associations in different paradigms (Schroeder et al., 2016, 2017). Although it may be surprising at first that the PFC would causally contribute to the seemingly automatic and unintended activation of implicit associations, actually, resembling stimulation effects were also expected by the polarity correspondence principle (Proctor & Cho, 2006).

Importantly, the observed results are not only consistent with the proposed stimulation rationale, but also with previous empirical findings. For instance, Gladwin and colleagues (2012) reported on a pattern of results effectively orthogonal to our findings and their study showed an enhancement of IAT effects by anodal tDCS of the same PFC target region in the insect-flower IAT. In the study by Sellaro et al. (2015), a cathodal tDCS configuration over medial PFC actually also induced a descriptive (yet non-significant) reduction of the racial bias. Since both tDCS configuration had relatively little spatial focality, a spill-over to more medial or lateral sites could not be excluded.

Theoretically, the present results also provide an important conceptual test of the observed effects of tDCS on spatial-numerical associations, which were attributed to depend on linguistic structures (such as small-large and before-after classification polarities). More precisely, tDCS effects reversed when classifications in the task instruction utilized reversed verbal polarities (Schroeder et al., 2017). However, it was not clear whether stimulation effects would generalize to non-spatial associations. In the IAT, *negative* and *insect* classifications are the more salient classification polarities, but their relative salience (and resulting IAT effects) can be temporally reversed by a search detection task (Rothermund & Wentura, 2001, 2004). In line with their regular verbal saliences, in fact, insect-flower IAT effects were even present in a statistical machine-learning model trained on large text corpora (Caliskan-Islam et al., 2017).

Importantly, we found moderate-to-large stimulation effects, but not a complete extinction of implicit associations during cathodal tDCS. On these grounds, our observations here are also congruent with theoretical IAT accounts including the assumption of spreading activation (Greenwald et al., 1998), salience asymmetry (Rothermund & Wentura, 2004), or similarity (De Houwer et al., 2005). A potential integrative account spanning different implicit spatial-numerical and non-spatial associations may also highlight multiple coding frameworks (Schroeder et al., 2017) and consider multiple cognitive processes reflected in socially sensitive IAT measures. Furthermore, we believe that implicit associations eventually reflect complex and long-term interactions between social, verbal-linguistic, behavioural, and cultural aspects that may require multidimensional approaches to overcome societal topics such as racial biases or the contribution of implicit associations to psychiatric conditions.

Potential relevance for cognitive and clinical tDCS trainings

The capability to reduce implicit associations with cathodal tDCS may be interesting for several applications. For instance, combined trainings in IAT tasks with tDCS have been explored in the treatment of addiction (den Uyl et al., 2015), but implicit associations may be involved in other clinically relevant behaviours as well (De Houwer, 2002). Nevertheless, the results reported here should be seen as a first starting point for theoretically motivated modification paradigms with cathodal tDCS for several reasons. (i) It is not yet established that the observed modulations are longer-lasting. Training studies achieved sustainability of 3-9 months after a combined tDCS cognitive training over three sessions (Ruf et al., 2017), but the current result was drawn from single-session observations. (ii) Furthermore, it is not clear whether the observed modulations of IAT effects also translate into relevant explicit behaviour, as already the transition between IAT measurements and explicit self-reports is often rather low (but incremental) (Fiedler et al., 2006; Greenwald et al., 2009). Possibly, a combined training might allow for reliable changes in IAT effects, which could also have effects on spontaneous behaviour in situations that are dominated by reflexive behaviour (e.g., binge eating), but this potential mechanism must be tested in respective studies first. (iii) Moreover, although theory and combined evidence from different previous tasks indicate a certain generalizability (Schroeder et al., 2016, 2017), it could be possible to obtain bolder or weaker modulations in different stimuli. This might be explained by additional codes that do not draw on implied mechanisms (e.g., salience) as much, or by more complex self-related behaviours. For example, Rothermund & Wentura (2004) acknowledged that some IAT effects may include emotional or self-relevant processing which could not be explained exhaustively by salience processing. In our previous elaboration of verbal markedness in spatial-numerical associations (Schroeder et al., 2017), we explicitly emphasize the necessity of multiple cognitive codes and the possibility of switching between them using tDCS. Moreover, posterior-parietal cathodal tDCS (with supraorbital return) was not equally effective to modulate both implicit spatial-numerical associations and parity-space markedness associations, but showed selectivity in another study (Di Rosa et al., 2017). (iv) Interestingly, in alcohol-addicted patients, a puzzling IAT effect pertains to the negative and avoidant evaluation of alcohol which is not accounted for by salience asymmetries but by alcohol use (Houben & Wiers, 2006). Thus, especially in patient populations that may have developed different cognitive processes to certain stimuli (e.g., compensation strategies), it must be established whether linguistic markedness, symmetry, or individually refined salience confines to any observed effect.

Finally, it should be recognized that implicit associations *per se* are not necessarily dysfunctional in all cases. Instead, implicit activations can also allow for low-cost and functional decision-making akin to heuristics (Gigerenzer & Gaissmaier, 2011), thus enabling rapid and adaptive action. For example, a negative association triggered by a spider or a wasp may guard an agent’s health in the first place by inducing avoidant behaviour. It will be mandatory to further investigate the personal and general processes that lead to potentially harmful implicit associations (e.g., approach biases in obese participants; Kemps & Tiggemann, 2015) in order to fully account for potential bias modifications with tDCS in the future.

Summary

In conclusion, the current study demonstrates the capability to reduce implicit associations in the IAT effect by means of cathodal prefrontal tDCS. Thus, we consistently complement a series of previous results. The present findings are in line with the modulation of spatial-numerical associations in single categorization tasks (Schroeder et al., 2016, 2017), with the effects of anodal tDCS on IAT biases (Sellaro et al., 2015; Gladwin et al., 2012; den Uyl et al., 2016), and with the proposed stimulation rationale of activity-decreasing cathodal tDCS. Although some interesting perspectives emerge for therapeutic applications, there is little evidence for long-term modulations of implicit associations, the link to external behaviours is unclear, and generalizability to clinical populations or to other socially sensitive IAT effects is likely to be examined in future clinical studies.

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Supplementary Materials

Supplementary Table 6.1. TDCS adverse effects. Adverse sensations were assessed on a 5-point Likert-like scale after each session (1=none, 5=extensive). Ratings from anodal and sham sessions were submitted to paired *t*-tests.

	sham tDCS	cathodal tDCS	
Adverse Sensation	M (SE)	M (SE)	*p*
Tingling at the site of the electrode	2.29 (0.16)	2.79 (0.23)	.037
Tingling elsewhere	1.09 (0.06)	1.23 (0.11)	.266
Exhaustion	2.09 (0.23)	1.91 (0.45)	.676
Itching	1.74 (0.25)	1.43 (0.16)	.148
Headache	1.17 (0.08)	1.30 (0.15)	.451
Nausea	1.00 (-)	1.00 (-)	-

GENERAL DISCUSSION

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Summary of Study Results

Table 7.1 summarizes the key empirical results of the previous chapters. Following a mini-review of available tES studies in the domain of numerical cognition in Chapter I, several experiments were conducted. I administered tDCS with an intensity of 1 mA to the left prefrontal cortex (*F3* according to the 10-20 international system for electrode placement) and the return electrode was fixed at the contralateral upper arm. Within and across experiments, the polarities of target and return electrodes were varied systematically (anodal vs. cathodal tDCS). An exception to this study design is Chapter III which describes behavioral data and individual differences analyses exclusively. Moreover, stimuli and tasks were varied to induce implicit spatial associations of numbers, non-numerical sequences, or non-spatial associations in the Implicit Association Test (IAT). The polarity-specific effects of cathodal tDCS were consistent over the conducted studies, but a dissociation was outlined for non-numerical ordinal sequence stimuli. Moreover, generalizability of the effects of cathodal tDCS were shown in the reduction of IAT effects (Chapter VI).

Table 7.1. Summary of empirical results gathered in Chapters II-VI.

	Chapter II	**Chapter III**	**Chapter IV**	**Chapter V**	**Chapter VI**
Polarity	Anodal - Cathodal	NA *(Individual-Differences Study)*	Anodal - Cathodal	Anodal	Cathodal
Stimuli	1-9	1-5, Mo-Fr	1-5, Mo-Fr	One-Five, Mo-Fr, Jan-Dec	Insect-Flower Negative-Positive
Tasks	Parity Judgment, Magnitude Judgment	Magnitude Judgment (Colour Judgment)	Magnitude Judgment (Colour Judgment)	Magnitude Judgment	IAT (Implicit Association Test)
Result	Reduced SNARC *Unaffected Simon*	Weak Correlation Between SNARCs	Dissociated SNARC Reversed Weeks *Unaffected Stroop*	Dissociated SNARC Modulated Months	Reduced IAT Effect
Implication	Polarity Dependence	Weak Construct Validity	Markedness Activity-Dependence	Multiple-Coding Polarity Asymmetry	Generalizability

In little more detail, Chapter II showed that the decreasing effect of cathodal tDCS on implicit spatial-numerical associations was polarity-specific and could not be obtained with anodal tDCS. A compatibility effect between numerical magnitude and spatial horizontal responding (i.e., SNARC effect) was observed during sham and anodal tDCS conditions, but not during prefrontal stimulation with cathodal tDCS. Interestingly, I could also observe task-selectivity and dissociate SNARC effects from Simon effects, where location-based spatial information was directly available in the stimulus and respective compatibility effects with spatial responding were maintained during tDCS. Although dissociations between SNARC and Simon effects were obtained before and it was established that SNARC differs significantly and should not be considered an exemplar of the Simon effect (Mapelli, Rusconi, & Umiltà, 2003), the chapter nicely illustrates the additional prefrontal effort for attaching a spatial code to number.

Chapters III – V focus on the distinction between purely ordinal vs. mixed ordinal-cardinal stimuli. The underlying rationale for these experiments was the notion that non-numerical sequences (weekdays and months) exhibit clear ordinal properties, but they do not refer to cardinality, which provides a mathematical and conceptual distinction with possible psychological relevance (see Patro et al., 2014, for theoretical elaboration and children data). In all three studies, this distinction was found to be highly relevant. First, I used an individual-differences approach to correlate weekday and number SNARC effects, but coefficients were remarkably low and thus, the observed construct validity was poor for an assumed common cognitive origin. Next, prefrontal tDCS produced orthogonal stimulation effects and the spatial association of a non-numerical sequence was reversed (Chapter IV) or at least modulated in opposite direction than the spatial-numerical associations of symbolic or written single-digits (Chapter V). Chapter V also includes a small meta-analysis across all studies using anodal tDCS to statistically confirm the pattern of enhanced spatial-numerical associations. Interestingly, this effect of anodal tDCS was estimated to be approximately three times smaller than the effect of cathodal tDCS at the same intensity (1 mA), which points to asymmetric polarity-dependent tDCS effects in cognition and will be discussed in greater detail in a later section (Clinical Implications II).

Finally, I generalized the effects of cathodal tDCS on implicit cognitive biases in the insect-flower Implicit Associations Test (IAT). In contrast to the other studies, the implicit associations measured by this paradigm are non-spatial (non-directional) and IAT effects are assessed in a specific double-classification tasks procedure. Nevertheless, mimicking the effects outlined in Chapters II and IV, a reduction of implicit associations was observed during cathodal tDCS. This result complements the previous stimulation capabilities modeled by the SNARC effect. As I will argue in the next sections, both anodal and cathodal tDCS effects across the studies can actually line up in a single stimulation rationale.

Theoretical Implications

Several topics appear relevant for discussion and in the next parts, I will separately present theoretical implications on SNARC effects and implicit cognition as well as clinical implications for future tDCS applications.

Prefrontal Spatial-Numerical Circuits

Limited by the spatial focality and large-scale network implications of the administered stimulations with tDCS, the gathered results complement previous studies on prefrontal spatial-numerical circuitry. Extending the availability of parietal number processing circuits (Dehaene et al., 2003; Hubbard et al., 2005), the current studies are in line with more recent proposals that consistently linked prefrontal areas to spatial-numerical processing and number representations in general (Nieder & Dehaene, 2009). Most prominently, non-human animals showed number-selective neurons in both prefrontal and parietal areas (Nieder, 2016). However, only prefrontal firing was indicative of a magnitude-related processing of absent stimuli (integrating the zero category as numerosity), whereas parietal firing patterns appeared to treat absent “zero” stimuli as a different object category than numerosity stimuli (Ramirez-Cardenas et al., 2016). In human subjects, theories on respective number processing networks were only recently updated to include prefrontal areas, which was proposed to account for white matter connectivity patterns observed following advanced diffusion tensor imaging (Klein et al., 2016). Moreover, TMS of prefrontal areas deteriorated spatial-numerical processing as well (Rusconi et al., 2011, 2013).

Along these lines, the notion of a prefrontal neurocognitive mechanism for implicit spatial-numerical associations accrues consistently and complementary. Furthermore, results are also corroborated by neuropsychological studies: For instance, physical and number magnitude line bisection performance was dissociated by prefrontal cortex damage (Doricchi et al., 2005). Regarding the dissociation between numerical and non-numerical sequences, again, the gathered results are consistent with neuropsychological studies in neglect patients (Zamarian, Egger, & Delazer, 2007; Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006). The modulation of SNARC by tDCS also offers a good opportunity to examine neurophysiological correlates, laterality, and cross-cortical stimulation effects with EEG and fNRIS in the future (e.g., Cutini, Scarpa, Scatturin, Dell’Acqua, & Zorzi, 2014; Keus, Jenks, & Schwarz, 2005).

Theories on the SNARC Effect

Previous theoretical accounts of the SNARC effect have assumed a single neurocognitive source underlying spatial-numerical associations. This reasoning is parsimonious and in line with the principle of Occam's razor, stating that simpler theories are to be preferred over complex ones. Regarding the origins of the SNARC effect, however, I argued that more than a single unified mechanism should be involved in generating spatial associations, at least two (Chapter IV) or up to five (Chapter V). This argumentation departs from the prominent view of a mental number line representation in memory (although it is also not necessarily incompatible with the view that such a representation may exist or not). The main necessity of this multiple-coding framework is based on the empirical observations of dissociating effects in different sequence stimuli induced by the same neurocognitive manipulation.

Origin of SNARC Effects: A Multiple-Coding Approach

More precisely, in the case of spatial-numerical (and space-metric) associations, it is hard to argue that less than two processes are available to produce SNARC effects. In Chapter IV, I observed that tDCS induced a reversed orientation of spatial associations in non-numerical ordinal stimuli, but not in cardinal numbers. It could be argued that this new behavior of a right-to-left directed spatial association was introduced by tDCS for the first time in the tested participants, but this is highly unlikely for two reasons. First, it was never documented that tDCS could *induce* a certain processing, but its mechanism of action rather allows to *modulate* pre-existing activities (but see footnote 3 in Chapter V). For example, the immediate effect of tDCS was attributed to slight modulations in the resting membrane potential by several millivolts, which does not externally induce action potentials, opposed to other transcranial brain stimulation technologies such as TMS. Second, actually, reversed spatial associations were also observed in different studies before, e.g., driven by cultural reading habits (Shaki & Gevers, 2011) or situated task context manipulations (Fischer et al., 2010), suggesting a general availability of both directionalities. Thus, it is more likely to assume that anodal tDCS would enhance a certain cognitive processing than to speculate that the stimulation would externally induce a new behavior.

In fact, multiple number activations in fMRI during a numerical single-task were observed before and suggested different numerical representations to subserve number processing in general (Wood, Nuerk, et al., 2008). The multiple-coding framework for SNARC effects, more specifically, was first introduced by Huber and colleagues following the observation that multiple spatial associations in a delayed working memory paradigm were based on both number magnitude und sequential order (Huber et al., 2016). Moreover, their result was consistent with the absence of both regular and reversed SNARC effects in conditions of a descending magnitude sequence (e.g., 6-5-4) and with the presence of regular SNARC effects in a randomized number sequences (e.g., 6-4-5) in a different study (Lindemann et al., 2008). The original suggestion of Huber et al. (2016) was that both long-term spatial number representations and temporary working memory associations of sequential position can influence behavior independently and even cancel each other out in respective paradigms. However, this model does not account for the reversal of non-numerical associations during anodal tDCS (Chapters IV and V), because neither long-term representations nor temporary sequential-order based associations are assumed to be reversed in those cases.

It is important to highlight that the general position of independent processes for numerical magnitude and sequential position in a multiple coding framework does not necessarily imply a long-term memory representation of number as the cause for spatial associations, as it was long conceptualized in the mental number line metaphor. Instead, it is (at least) equally possible that multiple spatial associations of number and serial order emerge at the level of working memory. The following augmented WM account of the SNARC effects elaborates this concept. Nevertheless, the necessity of a dual-processes (or multiple-processes) model is uncontested also in this account. A single process – as proposed by previous models – could not account convincingly for the discriminatory behavior in the explored combinations of stimuli and electric stimulation, even considering that slightly different long-term representations of sequential or numerical items were stored due to previous experience (Abrahamse et al., 2016). Eventually, the existence of multiple spatial coding mechanisms is also more compatible with neuropsychological evidence and situated modulations, because the account can easily incorporate the observed switching to previously indecisive at-rest processing routes. To consider the linguistic influences of markedness correspondence next to sequential-order working memory, the present model update proposes several mechanisms to flexibly coordinate available resources with environmental stimuli for implicit mental simulations, e.g., as indicated by SNARC or SNARC-like behavioral effects.

An Augmented WM Account of the SNARC Effects

Yet, another alternative to the proposed multiple-coding framework will be discussed here rather generally. Actually, particularly the minor inconsistencies in the replication of the reversal of the non-numerical sequence in Chapter V led me to believe that the presence of different tasks could modulate the processes involved in generating spatial associations. However, it could also be the case that the single process for implicit associations was already modulated by the presence of both numerical and non-numerical sequences. For example, when participants were confronted with numerical and non-numerical stimuli in the experiments, they might flexibly create a joint spatial representation of the two sequences to prepare and allow for optimal performance. In other psychological tasks, such context adaptation effects were readily observed when only the relative occurrence of types of trials was changed without informing participants in the context-specific proportion congruency Stroop paradigm (Crump, Gong, & Millken, 2006). In the present results, this form of context adaptation would be particularly compatible with a parallel session design in Chapter IV (i.e., participants knew with high fidelity during the stimulation session that two sequences were being tested from their previous experience in the baseline session). The joint spatial representation of all tested sequences could also explain different effect sizes of anodal tDCS across studies. Instead of modulating the spatial association mechanism, anodal tDCS could have then led to a more optimal strategy that incorporated all sequence items in a single framework, however, in (partially) opposed directionalities. Since single mechanisms are the more parsimonious explanation according to Occam’s principle, this possibility should be explored. For example, empirical tests of performance on a non-numerical sequence alone (and without another task requiring spatial associations) have to be examined concurrent to prefrontal neuromodulation with anodal tDCS and contrasted to the behavior which was observed in Chapter II (Exp. 2). This line of reasoning may also partially account for other results such as the observation of spatial-numerical associations (next to spatial-positional associations) in the delayed working memory paradigm by Huber et al. (2016). As it was also argued by Abrahamse et al. (2016), the presence of different sequence lengths within a session could have drawn attention to cardinal set-size information, rather than ordinal position information, and thus enhanced spatial associations of number magnitude (Huber et al., 2016).

In sum, however, a multiple coding framework is more likely than a single WM process that arranges all items alike onto mental space, given all present considerations. In particular, the low correlation between the cardinal and ordinal SNARC effects as well as their dissociations are hard to reconcile along a single WM mechanism. Rather, the distinctions between ordinality and cardinality and the psychological elaboration of salience or markedness appear to determine behavioral responses to tDCS, which are, in turn, best accounted for by the multiple-coding framework elaborated in Chapter IV. Interestingly, corroborating this notion of pre-existing distinctions, a recent study in preliterate children also demonstrated different spatial-numerical directionalities for counting activities incorporating ordanilities, numerosities, or fingers (Patro & Haman, 2018). Also consistent with tDCS results that were observed in studies by other research groups (i.e., Di Rosa et al., 2016), a hybrid and augmented WM account also considering markedness principles is required.

Furthermore, the suggestion of coding mechanisms for number and order independent from the visual spatial modality is underscored by results from blind participants. Here, consistent with the evidence for multiple codes involved in order-based and cardinal SNARC effects, associations between sequential order and space were not found in early-blind participants, but only in late-blind and sighted participants in an auditory variant of the delayed WM paradigm (Bottini, Mattioni, & Collignon, 2016). In contrast, SNARC effects were identical in sighted and early-blind participants in another study (Castronovo & Seron, 2007), which in sum nicely complements the outlined dissociations between spatial associations for ordinality and cardinality. Moreover, the presence of SNARC effects in congenitally blind participants is consistent with the proposal of non-visual spatial coding mechanisms based on verbal processing and markedness correspondence.

The original WM account of the SNARC effect only holds for certain conditions, e.g., additional Go-Nogo tasks (Ginsburg & Gevers, 2015). Moreover, the WM account could not explain the dissociations obtained in Chapters IV and V, as well as other results. Because further assumptions have to be made in order to account for findings such as parallel spatial associations of cardinality and ordinality (Huber et al., 2016), the theory is degenerative. An alternative proposal is made in Table 7.2 which augments the core assumptions explicated in Abrahamse et al. (2016). Moreover, the augmented assumption 2 also considers the enculturation perspective which was introduced to define directionality of spatial-numerical associations (Patro, Nuerk, & Cress, 2016).

Finally, another reconciliation of the sequential order working memory account of the SNARC effect was proposed by drawing onto long-term memory activations within working memory performance. Specifically, this generic proposal was supposed to include modern conceptions of working memory that include long-term memory activations by shifting the focus of attention and coordinating active and passive sets (e.g., stimuli and memories) within a flexible, capacity-limited region of direct access (e.g., Oberauer, 2002). Such accounts can easily also incorporate dissociations between SNARC effects by assuming long-term memory activations; however, the account does not explain reversals in directionality, because a reversed long-term representation based on (reversed) experience should be the exception in Western participants. Future designs may test whether there is a coordination of all sequential stimuli along spatial templates within the region of direct access or whether multiple mechanisms (such as polarity correspondence, implicit semantic spread of activation, or salience processing mechanisms) compete to contribute to implicit associations in different settings.

Table 7.2. Augmentation of Core Assumptions of the WM Account of the SNARC effect.

	Core Assumptions of Original WM Account (Abrahamse et al., 2016)	**Augmented Assumptions**
1	"Multiple number items are spatially coordinated at the level of working memory by binding them to an active spatial template from long-term memory"	Spatial associations can emerge from spatial templates or from markedness-based verbal association
2	"Number items trigger global left-to-right orientation in working memory due to experience"	Left-to-right orientation is based on experience, enculturation, or on the markedness of left-right and instruction polarities
3	"Long-term memory contains – besides item representations – a representation for ordered item sets that are used frequently and systematically (i.e., canonical number set 1–9)"	–
4	"Spatial codes are generated through referential coding of a current target's match in the working memory set relative to the item midway the set"	Associations emerge due to referential coding, visualization, spatial-verbal instruction, correspondence of markedness codes, or other (non-verbal) processes at the stage of working memory
5	"Multiple item sets can be active in working memory simultaneously"	Multiple spatial-coding strategies compete dependent on available neurocognitive resources

Table Note. – = no adjustment required.

Taxonomy of Spatial-Numerical Associations: Need for an Update?

According to the taxonomy of spatial-numerical associations (Cipora, Patro, & Nuerk, in press; Cipora et al., 2015, Patro et al., 2014), the implicit directional codings of cardinality vs. ordinality constitute different types of spatial associations. Furthermore, situated influences were documented for both types of processing (although most studies show situatedness of ordinality). These distinctions are in line with the results obtained in the current studies.

However, taking into account also the elaboration of potential mechanisms, it is currently unclear whether spatial coding processes can actually invoke both types of spatial associations (e.g., as proposed by Abrahamse et al., 2016) or whether distinct spatial coding processes are available (e.g., as suggested by Huber et al., 2016). Instead, it could be possible that both cardinality and ordinality information get flexibly mapped onto space by means of a verbal markedness mechanism (e.g., MARC effects), by means of a working memory mechanism, or a retrieval operation from long-term memory. The dominance of either coding strategy may be determined by contextual variables and neurocognitive resources. These possibilities are also sketched in Figure 7.1.

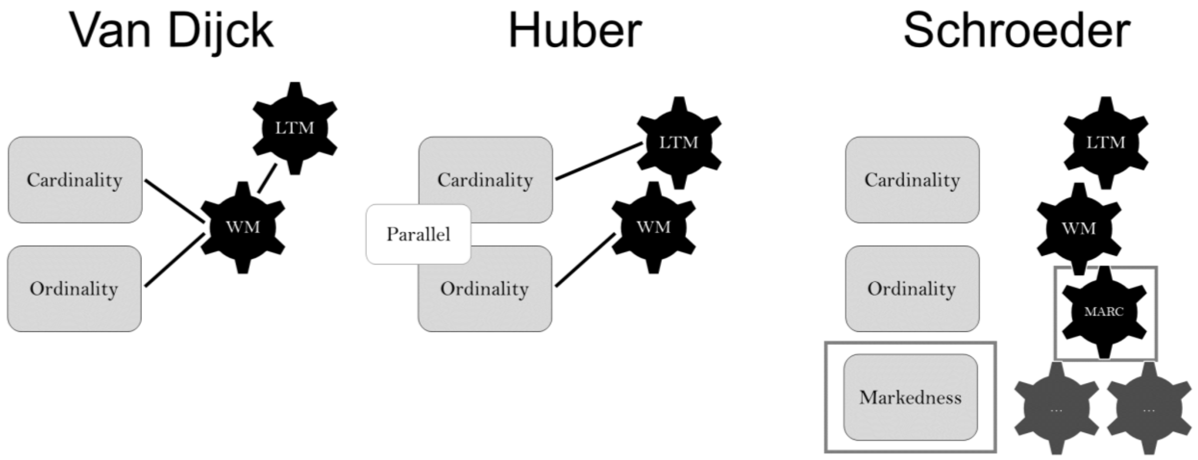

Figure 7.1. *Different WM accounts of spatial-numerical associations. Van Dijck et al.'s accounts (2011; Abrahamse et al., 2016) argue for a single WM mechanism that arranges cardinal and ordinal stimuli alike onto a spatial template drawn from long-term memory (LTM). Experience may also lead to a LTM mental number line. Huber et al. propose parallel associations that emerge from WM processes for ordinal information and LTM retrieval of cardinal spatial associations. The current proposal includes additional mechanisms such as MARC that can process features of both cardinal and ordinal information and possibly*

modulate WM, LTM, as well as their interactions with stimuli as well, but either code may become dominant during a measurement (trial) due to situated influences.

How to Reconcile tDCS Effects in Different Implicit Cognition Paradigms?

Since above discussion focused on implicit spatial associations in case of the SNARC effects, the generalization to non-spatial Implicit Association Test (IAT) effects in Chapter VI was not elaborated so far. In this experiment, relative implicit associations between insect pictures and negative words were referenced to flower pictures and positive words in different blocks of a double classification task. Similar to the effects of cathodal tDCS on spatial-numerical associations, I could show reductions of the implicit cognitive bias also in this paradigm. However, while this type of generalizability of stimulation effects appears to be quite consistent with the notion of implicit associations in general at face validity, the result is actually predicted by the polarity correspondence principle and, less obviously, it also lines up consistently with the observations of reversed tDCS effects in the non-numerical sequence.

Although IAT effects are often referred to as semantic mental links between objects and evaluations (i.e., in case of valence attribute decisions), other cognitive processes are thought to be at play as well. More precisely, behavioral performance in the test blocks of the classical insect-flower IAT may not exclusively reflect an automatic evaluation of insect vs. flower pictures as them being negative or positive. Instead, those categories also include a certain degree of asymmetry in terms of salience, which usually leaves one polarity of the two classification antagonisms more salient than the other. For instance, it is largely acknowledged that negative information would be more salient than positive information, e.g., which can lead to faster responses to negative stimuli in a negativity bias (Kanouse & Hanson, 1972).[16] The same type of asymmetry is assumed to be present in the artificial insect-flower dichotomy, with insects being more active, dangerous, self-relevant, thus also more salient. As a consequence, the respective two salient polarities (and the in-salient ones as well) share a common feature,

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[16] On this occasion, a first cross reference to the effects of linguistic markedness on cognitive processing speed may be appropriate: Here, the unmarked category member (e.g., a mark may be indicated by a pre- or suffix, or by more specific use cases) is usually faster responded to than the marked member, as exemplified by lengthened response times in the odd effect (German: “ungerade” = “uneven” = odd; Clark, 1969; Hines, 1990; Iversen et al., 2006). In the remainder of the discussion, I will introduce the possibility that these distinct effects may be traced back to a common origin in the cognitive fluent processing of psychological markedness.

which can speed up or interfere with fluent cognitive processing in the congruent and incongruent block constellations of the test, respectively.

Some experimental psychological findings can be referenced in order to corroborate this view: First, in the seminal study by Rothermund & Wentura (2004), the authors argued that several IAT effects rather indicated shared saliences between targets and attributes than semantic associations. This was reflected in correlations between search task performance for the different stimuli used in the test with the size of individual IAT effects (Experiments 2A & 2B). Moreover, the authors could impose a Go/ Nogo search detection task to change the underlying saliences of stimuli and thereby they successfully (temporally) reversed IAT effects (Exp. 3). The assumption of their figure-ground model is that *negative* and *insect* categories reflect the more salient *figure* category, possibly along with an increased self-relevance and a more fluent access to cognitive processing. The reversed IAT effects were then observed because *figure-ground* saliences were temporally reversed when attention had been allocated to one of the (per default) insalient categories in the search task.

This reasoning also accounted for another paradoxical result observed in a different IAT study that investigated the effects of replacing the flower category with a non-word category (e.g., insect names vs. meaningless letter sequences were classified as insects vs. non-words). Surprisingly at first, this manipulation led to faster responses (IAT effects) for shared responding to insect targets and positive attribute words (Brendl, Markmann, & Messner, 2001). This reversed effect was later replicated and accounted for by the assumption that non-words were relatively more salient than insect stimuli, allowing for responding based on salience asymmetries (Meissner & Rothermund, 2015). Thus, pairing of *insect-positive* and *non-word-negative* classifications to a more general *yes-no* classification could have facilitated the task and effectively produced the observed effects (this assumption was also referred to as recoding), which constituted one of the several mechanisms which are nowadays thought to be involved in IAT effects (Fiedler, Messner, & Bluemke, 2006; Meissner & Rothermund, 2013; Mierke & Klauer, 2001). A more general theoretical account elaborated the IAT measurements to indicate different conceptualizations of similarity, including semantic associations, perceptual similarity, and also the dynamic influences of salience asymmetries (De Houwer, Geldof, & De Bruycker, 2005).

Considering the markedness correspondence model as the most convincing explanation for the results in weekday and month series in Chapters IV and V, our previous suggestion was that the task instruction classification introduced marked vs. unmarked features in both stimulus-and response-dimensions, namely, in terms of the *earlier*-vs.-*later* classification and the *left*-vs.-*right* response hand decision. Although markedness was defined by drawing on linguistic features, it may be plausible to relate the concept to a psychologically relevant process of salience, similarity, or fluency (which may be informed by linguistic structures, or vice versa). In this case, effects of tDCS on implicit associations in general could actually reflect a modulation of similarity feature processing, akin to polarity correspondence. Possible psychological components of markedness may be continuously shaped, experience-based, prone to individual differences, embodied, and situated, whereas linguistically defined markedness may reflect its grounded compartment in an embodiment framework. Please note that, although this account further specifies the assumed mechanism at work, it is again only plausible within a multiple-coding framework because left-to-right oriented spatial associations of weekdays or months are not accounted for by the markedness correspondence.

Although a common framework based on polarity correspondence is appealing, some limitations have to be discussed as well. Eventually, the constraints that were outlined in different previous studies also affect this proposal of the stimulation framework.

Problems with Polarity Correspondence

The general conception of polarity correspondence was recently challenged by several empirical and theoretical constraints. Actually, already Chapter II includes a result which is inconsistent with the proposal of polarity correspondence by demonstrating a dissociation between location-based stimulus-response compatibility effects and the SNARC effect, which were subsumed to a common class of effects by the theory (Proctor & Cho, 2006). How can a markedness correspondence account based on salience asymmetries account for this dissociation and other challenging empirical findings?

First, regarding the present (and previous) dissociations between SNARC and Simon effects in terms of differential time courses, additivity (Mapelli et al., 2003), and distinct malleability to prefrontal cathodal tDCS (Chapter II), different mechanisms are likely involved in these two effects. However, this is already reflected in the physical availability of a spatial code vs. the mental availability of salience codes, which may be retrieved from a spatial response dimension. Thus, the markedness correspondence accounts actually posits a different form of neurocognitive processing at the core of explicit vs. implicit effects, in line with this basic distinction in the taxonomy of space-number associations (introduced by Cipora et al., 2015).

Next, different empirical and theoretical limitations of the polarity correspondence account were raised in research on embodied cognition of metaphorical thinking. Here, comparable to the SNARC effect, correspondence effects between abstract concepts and spatial dimensions are observed. The effects are thought to indicate spatial mental simulations as a grounded mechanism to achieve meaningful metaphorical mental representations. For example, in three experiments, Dolscheid & Casasanto (2015) observed associations between pitch and verticality (high vs. low, and tall vs. short), but they could not outline pitch associations with spatial frontoparallel (front vs. back) or spatial extension (big vs. small) dimensions. In their conclusion, this pattern of results favored metaphorical thinking over markedness or polarity correspondence (Dolscheid & Casasanto, 2015), because a markedness account would assume associations based on linguistic dimensions for all tested dimensions. In order to maintain a markedness correspondence view, it must be acknowledged that psychological markedness association processes can deviate from purely linguistic definitions and that certain criteria of similarity may have to be met such that associations actually become behaviorally relevant. For instance, I argued in Chapter IV that markedness-based spatial associations of temporal order (i.e., SNARC-like effects for weekdays and months) are deactivated by default and can be re-established, e.g., using cortical neuromodulation and task manipulations. In line with this sort of task-selectivity, spatial associations for grammatical number based on SNARC or on markedness correspondence appeared to compete with different outcomes for surface processing, lexical processing, or quantity-relevant and quantitiy-irrelevant semantic decision tasks (Roettger & Domahs, 2015).

In another critical approach, Santiago & Lakens (2015) studied the effects of response eccentricity on vertical location-based stimulus-response compatibility (orthogonal Simon) effects, on SNARC effects in parity and magnitude judgment tasks, and on SNARC-like effects for temporal order (past vs. future). Importantly, in contrast to the study of Schiller and colleagues (Schiller, Eloka, & Franz, 2016) who varied the distance between response keys without noting a modulation of SNARC effects, Santiago & Lakens (2015) manipulated response saliences by placing their participants' response keyboard on their left- vs. their right side (referred to as manipulation of eccentricity). In their first experiment, left-side responding to upwards presented targets produced faster responses (i.e., the orthogonal Simon effect), but this effect was dramatically abolished when the keyboard was placed to the participants' right-side (supposed to change left-right saliences), showing that their manipulation was effective. Still, neither SNARC effects in any of their three experiments were modulated, which basically dissociated with the observed modulation of location-based spatial compatibility effects in Exp. 1 and provided evidence against a pure polarity correspondence account of the effects under study (Santiago & Lakens, 2015). Note that Proctor & Xiong argued that the modulation of SNARC effects by keyboard eccentricity was predicted by polarity correspondence only for the magnitude judgment task and that a numerical difference was actually present as hypothesized in the respective data, leaving the actual presence or absence of this effect unclear (Proctor & Xiong, 2015).

Complementary to the explanations provided by the authors (Santiago & Lakens, 2015), the polarity correspondence account of the orthogonal Simon effect reversal (e.g., the notion that salience would be increased for placing response sets on different relative locations) was actually not identical with the markedness-based view. More precisely, if verbal processing was dominant in markedness-based correspondence effects such as SNARC (or also future-past temporal order classifications), physical salience modulations should not be effective in changing linguistic markedness patterns. In contrast, the location-based orthogonal Simon effect includes spatial codes in the visual dimension, raising the possibility of modality-specific processing and correspondence effects that are guided by the visual modality as well, where a left-right salience may indeed inverse for attending to left-side or right-side locations (but a verbal linguistic-based salience may remain stable for this manipulation).[17] Moreover, as noted above, whereas it is true that the original polarity correspondence account does not account for the observations of Santiago & Lakens (2015; pending the debated presence or absence of effects in magnitude judgment SNARC tasks), the notion of markedness-based salience asymmetries does consider their observed dissociation between experiments as well as their proposed alternatives and the conceptual metaphor view. Precisely, the proposed multiple coding framework supposes that certain test situations and stimuli allow for different processing such as verbal markedness, flexible or automatic retrieval of spatial associations, or WM processing of verbal or nonverbal aspects (such as metaphorical spatial simulation).

Thus, as it was explicated above, the presented markedness correspondence account eventually lines up also with the generalized effects when considering salience asymmetries in a shared theoretical model. Regarding tDCS effects, this model and the underlying verbal-linguistic

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[17] One could even consider the reverse case that linguistic markedness-based polarities were reversed for placing a keyboard to the right and framing the left-hand key as being *close* to the center.

processes are consistent with a reduced (or increased) left-hemispheric verbal processing of markedness and IAT effects. Although some empirical questions remain unaddressed so far, I will proceed with a theoretical elaboration of the consequences in a preliminary neuropsychological appreciation of markedness and markedness correspondence, based on psycholinguistic, experimental psychological, and neurocognitive evidence.

Towards a Psychology of Markedness

Linguistic studies offer precise (yet partially varying) definitions on the concept of markedness. Mostly accepted key aspects include formal, distributional, and semantic marking of language. For example, unmarked terms are void of pre- and suffixes, less restricted in use (or independent of the complementary term), or less specific in semantic meaning (Lyons, 1977). However, in the field of linguistics, the markedness concept was also exposed to criticism. Recently, Haspelmath carved out 12 distinct senses of markedness covered by complexity, difficulty, abnormality, and multidimensional correlation, but he acknowledged that structural markedness asymmetries may be better and more directly accounted for by other factors such as frequency asymmetries or phonetics (Haspelmath, 2006). Regarding psychological effects, not all of those senses of linguistic markedness are systematically evaluated in terms of their behavioral outcome, latent structure such as constructive or divergent validity, or consequences in applied settings. In principle, marked features are acquired later in development and lead to worse performance. Particularly later Chomskyan views reflected markedness as generative structure in procedural discovery and learning (Battistella, 1995; Chomsky, 1965; Jakobson, 1932). However, it is not yet sufficiently examined whether a common neuropsychological substrate was involved in cognitive processing beyond the distinct formal senses of markedness. Furthermore, different linguistic constellations can impair otherwise unrelated topics such as mathematics education (Daroczy, Wolska, Meurers, & Nuerk, 2015). Regardless of the underlying linguistic controversy, markedness taxonomies provide a powerful explanatory framework for psychological observations as well (see also Chapters IV and V).

Despite this, linguistic markedness alone comes short in explaining key experimental findings which appear to indicate that marking can also result from nonlinguistic psychological processes. As described above, reversals of the vertical location-based Simon effects from eccentricity manipulations (i.e., relative response device position) were attributed to changes in the saliences of the responses (Santiago & Lakens, 2015). Such manipulations must draw on nonlinguistic factors, since the verbal markedness of horizontal response labels hardly vary by a perceptual and situational manipulation such as eccentricity, unless participants (or instructions) utilized inverse global spatial frames of reference or actively recoded left vs. right response labels; this is highly unlikely to be the source of variation in the respective experiments (Proctor & Cho, 2003; Santiago & Lakens, 2015). Thus, the effects of relative response eccentricity on orthogonal Simon effects constitute a first example of nonlinguistic sources of markedness correspondence, if the orthogonal Simon effect was at all considered to be markedness-based (but see Proctor & Cho, 2006; Umiltà, 1991; Weeks & Proctor, 1990). Some additional results are discussed in the following which are more directly linked to the cognitive markedness processing in stimulus-response compatibility effects.

First, one primary and possibly the most established index of markedness correspondence is present in the parity-space associations also sometimes referred to as MARC effect (Berch, Foley, Hill, & McDonough Ryan, 1999; Nuerk et al., 2004). Its central result describes relatively faster left-hand than right-hand responses to odd digits and relatively faster right-hand than left-hand responses to even digits. This pattern was best accounted for by linguistic markedness and correspondence effects between the marked (left-hand + odd) and unmarked classification dimensions (right-hand + even). However, a purely linguistic account was ruled out by the observation of reversed parity-space associations in strong left-handers (Huber et al., 2014). Moreover, spatial associations of emotional valence (right-hand + good, left-hand + bad) were found to co-vary with individual handedness (Casasanto, 2009). Interestingly, also in deaf signers, a reversed parity-space MARC effect was found (Iversen, Nuerk, Jäger, & Willmes, 2006). It was suggested that this reversal was related to the specific way of displaying “1” as the prototypical odd number in DGS sign (1 = thumbs up), which is also used to indicate “good”, “okay”, and other unmarked features (see Leth-Steensen & Citta, 2016, for even-is-good association). In addition, the DGS sign “left hand” implied touching the left arm with the right hand, leaving some ambiguity regarding encoding of linguistic markedness features (Iversen et al., 2004, 2006).

Next, situatedness of spatial associations challenges the assumed fixed nature of markedness-based associations and shows flexibility, possibly involving different coding strategies (see Chapter VI for suggestions). It was hypothesized that right-handed bodily experiences may shape a stance of markedness through motor fluency (de la Fuente, Casasanto, Martínez-Cascales, & Santiago, 2016; de la Fuente, Casasanto, & Santiago, 2015). Conversely, valence words biased perceptual judgments through activation of motor fluency simulations (Milhau, Brouillet, Dru, Coello, & Brouillet, 2017) and a response device artificially hindering motor fluency modulated spatial associations of valence temporally (Casasanto & Chrysikou, 2011; Milhau, Brouillet, & Brouillet, 2014). At least in these first study results, the temporary coding of horizontal markedness was related to both long-term and short-term motor fluency.

If linguistic markedness was their exclusive source, SNARC and MARC effects should not be observed in nonverbally communicating non-human animals. Yet, chimpanzees showed better performance when small-to-large magnitudes in a visual display were arranged from left-to-right, mimicking the typical shape of the SNARC effect (Adachi, 2014). Notably, a recent investigation in nine gorillas and orangutans documented horizontal SNARC-like effects in a non-symbolic magnitude judgment task, but also remarkable amount of individual variability (Gazes et al., 2017). In a highly influential study, newly hatched chicks showed a leftwards (rightwards) directed preference for relatively smaller (larger) nonsymbolic magnitude displays (Rugani et al., 2015) and eye-tracking/ habituation studies revealed similar results in new-born children (Rugani & de Hevia, 2017). In preverbal children, a short training further induced directed and reversed SNARC-like effects (Patro, Fischer, Nuerk, & Cress, 2015). A possible general influence was discussed in the functional lateralization of brain regions, which, however, does not offer a unified view because within- and across-species variability has to be accounted for (Patro & Nuerk, 2016). Also in the avian brain, it was shown that most chicks would count from left-to-right in experiments on ordinal pecking of the 4th element in frontoparallel rotated search task. In the same study, interestingly, a minority of right monocular chicks pecked at the 4th right element (Rugani, Vallortigara, & Regolin, 2016), lending evidence on the hemispheric asymmetry hypothesis, but also somewhat reflecting handedness effects in human adults. Note that the lack of corpus callosum in chicks and other methodological challenges restrict the significance of inferences drawn from these animal studies for conceptions of human cognition, e.g., because novelty-based processing may determine chicks' leftward orienting in some stimulus conditions more often than in other ones (Patro & Nuerk, 2016; Núñez & Fias, 2017). A more general psychological conception of markedness including motor and perceptual difficulty, possibly influenced by fluent brain lateralization, may conveniently enfold these findings from animal studies as well. This may particularly dovetail with the Chomskyan approach to markedness as a psychological principle which defines defaults and preferences in language acquisition (Battistella, 2005, p. 65; see also Jakobson, 1968). It may prove further insightful to differentiate psychological effects that seem to draw on linguistic markedness in terms of the detailed descriptions of rarity, difficulty, or complexity (or other detailed feature) of verbal material instead (Haspelmath, 2006).

Finally, it is important to consider that neurocognitive mechanisms of the IAT effect along a difficulty or salience asymmetry perspective departs from the most prevailing view that IAT effects would reflect a long-term memory existence of covert attributes much like personality variables. Nevertheless, also non-spatial implicit associations in the IAT effect include nonlinguistic personal moderators.[18] For example, in the assessment of evaluative IAT effects for East- and West-Germany (which were politically and physically divided until 1989), the habitants of each respective country side showed orthogonal effects, effectively always showing faster responses to positive stimuli paired with their residence, and vice versa (Rothermund & Wentura, 2004). Interestingly, variability in specific IAT effects was related to symptomatology or behavior in psychiatric conditions (De Houwer, 2002; Roefs et al., 2011).

To conclude the discussion, a careful first suggestion of a psychological account of markedness appears to involve linguistic processes in terms of difficulty, but also perceptual and motor fluency in terms of their asymmetric coding in categorical dimensions. Eventually, psycholinguistics may reflect mutual language-culture dependencies and developments, which could inspire further psychological studies. Neural networks may preferentially respond to easier stimuli as conceptualized by psychological markedness, which is flexibly encountered for by prefrontal activity patterns.

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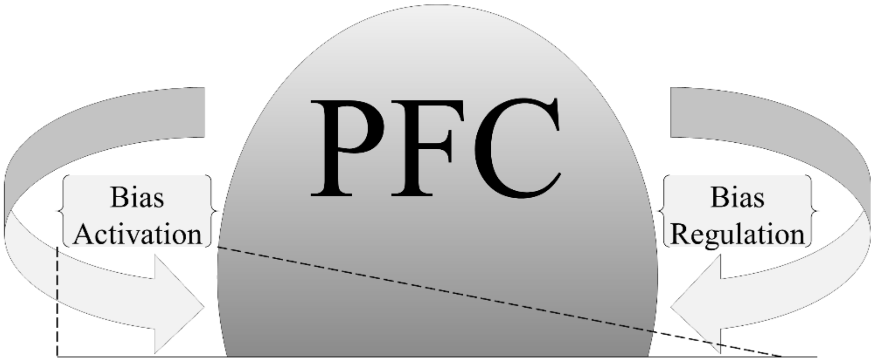
[18] Certainly, the comparability between IAT effects and much simpler stimulus-response compatibility effects like SNARC or MARC effects is not clear and there are no diagnostic studies so far. However, at group level, also respective IAT procedures yielded parity-space associations (e.g., MARC effects; Kinoshita & Peek-O'Leary, 2006) as well as number-space associations (e.g., SNARC effects; Fischer & Shaki, 2016), which provides some preliminary hints that the different tasks may involve one or more common source(s) of cognitive processing.

Clinical Implications I: Balancing Bias Regulation and Bias Activation

Executive functions play a central role in higher-order cognitive processes. Deficits in executive functions such as cognitive control are hypothesized to pervade psychiatric conditions in various forms, either specifically as for instance related to emotional control in major depression, or generally as for instance related to working memory deficits and hypofrontality in schizophrenia. Thus, the perspective to enhance (or rehabilitate) executive functions is one major pillar of contemporary neuropsychiatric therapies, including stimulation with tDCS (Plewnia, Schroeder, & Wolkenstein, 2015). Bottom-up processing, in contrast, is not always considered as malleable by therapeutic and neurophysiological intervention.

Given their automatic and unintended character, implicit cognitive biases could be seen as bottom-up processing as well. Despite this, even computational models of cognitive control acknowledge a central role of PFC firing for the active maintenance of internal patterns (Botvinick & Cohen, 2014). In fact, the PFC was thought to serve to the “active maintenance of patterns of activity that represent goals and the means to achieve them” already in early models of conflict monitoring (Miller & Cohen, 2001, p. 171). Possibly, it would be more appropriate to conceptualize such maintenance processes to the neuroscientific elaboration of working memory networks (D’Esposito & Postle, 2015). In any case, activation and/ or maintenance of implicit biases offers a target for neuropsychiatric rehabilitation. Arguably, my studies show that this type of *bias activation* can be targeted directly with cathodal tDCS.



„Implicit Associations“
- Domain-General
  - Verbal Processes
    - SNARC Effect: Markedness Polarities
    - IAT Effect: Figure-Ground Reversal
- Domain-Specific
    - SNARC Effect: Finger Counting, Mental Number Line, etc.
    - IAT Effect: Personal Group Membership, Disease, etc.

Figure 7.2. *Bias regulation and activation could both draw on prefrontal cortex activation. Maintenance of biased signals is conceptualized in and subserved by WM processes. Implicit associations furthermore include domain-general processes such as verbal salience markedness processing, but there are also domain-specific influences. Examples include situated, embodied, and grounded influences in the SNARC effect, or personal group membership and psychiatric condition in IAT effects. Reversed stimulation effects could be suspected in tasks that reverse figure-ground categories in the IAT effect (e.g., Rothermund & Wentura, 2004), comparable to the differential effects in numerical magnitude vs. sequential order judgment (Chapters VI and V). Importantly, due to the lack of empirical tDCS evidence, lateralization of bias activation vs. regulation is not clarified and likely more complex than suggested by the figure.*

In dual-process models of cognition, a balance between controlled processing and automatic activations is described (e.g., Strack & Deutsch, 2004), and such models have also motivated respective modification paradigms with therapeutic potential (Friese, Hofmann, & Wiers, 2011). Notably, implicit processes are already documented to play a role in several neuropsychiatric conditions such as eating disorders or addiction (De Houwer, 2002), at least as evidenced by group differences and by some positive correlations with explicit behavior or symptoms (Greenwald, Poehlman, Uhlmann, & Banaji, 2009; Vahey, Nicholson, & Barnes-Holmes, 2015). For example, implicit associations could influence decision-making and critical behaviors in the domains of eating (Hofmann, Rauch, & Gawronski, 2007), spontaneous shyness (Asendorpf, Banse, & Mücke, 2002), or alcohol consumption (De Houwer, Crombez, Koster, & De Beul, 2004; Wiers, Van Woerden, Smulders, & De Jong, 2002). In a meta-analysis comprising 122 research reports, the predictive validity of IAT measures for later behaviours was particularly pronounced for socially sensitive topics (such as intergroup behaviour) and incremental to the predictive validity of self-reports (Greenwald et al., 2009). Conversely, changes in implicit associations of panic could significantly predict amelioration of panic symptom severity (Teachman, Marker, & Smith-Janik, 2009). A more recent special issue highlighted diversity and promise of implicit measures for understanding and implementing health behavior based on methodological sound investigations (Sheeran et al., 2016).

Extending this framework, the current series of stimulation results implies that the implicit, unintended, and presumably automatic activation of cognitive processes could be blocked by application of cathodal tDCS. Intriguingly, although tDCS was administered to the same anatomical structure (dLPFC), anodal and cathodal tDCS could still encompass different functional targeting (and anatomical targeting) due to concurrent task-induced neurocognitive activities. Nevertheless, anodal tDCS over medial PFC significantly reduced IAT effects in the racial bias (Sellaro et al., 2015) whereas anodal tDCS over dorsolateral PFC increased non-emotional IAT effects (Gladwin, den Uyl, & Wiers, 2012), orthogonal to the effect of cathodal tDCS reported in Chapter VI. In sum, these studies present first promising evidence, but further dissociative results in identical task settings are required to convincingly distinguish a medio-lateral prefrontal gradient for bias regulation vs. bias activation stimulation rationales. In addition, it is currently not known whether cathodal tDCS exerts serviceable results in clinical populations as well and studies on implicit processes in psychopathological conditions need to be performed in patient populations who may respond differentially. The bias activation rationale could amend other possible approaches to utilize the inhibitory effects of cathodal tDCS in neuropsychiatric conditions (Schroeder & Plewnia, 2016).

Finally, acknowledging that IAT effects and SNARC effects both constitute indirect evidence of implicit associations in distinct domains and instruments, it is important to acknowledge the presence of multiple mechanisms beyond individual effects both in general, but also individually (Figure 7.2). More precisely, the neuromodulation capability of both effects by tDCS could indicate the presence of one shared mechanism, which is most likely instantiated through verbal working memory processing. Domain-specific mechanisms, on the other hand, should not be entirely neglected, as those may also render the direction of a stimulation outcome, as observed in Chapters IV and V. Note that the dissociating stimulation effects for ordinality-based classifications were actually consistent with a common stimulated markedness correspondence process, for which linguistical markedness poles were reversed in the before-after classification task and thus process was inactive during sham stimulation. However, differences in the spatial associations of these numerical and non-numerical sequential stimuli also indicate that other cognitive mechanisms (next to the stimulated verbal code) are dominant in the ordinal month name / weekday vs. cardinal number series without stimulation. More precisely, if the verbal markedness process was most dominant in assessments without concurrent tDCS, SNARC effects should be oriented leftwards for numbers, but rightwards for weekdays. In behavioral experiments, this was not the case (e.g., Gevers et al., 2003, 2004; Chapter III), suggesting that the verbal markedness process was not active or suppressed in non-numerical sequence stimuli without concurrent tDCS.

Finally, entirely domain-specific processing should be briefly mentioned, for instance, given the link between embodied number processing and spatial-numerical associations in finger counting. Likewise, domain-specific processes should be also attended when applying the developed stimulation rationale to other IAT effects, such as alcoholism, math-gender associations, or other types of implicit bias.

Limitations of the Bias Activation Approach

For several reasons, the current results are still insufficient for practical realization of this stimulation rationale in respective clinical trials and protocols. First, although some generalizability was shown, it is currently not examined whether critical tests of derailed implicit associations in different disorders are malleable by tDCS as well. Next, it is not established whether there is a long-term effect or whether the stimulation effects can be transferred to symptom amelioration. This is particularly critical in the case of the IAT, whose predictive validity was criticized before (Fiedler et al., 2006). For example, it could not be excluded that a modulation of implicit associations by cathodal tDCS constitutes an epiphenomenon (possibly due to recoding of task labels or verbal processes) without actual relevance to direct impairments or symptoms. Thus, basic research is still required before the efficacy of the cathodal tDCS configuration can be systematically examined in clinical trials.

External validity. By examining well-established computerized measurement tasks in experimental psychology, it remains ambiguous how a possible stimulation effect would translate into observable behavior under non-laboratory circumstances. Regarding spatial-numerical associations, it was observed that implicit effects could also influence overt action decisions, e.g., when deciding between players that are situated on a leftward and a rightward location from oneself (Schroeder & Pfister, 2015) or when turning to the left or right without intention (Shaki & Fischer, 2014). However, correlations with arithmetic skill are scarce (Cipora et al., 2015). In research on the IAT, transfer to overt behaviors was more throroughly assessed (at least regarding stereotypes and clinical psychology). More elaborated theories on external validity state in their essence that the real-world implication of implicit associations in the IAT are most relevant to situations in which fast decisions are required, possible under cognitive load (Greenwald et al., 2009). Moreover, implicit associations deviate from explicit self-reports (divergent validity), thus highlighting that under usual circumstances, cognitive control processes allow for deliberate decisions different from the test situation, where the implicit association is more influential and less relevant to the actual task. In explicit assessments, it is also possible to bias the own self-reports (regarding both actual beliefs or intended misreport) to comply with socially acceptable views.

Finally, some correlations were observed in clinical symptoms. For example, implicit associations indicating drinking identity predicted alcohol consumption (Lindgren et al., 2015), (under)weight-based positive associations predicted drive for thinness (Ahern, Bennett, & Hetherington, 2008), and implicit associations between approach words and high-calorie palatable food were documented in obese participants (Kemps & Tiggemann, 2015). Conversely, reductions in self-anxious implicit associations accompanied successful psychotherapy of social anxiety (Gamer, Schmukle, Luka-Krausgrill, & Egloff, 2008).

Long-term effects. Obviously, longevity is a critical aspect of any training or therapy. Longer lasting effects must be examined in longitudinal designs including standard clinical parameters such as relapse rates after a year. In alcohol addiction, exploratory analyses showed interesting effects for the combination of anodal tDCS and cognitive bias modification (den Uyl, Gladwin, Rinck, Lindenmeyer, & Wiers, 2016) and WM training in healthy participants showed elevated effects after 3-to-9 months (Ruf et al., 2017). To date, long-term effects of cathodal tDCS in combination with respective psychiatric trainings are not known.

Disease-specific symptomatology. Generally, it is likely that different types of symptomatology in specific disorders also include different effectivities of the bias activation vs. regulation stimulation rationale. For instance, eating-related disorders include facets of emotional and body-related processing (e.g., Riva, 2014) that are likely to differ from other psychiatric conditions such as addiction or major depression. Thus, adjustments are not only required on the side of stimuli and associations, but also in considering additional processes and studying potential cross-diagnostic mechanisms.

Psychoeducation. Finally, the stimulation approach requires careful psychoeducation, in particular because self-reports and indirect measurements of implicit associations deviate. Moreover, I observed in Chapter VI that the stimulation was not subjectively discriminated from a sham tDCS. Instead (and even more critically), although behavioral effects of the stimulation were relatively clear, participants could not subjectively perceive changes in their cognitive processing. Although the subtle influences of implicit cognitive processing and its deviations from deliberate thought are a consistent result well-known in implicit cognition research, therapeutic progress without noticeable change could drain on lacks of motivation, which reiterates the needs for appropriate psychoeducation.

Clinical Implications II: Neuromodulation as a Tool in Psychiatry

Transcranial electric stimulation – tDCS and tRNS in particularly – encompasses interesting tools for neurological and psychiatric rehabilitation, next to their implementations as basic research instruments as utilized in the current thesis. Relevant translational aspects can be deducted from the presented studies which will relate to therapies and basic research. In amendment to the established operational rationales of application of tDCS as introduced in the beginning, the following list highlights four prevailing (but not necessarily trivial) basic principles for applications of tDCS drawn from my studies.

Polarity-Dependent Effects

Polarity-dependency was a basic physiological principle governing the effects of tDCS on motor cortex excitability, basically giving rise to the anodal-excitability cathodal-inhibitory dichotomy (Nitsche & Paulus, 2000). Cellular modeling of uniform extracellular DC fields confirms this physiological dichotomy of polarity-dependent stimulation effects (Bikson et al., 2004). To date, however, polarity-dependent effects are not always observed in the cognitive domain, but studies rather show a general superiority of anodal tDCS and smaller or no effects of cathodal tDCS (Jacobson et al., 2012). Moreover, cognitive effects of tDCS certainly include additional non-linear processes (Fertonani & Miniussi, 2016) and it was even observed that both tDCS polarities appeared to induce comparable effects at the behavioral level. On these grounds, it is important to highlight that all studies performed here yielded polarity-specific effects in orthogonal directionalities.

Moreover, the current research substantiates the hypothesis that cathodal tDCS can improve cognitive processing. Although this potential application of cathodal stimulation was noted from early on (Nitsche, Nitsche, et al., 2003), my studies (and others as well) point beyond reductions of hyper-excitability in certain brain regions as disease biomarker and I have extended on this discussion in another article (Schroeder & Plewnia, 2016).

➔ See polarity-dependent effects in Chapters I, II, & IV

Asymmetrical Cognitive Effects

However, it is also noteworthy that the observed effects for anodal vs. cathodal polarities at the same intensities (1 mA) were not symmetrical in their effect sizes. Instead, actually, the unique effect of anodal tDCS on spatial-numerical associations was only ascertained by incorporating data from three individual studies in the least conservative test. Moreover, the effect size estimate of this enhancement with anodal tDCS was approximately a third of the effect size estimate of the reductions with cathodal tDCS.

Again, this result of polarity asymmetry can be reconciled with the previous literature. However, in previous studies, it was rather observed that anodal tDCS was superior than cathodal tDCS in cases of polarity-specificity (Jacobson et al., 2012). The sources of such asymmetrical cognitive effects are subject to speculation given current empirical efforts, but it is likely that compensatory cognitive processes – possibly along with cross-cortical regulation networks – are readily available to maintain the most important functional cognitive states. Furthermore, inhomogenities of cortical areas which differentially respond to anodal vs. cathodal tDCS may well play into the different net outcomes of stimulation interactions (Bestmann et al., 2015). Vice versa, it could be explored whether polarity-asymmetric stimulation effects in respective therapeutic applications could produce stimulation outcomes with less intense dosage, e.g., by switching to cathodal tDCS configurations instead of anodal tDCS configurations, where applicable based on theoretical stimulation rationales.

It is interesting to note that polarity asymmetric effects were also observed in some other study designs with more physiological measures and other cortical configurations. For example, in one early study testing excitability changes from anodal or cathodal tDCS of the sensorimotor cortex (target: C4, return: SO), only cathodal tDCS was able to modulate (and impair) tactile discrimination (Rogalewski et al., 2004). In another study testing motion perception changes from tDCS of the visual cortices (target: ~ V5, return: Cz), 2 out of 3 experiments showed polarity-asymmetric discrimination improvements during and following 7 minutes of cathodal tDCS (Antal, Nitsche, et al., 2004). Both studies required preceding trainings (in separate sessions or before the test session, respectively) to achieve a stable level of discrimination performance.

- ➔ See asymmetrical cognitive effects in Chapters II, IV & V

Task Relevance Determines Stimulation Outcome

Baseline cortical activity influences the effects of transcranial brain stimulation, which was also termed state-dependency and already coined relevant for TMS (Silvanto & Pascual-Leone, 2008). In tES, activity-dependence can be considered even more relevant because a stimulation could not induce a certain processing, but rather modulate pre-existing patterns of activity. In Chapter IV, this principle becomes apparent in the color judgment task: Here, given that the relevant task dimension (color) is not influenced by a numerical processing network, spatial associations are not pronounced (see also Chapter III). In this case, neither anodal nor cathodal tDCS can induce a different form of processing and the application of tDCS is ineffective, although the exact same stimulation produced significant effects in other, order-relevant magnitude classification tasks in the same participants.

In fact, this result reiterates previous observations of most pronounced stimulation effects in the most active and difficult task instructions (e.g., Zwissler et al., 2014). Consistently, state-dependent effects are also apparent in neural responses: For example, in a combined fMRI-tDCS experiment, Hauser and colleagues (2016) could observe activation changes underneath the cathode (placed over the inferior prefrontal cortex), but such modulations were observed only for novel and not for repeated subtraction operations. This result is particularly relevant to the current studies because it shows task-induced activity-dependence also on a neural level and the imaging result nicely illustrates the effect of cathodal tDCS on neural tissue, when combined with a respective task (Hauser et al., 2016).

In broader terms, these mutual interactions between resting state networks, task-induced brain activity, and their dynamic interactions with membrane potential modulations by external DC fields are described by meta-plasticity (Miniussi et al., 2013).

➔ See effects of task relevance in Chapter IV

Task Properties Inverse Stimulation Outcome

Further extending the premise of state-dependency, results from the earlier-later classifications of ordinal stimuli in Chapters IV & V demonstrate that the observed behavioral result of tDCS can be inversed by choosing different task properties. Next to highlighting the importance of exact task characteristics and instruction, this finding also increases the available parameters for shaping stimulation protocols (e.g., functional targeting).

At a cognitive level, both above mentioned findings indicate that state-dependent results can be obtained by rendering modulated areas relevant or irrelevant to the ongoing cognitive activity. Furthermore, I also showed that task instruction can be an effective way to vary properties of stimulus material (e.g., ordinal vs. cardinal information) or by incorporating different depths of cognitive processing of given information (color judgment vs. comparison tasks). It would be interesting to investigate whether also the physiological effects of stimulation – such as excitability and plasticity – interact with task instruction in comparable ways and whether the combination of task and stimulation can provide superior (and likely also more targeted) outcomes of a stimulation. However, there are only few systematic reports and overall mixed results on this interaction (Cappelletti et al., 2013; Segrave, Arnold, Hoy, & Fitzgerald, 2014). At least in the arithmetic domain and with tRNS, the combined administration of a cognitive training task and stimulation had superior effects and was longer-lasting than both sham training or stimulation (Cappelletti et al., 2013).

- ➔ See inversion effects of task properties in Chapters IV & V

Together, these aspects observed in cognitive studies (Figure 7.3) are partially compatible with theoretical models. Some aspects – such as the inversion of stimulation outcomes by task properties and mutual non-linear interactions – require further validation to specify underlying mechanisms and to clarify the breadth and relevance of implications.

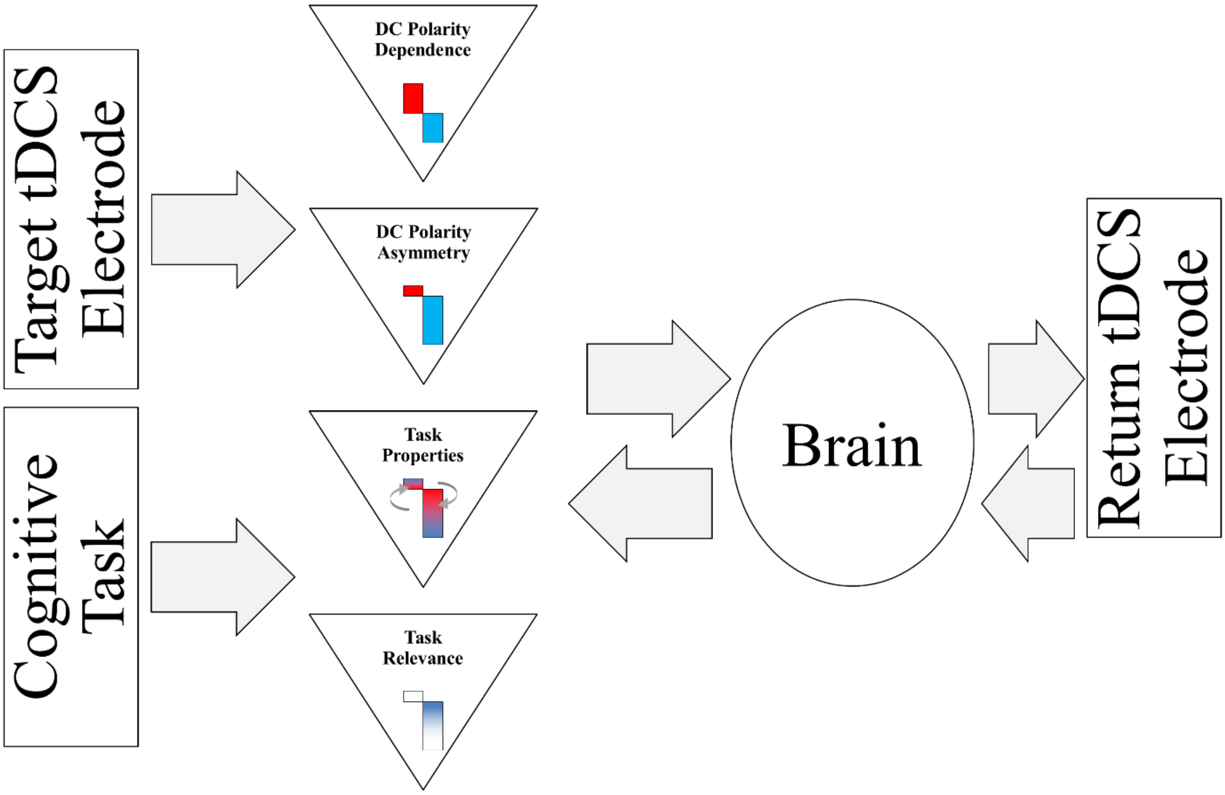


Figure 7.3. *Four basic principles of tES applications garnered in the present research. Note that non-linear effects can be present already at the stage of (physiological) DC polarity dependence, at least for excitability changes meeting certain technical parameters (current duration and intensity) and after-effects. The current flow mediated by electrode placement and technical characters, cognitive task mediated by stimuli and instruction, as well as initial brain states and their mutual interactions are supposed to render behavioral outcomes.*

Controversy: Is tDCS Effective?

Accumulating reports of null findings cast doubt on the efficacy of tDCS for modulating cognitive functions. For instance, a controversial quantitative review on 271 single-session tDCS studies found no support for reliable modulations of cognition (Horvath et al., 2015). Although their bold conclusions were attenuated by several methodological problems and conceptual shortcomings (Antal, Keeser, & Padberg, 2015; Price & Hamilton, 2015), including the fact that little-to-none direct study replications with identical technical implementation exist, tDCS effectivity is a recurring theme in contemporary neuroscience research. This becomes especially apparent when also considering commercial devices for cognitive enhancement with opaque placement and DC generation implementations that produce detrimental performance in standardized tests (Steenbergen et al., 2015). Briefly, in the following paragraph, I will attempt to amend to this discussion from the research reported in this thesis. Obviously, having reported on effective tDCS procedures in the preceding research, I will argue for the effectivity of tDCS. However, the discussion on research practices, technical parameters, and task-dependent interactions will also point to evaluative considerations that may improve the quality of future research.

Why are some Cognitions Malleable by tDCS and Others are not?

In the previous chapters, I demonstrated the capability of tDCS to modulate implicit associations in terms of both SNARC and IAT effects. My study results on implicit cognitive biases were overall relatively clear and statistically robust in this regard. Nevertheless, some other tDCS effects were not as consistent. For instance, opposite stimulation effects for the modulation of explicit stimulus-response compatibility in the Simon task in Chapter II were never observed, although there is good theoretical rationale derived from the well-known conflict monitoring theory (Botvinick, Braver, Barch, Carter, & Cohen, 2001) to expect that the PFC would be involved in regulating such conflict effects. In fact, a recent study using more focal high-definition tDCS and a large cohort of 120 participants observed only a small effect (~ 5ms) on conflict monitoring (Gbadeyan et al., 2016). Why was conventional tDCS not so effective in modulating this effect, which was consistently linked to prefrontal areas both empirically in fMRI studies (Liu, Banich, Jacobson, & Tanabe, 2004) and theoretically in computational modeling (Botvinick et al., 2001)?

Eventually, this mismatch between theory and behavioral stimulation results must point to some neurocognitive differences in the underlying structures and/ or specific stimulation characteristics. Similarly, dissociable cognitive control systems were found for emotional and non-emotional tasks (such as the Simon task; Egner, Etkin, Gale, & Hirsch, 2008), and tDCS was capable to modulate emotional cognitive control in respective studies (Plewnia, Schroeder, Kunze, et al., 2015; Plewnia, Schroeder, & Wolkenstein, 2015).

Although puzzling at first, it is important to resolve the discrepancies between different stimulation effectivities, since such patterns can also inform the basic principles of tDCS. For example, could neuron populations involved in one behavioral effect possess certain properties that immunize them for transcranial electric stimulation? At first, this seems improbable, because electric signal transmission is key to neuronal communication overall. However, for some specific configurations of electric stimulation, this assumption may actually hold true to allow the self-organizing neural system to particularly shield some networks that are more vital than others. Possibly, adaptive cortical strategies (e.g., myelination of some structures, or another neurochemical or physical process) could protect some networks better against external modulation than others.

Vice versa, it may also be possible that some neurocircuits are particularly malleable by external influences, so to allow for flexible adjustments due to environmental events. This view is corroborated by the cultural recycling hypothesis and the accumulating evidence that fixed brain circuits (e.g., for sensory processing) are adaptively remapped for other processes (Dehaene & Cohen, 2007). Evolutionary, it would be sensible that different neuronal systems evolve to a rather fixed state (such as conflict monitoring loop) whereas other systems remain flexible to account for different kinds of situations (such as implicit cognitive biases). Finally, some first physiological evidence supporting this view can be mentioned, because *in vitro* DC polarizations were dependent on cell morphology and it was predicted that layer V pyramidal soma would be most sensitive to DC fields (Radman, Ramos, Brumberg, & Bikson, 2009). Consequently, also cognitive networks that invoke respective neurons at layer V should be most sensitive to tDCS configurations.

Although I provide more suggestions in Chapters II and V regarding the question why tDCS is effective in some domains (or study designs) and not effective in others, there is a great need for more exhaustive research programs. Eventually, it is equally important to pay close attention to the exact methods, such as choice of electrode size, duration, intensity, and return placement. In reviews that claim for in-effectivity of tDCS, reviewed studies can often incorporate bipolar electrode configurations – such that two brain regions are being modulated in opposite direction. To avoid such ambiguity, extracephalic electrode configurations are much clearer with regard to their potential effects (as are concentric electrodes), and I look forward to upcoming factorial comparisons of different electrode configurations (e.g., see Leite et al., in press, for effects of unilateral vs. bilateral tDCS on switch costs).

Scientific Skepticism in other Domains

In principle, interference with brain activity can provide causal evidence for the involvement of brain regions in certain cognitive operations. For scientific avenues, the possibility to experimentally manipulate brain regions and observe effects provides an important tool in order to investigate the decisive influence of brain regions. This feature is distinct to studies with tDCS and in particular also TMS, because evidence collected with neuroimaging techniques (such as EEG, fMRI, fNIRS, or MEG) is always correlative and thus it is not clear whether an observed signature is necessarily involved in the behavior. In the case of interference with tDCS, however, following this rationale requires additional care and may not be sufficient in some cases. Instead, the intricated nature of tDCS effects on the CNS may be perceived as a modulation of large-scale network, which can also produce distant effects in other brain regions and largely depend on the a-priori state of the brain and its involvement with externally and internally imposed cognitive operations. How should a post-mortem cadaver then respond to subthreshold resting membrane modulations by tDCS (Vöröslakos et al., 2018)?

Other neuroscientific methods are subject to skepticism and controversy as well. For instance, fMRI measurements of the amygdala as a popular area for emotional processing were only recently implied to include a dramatic confound by means of the basal vein of Rosenthal (Boubela et al., 2015), which could partially account for observed activations in previous studies. But particularly cost-efficient methods (such as also heart-rate variability measurements or supplementary nutrition) could easily attract consumer-market manufacturing loosely based on scientific evidence, potentially harnessing the real merit of the respective methods and leading to premature public and scientific discredit. This has certainly been the case in tDCS as well (e.g., Steenbergen et al., 2015). Eventually, continuous skepticism is due to scientific nature and allows also in apparently established methods for identification of artifacts, as this example illustrates. Moreover, it is equally important to stress that some scientific questions or societal challenges simply could not benefit from studying neurophysiological correlates. Thus, it is mandatory to refine the hypotheses that can and can’t be addressed with tES, and to realistically outline implications.

Why is tDCS not ‘one for all’?

The general idea of using electricity to modulate cognitive processes is intuitive, since majority of neural signaling relies on action potentials. Impressively, this general mechanism naturally produces quite diverse results regarding cognitive proficiencies. Presumably, all of these processes can be actually changed using externally injected electricity in some configuration.

One overlooked feature of the current research literature is the potential generativity of tES configurations and training combinations. For example, an effective training procedure could even consist in combinations of different electrode configurations that are adapted during progress in a mathematical training, e.g., by stimulating frontal cortices during the first sessions and then stimulating parietal cortices during later sessions (Popescu et al., 2016) or cathodal in the first and anodal in the later sessions (Dockery et al. 2009). It may be more instructive not to classify the different types of stimulation into a single intervention category, but rather acknowledge the variety of parameters. Based on basic principles, theoretical models of the neurocognitive impairment under study, and individual parameters, targeted interventions can be developed, validated, and delivered.

Finally, the pace of technological discovery should be considered. When the usefulness of fire was discovered ~1.5 millions of years ago by humans, there was certainly poor control over fire parameters. Application of fire to various materials may have shown effectivity, but some materials such as wet timber or stones would require more time or intensity of fire. Moreover, it then took some time and further development until fire technology and the subsequent discovery of boiling water were advanced to a state that pasta was cooked al dente or that the correct procedure for soft eggs was identified. Neuromodulation of brain areas with tDCS is still in its infancy and there remain tremendous possibilities, but certainly there also exist unexplored and ineffective procedures. Using scientific methods in systematic ways will allow us to better characterize, parametrize, and advance potential use cases for tDCS in the future.

Adverse Events of tDCS Applications

Of all 288 tDCS sessions conducted in the present thesis, one single (additional) experiment had to be aborted because the participant felt dizzy, uncomfortable, and reported a narrowed visual perception. Interestingly, this event took place concurrent to a sham tDCS session and thus it cannot be attributed to the stimulation. The experiment in this participant was aborted and (s)he quickly recovered by means of H_2O delivery.

In the individual chapters, I have reported on adverse sensations of sham and anodal / cathodal tDCS that mostly included tingling and burning sensations at the site of the electrodes. The adverse sensations were particularly pronounced in the beginning of stimulation, according to participants’ self-reports. There were no indications of polarity differences in adverse sensations. However, some participants reported higher values during active tDCS than during sham tDCS. Apparently, this result did not necessarily preclude effective blinding. Internally in the lab, improved realization of the sham stimulation (Gandiga, Hummel, & Cohen, 2006) with intermittent phase–in and –out were developed and already incorporated to prospective study protocols which will be reported on in the future.

In my view, the more serious concerns are unintended and unexplored side effects of tDCS. Since tDCS is considered to be safe and easy-to-apply, a remarkable do-it-yourself community has evolved. However, until the parameters and working mechanisms are not fully understood, it is simply not known which long-term effects may be provoked by these kinds of applications. Critically, since the effects studied in the present research are not always available to introspective processing, they constitute a likely overseen process that gets modulated. Consequences are not known, for instance, if individual SNARC effects or implicit associations are reduced involuntarily, but it is possible that also overt behaviors are then altered (e.g., in the same way that the existence of implicit associations in the first place can influence overt behaviors, such as stereotypes). This potential mechanism has to be weighed against interactions with task-induced activity and potentially covert participant characteristics. For instance, unknown individual differences in certain personality traits or level of skill can render the same stimulation helpful in one group, but detrimental to others (Iuculano & Cohen Kadosh, 2013; Weidacker, Weidemann, Boy, & Johnston, 2016). Moreover, it is hard to exclude potential interactions with learning mechanisms and neuroplastic offline effects.

Certainly, comparable neuroplastic processes are also apparent in other methods than tDCS, such as training or education. Other ethical issues include accessibility and regulation of tDCS, the question whether and how it should be coupled with education and in at-risk children, and applications in non-clinical populations (Antal et al., 2017; Cohen Kadosh, Levy, O’Shea, Shea, & Savulescu, 2012). In clinical populations, however, it is utmost critical to also acknowledge positive effects that could not be achieved otherwise. For example, more than 1,000 sessions of tDCS home treatment were tolerated well in a treatment-resistant schizophrenia patient who could experience some relief from his symptoms during tDCS (Schwippel, Wasserka, Fallgatter, & Plewnia, 2017). Such individual results reiterate the urgent need to further investigate possible (cognitive) side effects of tDCS and continue systematic monitoring of all adverse events.

Concluding Remarks

The concealed presence of implicit cognitive biases in various domains constitutes a fascinating phenomenon of human cognition and behavior. In the present thesis, cathodal transcranial direct current stimulation (tDCS) to the left prefrontal cortex reduced implicit biases as modelled by spatial-numerical associations in the SNARC effect. However, spatial associations appeared bolstered by multiple coding mechanisms, because excitability-enhancing anodal tDCS dissociated ordinality-based from cardinality-based SNARC effects. Finally, generalizability was shown in the non-spatial and non-directional implicit association test (IAT) effect, which was consistently reduced by application of cathodal tDCS.

The outlined interactions between stimulation, task demands, and verbal markedness in the studies encompass the dependency of tDCS effects on task-induced activities. Functional targeting based on psychological principles can render stimulation protocols more effective. Eventually, also the capability of cathodal tDCS may compile to respective combined therapeutic approaches.

Contemporary psychiatric theories often consider the reflective-impulsive dual-coding model. One key axiom of the present research was the assumption of respective prefrontal cortex networks for bias regulation and bias activation. By drawing on implicit cognitive biases, I could demonstrate how the latter activation of implicit cognitive processing modulates behavioral decisions, but prefrontal neuromodulation was effective to alter such processing. The results were particularly informative for the elaboration of a bias activation hypothesis, which was compatible with previous models. Markedness correspondence, in a psychological interpretation as the definition of default, fluent characteristics being aligned and more accessible in neurocognitive processing, was argued to be one of multiple codes to render implicit associations in general and to be particularly malleable by prefrontal tDCS.

Regarding the neurocognitive mechanisms underlying implicit associations, an important and unresolved question pertains to the situation where several different markedness codes interact with each other and/ or compete for task relevance. This issue is not only theoretically important, but also of practical relevance for avoiding confounds in experimental designs. For example, SNARC effects in native Hebrew participants were partialled out by the presence of parity-space MARC effects (Zohar-Shai, Tzelgov, Karni, & Rubinsten, 2017). Moreover, even in non-spatial Go-Nogo tasks, marked information is still available in both instruction and response domains (i.e., the marked prefix of No-go and unmarked motor fluency in pressing a key in response to visual stimulation), which presents a confound for conceptual measures of implicit spatial-numerical associations (Fischer & Shaki, 2016), but also for the combined delayed working memory assessment of spatial-positional associations (Ginsburg & Gevers, 2015; van Dijck & Fias, 2011).

To conclude, I characterized the involvement of prefrontal circuits in the activation of implicit cognitive biases as modeled by the SNARC effects for numerical and non-numerical sequences as well as the implicit association effect between insect-flower and negative-positive categories. External modulation of brain patterns with tDCS showed online capability to directly change these biases. Future research and applications can utilize this mechanism to replace dysfunctional implicit cognitive biases flexibly and to potentially enhance goal-directed cognitive processing.

REFERENCES

Abrahamse, E. L., van Dijck, J. P., & Fias, W. (2017). Grounding verbal working memory: The case of serial order. *Current Directions in Psychological Science, 26*(5), 429-433. doi:10.1177/0963721417704404

Abrahamse, E. L., van Dijck, J. P., & Fias, W. (2016). How Does Working Memory Enable Number-Induced Spatial Biases? *Frontiers in Psychology, 7*(June), 1–11. doi:10.3389/fpsyg.2016.00977

Abrahamse, E. L., van Dijck, J. P., Majerus, S., & Fias, W. (2014). Finding the answer in space: the mental whiteboard hypothesis on serial order in working memory. *Frontiers in Human Neuroscience, 8*, 1–12. doi:10.3389/fnhum.2014.00932

Adachi, I. (2014). Spontaneous spatial mapping of learned sequence in chimpanzees: Evidence for a SNARC-Like effect. *PLoS ONE, 9*(3), 1–4. doi:10.1371/journal.pone.0090373

Ahern, A. L., Bennett, K. M., & Hetherington, M. M. (2008). Internalization of the Ultra-Thin Ideal: Positive Implicit Associations with Underweight Fashion Models are Associated with Drive for Thinness in Young Women. *Eating Disorders, 16*(4), 294–307. doi:10.1080/10640260802115852

Agrillo, C., Miletto Petrazzini, M. E., & Bisazza, A. (2017). Numerical abilities in fish: A methodological review. *Behavioural Processes, 141*, 161–171. doi:10.1016/j.beproc.2017.02.001

Ali, M. M., Sellers, K. K., & Fröhlich, F. (2013). Transcranial Alternating Current Stimulation Modulates Large-Scale Cortical Network Activity by Network Resonance. *Journal of Neuroscience, 33*(27), 11262–11275. doi:10.1523/JNEUROSCI.5867-12.2013

Almeida, J., Martins, A. R., Bergström, F., Amaral, L., Freixo, A., Ganho-Ávila, A., Kristensen, S., ... Ruttorf, M. (2017). Polarity-specific transcranial Direct Current Stimulation effects on object-selective neural responses in the Inferior Parietal Lobe. *Cortex*. doi:10.1016/j.cortex.2017.07.001

Ansari, D. (2008). Effects of development and enculturation on number representation in the brain. *Nature Reviews Neuroscience, 9*(4), 278–291. http://doi.org/10.1038/nrn2334

Ansorge, U., & Wühr, P. (2004). A response-discrimination account of the Simon effect. *Journal of Experimental Psychology: Human Perception and Performance*, 30(2), 365–377. doi:10.1037/0096-1523.30.2.365

Antal, A., Alekseichuk, I., Bikson, M., Brockmöller, J., Brunoni, A. R., Chen, R., Cohen, L. G., ... Paulus, W. (2017). Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines. *Clinical Neurophysiology, 128*(9), 1774-1809. doi:10.1016/j.clinph.2017.06.001

Antal A, & Herrmann CS (2016) Transcranial Alternating Current and Random Noise Stimulation: Possible Mechanisms. *Neural Plasticity*, 2016, Article ID 3616807. doi: 10.1155/2016/3616807

Antal, A., Keeser, D., & Padberg, F. (2015). Conceptual and Procedural Shortcomings of the Systematic Review "Evidence That Transcranial Direct Current Stimulation (tDCS) Generates Little-to-no Reliable Neurophysiologic Effect. *Brain Stimulation*, *8*(July), 27–31. http://doi.org/10.1016/j.brs.2015.05.010

Antal, A., Kincses, T. Z., Nitsche, M. A., Bartfai, O., & Paulus, W. (2004). Excitability changes induced in the human primary visual cortex by transcranial direct current stimulation: direct electrophysiological evidence. *Investigative Ophthalmology & Visual Science*, *45*(2), 702–707. http://doi.org/10.1167/iovs.03-0688

Antal, A., Nitsche, M. A., Kruse, W., Kincses, T. Z., Hoffmann, K.-P., & Paulus, W. (2004). Direct current stimulation over V5 enhances visuomotor coordination by improving motion perception in humans. *Journal of Cognitive Neuroscience*, *16*(4), 521–7. http://doi.org/10.1162/089892904323057263

Antal, A., Nitsche, M. A., & Paulus, W. (2001). External modulation of visual perception in humans. *Neuroreport*, *12*(16), 3553–5.

Arsalidou, M., & Taylor, M. J. (2011). Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations. *NeuroImage*, *54*(3), 2382–93. doi:10.1016/j.neuroimage.2010.10.009

Artemenko, C., Moeller, K., Huber, S., & Klein, E. (2015) Differential influences of unilateral tDCS over the intraparietal cortex on numerical cognition. *Frontiers in Human Neuroscience*, 9, 110. doi: 10.3389/fnhum.2015.00110

Asendorpf, J. B., Banse, R., & Mücke, D. (2002). Double dissociation between implicit and explicit personality self-concept: The case of shy behavior. *Journal of Personality and Social Psychology*, *83*(2), 380–393. http://doi.org/10.1037/0022-3514.83.2.380

Bachot, J., Gevers, W., Fias, W., & Roeyers, H. (2005). Number sense in children with visuospatial disabilities: orientation of the mental number line. *Psychology*, *47*(1), 172–183.

Bächtold, D., Baumüller, M., & Brugger, P. (1998). Stimulus-response compatibility in representational space. *Neuropsychologia*, *36*, 731–735. doi:10.1016/S0028-3932(98)00002-5

Baddeley, A. D. (1992). Working memory. *Science*, *255*(5044), 556–559. doi:10.1126/science.1736359

Baddeley, A. D. (2000). The episodic buffer: A new component of working memory? *Trends in Cognitive Sciences*. doi:10.1016/S1364-6613(00)01538-2

Baddeley, A. (2003). Working memory: Looking back and looking forward. *Nature Reviews Neuroscience*, *4*(10), 829–839. http://doi.org/10.1038/nrn1201

Badets, A., Koch, I., & Philipp, A. M. (2016). A review of ideomotor approaches to perception, cognition, action, and language: advancing a cultural recycling hypothesis. *Psychological Research*, *80*(1), 1–15. doi:10.1007/s00426-014-0643-8

Baker, J. M., Rorden, C., & Fridriksson, J. (2010). Using transcranial direct-current stimulation to treat stroke patients with aphasia. *Stroke*, *41*(6), 1229–1236. doi:10.1161/STROKEAHA.109.576785

Barker, A. T., Jalinous, R., & Freeston, I. L. (1985). Non-Invasive Magnetic Stimulation of Human Motor Cortex. *The Lancet*, *325*(8437), 1106–1107. http://doi.org/10.1016/S0140-6736(85)92413-4

Barsalou, L. W. (1999). Perceptual symbol systems. *Behavioral and brain sciences*, *22*(4), 577-609-660. doi:10.1017/S0140525X99252144

Barsalou, L. W. (2008). Grounded cognition. *Annual review of psychology*, *59*, 617–45. doi:10.1146/annurev.psych.59.103006.093639

Batsikadze, G., Moliadze, V., Paulus, W., Kuo, M.-F., & Nitsche, M. A. (2013). Partially non-linear stimulation intensity-dependent effects of direct current stimulation on motor cortex excitability in humans. *The Journal of physiology, 591*(7), 1987–2000. doi:10.1113/jphysiol.2012.249730

Battistella, E. (1995). Jakobson and Chomsky on Markedness. In E. Hajičová, M. Červenka, O. Leška, & P. Sgall (Eds.), *Prague Linguistic Circle Papers: Travaux du cercle linguistique de Prague nouvelle série*. Volume 1 (pp. 55–72).

Battleday, R. M., Muller, T., Clayton, M. S., & Cohen Kadosh, R. (2014) Mapping the mechanisms of transcranial alternating current stimulation: A pathway from network effects to cognition. *Frontiers in Psychiatry,* 5, 162. doi: 10.3389/fpsyt.2014.00162

Benson-Amram, S., Heinen, V. K., Dryer, S. L., & Holekamp, K. E. (2011). Numerical assessment and individual call discrimination by wild spotted hyaenas, Crocuta crocuta. *Animal Behaviour, 82*(4), 743–752. http://doi.org/10.1016/j.anbehav.2011.07.004

Benwell, C. S. Y., Learmonth, G., Miniussi, C., Harvey, M., & Thut, G. (2015). Non-linear effects of transcranial direct current stimulation as a function of individual baseline performance: Evidence from biparietal tDCS influence on lateralized attention bias. *Cortex, 69,* 152–165. doi:10.1016/j.cortex.2015.05.007

Berch, D. B., Foley, E. J., Hill, R. J., & Ryan, P. M. (1999). Extracting parity and magnitude from Arabic numerals: developmental changes in number processing and mental representation. *Journal of experimental child psychology, 74*(4), 286–308. doi:10.1006/jecp.1999.2518

Bestmann, S., de Berker, A. O., & Bonaiuto, J. (2015). Understanding the behavioural consequences of noninvasive brain stimulation. *Trends in Cognitive Sciences*, *19*(1), 13–20. doi:10.1016/j.tics.2014.10.003

Bikson, M., Datta, A., Rahman, A., & Scaturro, J. (2010) Electrode montages for tDCS and weak transcranial electrical stimulation: Role of "return" electrode's position and size. *Clinical Neurophysiology,* 121(1),1976–1978. doi: 10.1097/MPG.0b013e3181a15ae8.

Bikson, M., Inoue, M., Akiyama, H., Deans, J. K., Fox, J. E., Miyakawa, H., & Jefferys, J. G. R. (2004). Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices in vitro. *The Journal of Physiology*, *557*(Pt 1), 175–90. doi:10.1113/jphysiol.2003.055772

Bikson, M., Rahman, A. (2013) Origins of specificity during tDCS: anatomical, activity-selective, and input-bias mechanisms. *Frontiers in Human Neuroscience*, 7, 688. doi: 10.3389/fnhum.2013.00688

Bikson, M., Grossman, P., Thomas, C., Zannou, A. L., Jiang, J., Adnan, T., … Woods, A. J. (2016). Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016. *Brain Stimulation*, *9*(5), 641–661. http://doi.org/10.1016/j.brs.2016.06.004

Boggio, P. S., Bermpohl, F., Vergara, A. O., Muniz, A. L. C. R., Nahas, F. H., Leme, P. B., Rigonatti, S. P., ... Fregni, F. (2007). Go-no-go task performance improvement after anodal transcranial DC stimulation of the left dorsolateral prefrontal cortex in major depression. *Journal of affective disorders*, *101*(1–3), 91–8. doi:10.1016/j.jad.2006.10.026

Bonato, M., Zorzi, M., & Umiltà, C. (2012). When time is space: Evidence for a mental time line. *Neuroscience and Biobehavioral Reviews*, *36*(10), 2257–2273. doi:10.1016/j.neubiorev.2012.08.007

Borckardt, J. J., Bikson, M., Frohman, H., Reeves, S. T., Datta, A., Bansal, V., Madan, A., … George, M. S. (2012). A pilot study of the tolerability and effects of high-definition transcranial direct current stimulation (HD-tDCS) on pain perception. *Journal of Pain*, *13*(2), 112–120. doi:10.1016/j.jpain.2011.07.001

Bortoletto, M., Rodella, C., Salvador, R., Miranda, P. C., & Miniussi, C. (2016). Reduced Current Spread by Concentric Electrodes in Transcranial Electrical Stimulation (tES). *Brain Stimulation*. doi:10.1016/j.brs.2016.03.001

Bottini, R., Mattioni, S., & Collignon, O. (2016). Early blindness alters the spatial organization of verbal working memory. *Cortex*. doi:10.1016/j.cortex.2016.08.007

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological review*, *108*(3), 624–52.

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. *Trends in Cognitive Sciences*, *8*(12), 539–46. doi:10.1016/j.tics.2004.10.003

Botvinick, M. M., & Cohen, J. D. (2014). The computational and neural basis of cognitive control: Charted territory and new frontiers. *Cognitive Science*, *38*(6), 1249–1285. doi:10.1111/cogs.12126

Boubela, R. N., Kalcher, K., Huf, W., Seidel, E.-M., Derntl, B., Pezawas, L., … Moser, E. (2015). fMRI measurements of amygdala activation are confounded by stimulus correlated signal fluctuation in nearby veins draining distant brain regions. *Scientific Reports*, (March), 1–15. doi:10.1038/srep10499

Brendl, C. M., Markmann, A. B., & Messner, C. (2001). How Do Indirect Measures of Evaluation Work? Evaluating the Inference of Prejudice in the Implicit Association Test. *Journal of Personality and Social Psychology*, *81*(5), 760–773.

Brunoni, A. R., Amadera, J., Berbel, B., Volz, M. S., Rizzerio, B. G., & Fregni, F. (2011). A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. *The International Journal of Neuropsychopharmacology*, *14*(8), 1133–45.

Brunoni, A. R., & Vanderhasselt, M. A. (2014). Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: a systematic review and meta-analysis. *Brain and cognition, 86*, 1-9.

Bueti, D., & Walsh, V. (2009). The parietal cortex and the representation of time, space, number and other magnitudes. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *364*(1525), 1831–40. doi:10.1098/rstb.2009.0028

Bull, R., Cleland, A. A., & Mitchell, T. (2013). Sex differences in the spatial representation of number. *Journal of Experimental Psychology. General*, *142*(1), 181–92. doi:10.1037/a0028387

Bynner, J., & Parsons, S. (1997) *Does Numeracy Matter? Evidence from the National Child Development Study on the Impact of Poor Numeracy on Adult Life*. Basic Skills Agency, Commonwealth House, London WC1A 1NU, London, United Kingdom

Caliskan-Islam, A., Bryson, J.J., & Narayanan, A. (2017). Semantics derived automatically from language corpora necessarily contain human biases. *Science, 356*(6334), 183–86. doi:10.1126/science.aal4230.

Cantlon, J. F., & Brannon, E. M. (2006). Shared System for Ordering Small and Large Numbers in and Humans Monkeys. *Psychological science*, *17*(5), 401–406. doi:10.1111/j.1467-9280.2006.01719.x

Cattaneo, Z., Mattavelli, G., Platania, E., & Papagno, C. (2011). The role of the prefrontal cortex in controlling gender-stereotypical associations: A TMS investigation. *NeuroImage, 56*(3), 1839–1846. doi:10.1016/j.neuroimage.2011.02.037

Cappelletti, M., Barth, H., & Spelke, E. S. (2008). rTMS over the intraparietal sulcus disrupts numerosity processing. *Experimental Brain Research*, *179*, 631–642.

Cappelletti, M., Gessaroli, E., Hithersay, R., Mitolo, M., Didino, D., Kanai, R., Cohen Kadosh, R., & Walsh, V. (2013). Transfer of Cognitive Training across Magnitude Dimensions Achieved with Concurrent Brain Stimulation of the Parietal Lobe. *The Journal of Neuroscience*, *33*(37), 14899–14907. doi:10.1523/JNEUROSCI.1692-13.2013

Carlson, K. D., & Herdman, A. O. (2012). Understanding the Impact of Convergent Validity on Research Results. *Organizational Research Methods*, *15*(1), 17–32. doi:10.1177/1094428110392383

Casasanto, D. (2009). Embodiment of abstract concepts: good and bad in right- and left-handers. *Journal of Experimental Psychology: General*, *138*(3), 351–67. doi:10.1037/a0015854

Casasanto, D., & Chrysikou, E. (2011). When left is “right”: Motor fluency shapes abstract concepts. *Psychological Science*, *22*(4), 419–422. doi:10.1177/0956797611401755

Castronovo, J., & Seron, X. (2007). Semantic numerical representation in blind subjects: the role of vision in the spatial format of the mental number line. *Quarterly journal of experimental psychology (2006)*, *60*(1), 101–19. doi:10.1080/17470210600598635

Chaieb, L., Antal, A., & Paulus, W. (2015) Transcranial random noise stimulation-induced plasticity is NMDA-receptor independent but sodium-channel blocker and benzodiazepines sensitive. *Frontiers in Neuroscience*, 9, 125. doi: 10.3389/fnins.2015.00125

Chee, M.W., Sriram, N., Soon, C.S., & Lee, K.M. (2000). Dorsolateral prefrontal cortex and the implicit association of concepts and attributes. *Neuroreport, 11*(1), 135–40.

Cho, Y. S., & Proctor, R. W. (2007). When is an odd number not odd? Influence of task rule on the MARC effect for numeric classification. *Journal of experimental psychology. Learning, memory, and cognition*, *33*(5), 832–42. doi:10.1037/0278-7393.33.5.832

Chomsky, N. (1965). *Aspects of the Theory of Syntax.* (Vol. 11). http://doi.org/10.1016/0732-118X(86)90008-5

Chrysikou, E.G., Hamilton, R.H., Coslett, H.B., Datta, A., Bikson, M., & Thompson-Schill, S. L. (2013). Noninvasive transcranial direct current stimulation over the left prefrontal cortex facilitates cognitive flexibility in tool use. *Cognitive neuroscience, 4*(2), 81–89. doi:10.1080/17588928.2013.768221

Cipora, K., Hohol, M., Nuerk, H.-C., Willmes, K., Brożek, B., Kucharzyk, B., & Nęcka, E. (2015). Professional mathematicians differ from controls in their spatial-numerical associations. *Psychological Research*. doi:10.1007/s00426-015-0677-6

Cipora, K., & Nuerk, H.-C. (2013). Is the SNARC effect related to the level of mathematics? No systematic relationship observed despite more power, more repetitions, and more direct assessment of arithmetic skill. *The Quarterly Journal of Experimental Psychology, 66*(10), 1974–91. doi:10.1080/17470218.2013.772215

Cipora, K., Patro, K., & Nuerk, H.-C. (2015). Are Spatial-Numerical Associations a Cornerstone for Arithmetic Learning? The Lack of Genuine Correlations suggests: No. *Mind, Brain, & Education*, *9*(4), 190–207.

Cipora, K., Patro, K., & Nuerk, H.-C. (in press). Situated influences on spatial-numerical associations. In T. Hubbard (Ed.), *Spatial Biases in Perception and Cognition*. Cambridge, UK: Cambridge University Press.

Cipora, K., Schroeder, P. A., Soltanlou, M., & Nuerk, H.-C. (in press). More space, better math: Is space a powerful tool or a cornerstone for understanding arithmetic? In M. Battista & K. S. Mix (Ed.), *Visualizing Mathematics* (working title).

Cipora, K., & Wood, G. (2017). Finding the SNARC instead of hunting it: A 20*20 Monte Carlo Investigation. *Frontiers in Psychology, 8,* 1194. doi:10.3389/fpsyg.2017.01194

Clark, H. H. (1969). Linguistic processes in deductive reasoning. *Psychological Review*, *76*(4), 387–404. doi:10.1037/h0027578

Clemens, B., Jung, S., Zvyagintsev, M., Domahs, F., & Willmes, K. (2013) Modulating arithmetic fact retrieval: A single-blind, sham-controlled tDCS study with repeated fMRI measurements. *Neuropsychologia* 51:1279–1286. doi: 10.1016/j.neuropsychologia.2013.03.023

Coffman, B. A., Trumbo, M. C., & Clark, V. P. (2012). Enhancement of object detection with transcranial direct current stimulation is associated with increased attention. *BMC Neuroscience*, *13*(1), 108. doi:10.1186/1471-2202-13-108

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Lawrence Earlbaum Associates. Hillsdale, NJ.

Cohen Kadosh, R. (2008). The laterality effect: Myth or truth? *Consciousness and Cognition*, *17*(1), 350–354. doi:10.1016/j.concog.2007.03.008

Cohen Kadosh, R., Cohen Kadosh, K., Kaas, A., Henik, A., & Goebel, R. (2007). Notation-dependent and -independent representations of numbers in the parietal lobes. *Neuron*, *53*(2), 307–14. doi:10.1016/j.neuron.2006.12.025

Cohen Kadosh, R., Lammertyn, J., & Izard, V. (2008). Are numbers special? An overview of chronometric, neuroimaging, developmental and comparative studies of magnitude representation. *Progress in Neurobiology*, *84*(2), 132–47. doi:10.1016/j.pneurobio.2007.11.001

Cohen Kadosh, R., Levy, N., O'Shea, J., Shea, N., & Savulescu, J. (2012). The neuroethics of non-invasive brain stimulation. *Current Biology*, *22*(4), R108-11. doi:10.1016/j.cub.2012.01.013

Cohen Kadosh, R., Soskic, S., Iuculano, T., Kanai, R., & Walsh, V. (2010). Modulating neuronal activity produces specific and long-lasting changes in numerical competence. *Current Biology*, *20*(22), 2016–2020. doi:10.1016/j.cub.2010.10.007

Cohen Kadosh, R., & Walsh, V. (2009). Numerical representation in the parietal lobes: abstract or not abstract? *Behavioral and BrainSsciences*, *32*(3–4), 313-28-73. doi:10.1017/S0140525X09990938

Craeynest, M., Crombez, G., De Houwer, J., Deforche, B., Tanghe, A., & De Bourdeaudhuij, I. (2005). Explicit and implicit attitudes towards food and physical activity in childhood obesity. *Behaviour Research and Therapy*, *43*(9), 1111–1120. doi:10.1016/j.brat.2004.07.007

Crescentini, C., Aglioti, S.M., Fabbro, F., & Urgesi, C. (2014). Virtual lesions of the inferior parietal cortex induce fast changes of implicit religiousness/spirituality. *Cortex, 54*, 1–15 doi: 10.1016/j.cortex.2014.01.023

Crump, M. J. C., Gong, Z., & Milliken, B. (2006). The context-specific proportion congruent Stroop effect: location as a contextual cue. *Psychonomic Bulletin & Review, 13*(2), 316–321. http://doi.org/10.3758/BF03193850

Cutini, S., Scarpa, F., Scatturin, P., Dell'Acqua, R., & Zorzi, M. (2014). Number-space interactions in the human parietal cortex: Enlightening the SNARC effect with functional near-infrared spectroscopy. *Cerebral Cortex, 24*(2), 444–51. doi:10.1093/cercor/bhs321

Daroczy, G., Wolska, M., Meurers, W. D., & Nuerk, H. C. (2015). Word problems: A review of linguistic and numerical factors contributing to their difficulty. *Frontiers in Psychology*, *6*(APR), 1–13. doi: 10.3389/fpsyg.2015.00348

Davis, N. J. (2014) Transcranial stimulation of the developing brain: a plea for extreme caution. *Frontiers in Human Neuroscience,* 8, 8–11. doi: 10.3389/fnhum.2014.00600

Davis, N. J., & van Koningsbruggen, M. G. (2013). "Non-invasive" brain stimulation is not non-invasive. *Frontiers in Systems Neuroscience, 7*, 76. doi:10.3389/fnsys.2013.00076

D'Esposito, M., Aguirre, G. K., Zarahn, E., Ballard, D., Shin, R. K., & Lease, J. (1998). Functional MRI studies of spatial and nonspatial working memory. *Cognitive Brain Research, 7*(1), 1–13. http://doi.org/10.1016/S0926-6410(98)00004-4

D'Esposito, M., & Postle, B. R. (2015). The Cognitive Neuroscience Of Working Memory. *Annual review of psychology*, *66*, 115–142. doi:10.1146/annurev-psych-010814-015031

De Houwer, J. (2002). The Implicit Association Test as a tool for studying dysfunctional associations in psychopathology: Strengths and limitations. *Journal of Behavior Therapy and Experimental Psychiatry, 33*(2), 115–133. doi:10.1016/S0005-7916(02)00024-1

De Houwer, J., Crombez, G., Koster, E. H. W., & De Beul, N. (2004). Implicit alcohol-related cognitions in a clinical sample of heavy drinkers. *Journal of Behavior Therapy and Experimental Psychiatry, 35*(4), 275–286. doi:10.1016/j.jbtep.2004.05.001

De Houwer, J., Geldof, T., & De Bruycker, E. (2005). The implicit association test as a general measure of similarity. *Canadian Journal of Experimental Psychology, 59*(4), 228–39. doi:10.1037/h0087478

de la Fuente, J., Casasanto, D., Martínez-Cascales, J. I., & Santiago, J. (2016). Motor Imagery Shapes Abstract Concepts. *Cognitive Science*, 1–21. doi:10.1111/cogs.12406

de la Fuente, J., Casasanto, D., & Santiago, J. (2015). Observed actions affect body-specific associations between space and valence. *Acta psychologica, 156*, 32–36. doi:10.1111/cogs.12177

Dehaene, S. (1992). Varieties of numerical abilities. *Cognition, 44*(1–2), 1–42. doi:10.1016/0010-0277(92)90049-N

Dehaene, S. (1997). *The number sense. How the mind creates mathematics.* Oxford: Oxford University Press.

Dehaene, S., Bossini, S., & Giraux, P. (1993). The mental representation of parity and number magnitude. *Journal of Experimental Psychology: General, 122*(3), 371–396. doi:10.1037/0096-3445.122.3.371

Dehaene, S., & Cohen, L. (1997). Cerebral Pathways for Calculation: Double Dissociation Between Rote Verbal And Quantitative Knowledge of Arithmetic. *Cortex, 33*, 219–250.

Dehaene, S., & Cohen, L. (2007). Cultural recycling of cortical maps. *Neuron, 56*(2), 384–398. doi:10.1016/j.neuron.2007.10.004

Dehaene, S., Piazza, M., Pinel, P., & Cohen, L. (2003). Three parietal circuits for number processing. *Cognitive Neuropsychology, 20*(3), 487–506. doi:10.1080/02643290244000239

den Uyl, T. E., Gladwin, T. E., Rinck, M., Lindenmeyer, J., & Wiers, R. W. (2016). A clinical trial with combined transcranial direct current stimulation and alcohol approach bias retraining. *Addiction Biology*, 1–9. doi:10.1111/adb.12463

den Uyl, T.E., Gladwin, T.E., & Wiers, R.W. (2015). Transcranial direct current stimulation, implicit alcohol associations and craving. *Biological Psychology*, 105, 37–42. doi: 10.1016/j.biopsycho.2014.12.004

D’Esposito, M., & Postle, B. R. (2015). The Cognitive Neuroscience Of Working Memory. *Annual Review of Psychology, 66*, 115–142.

Di Bono, M. G., & Zorzi, M. (2013). The spatial representation of numerical and non-numerical ordered sequences: Insights from a random generation task. *The Quarterly Journal of Experimental Psychology, 66*(12), 2348–2362. doi:10.1080/17470218.2013.779730

Dockery, C. A., Hueckel-Weng, R., Birbaumer, N., & Plewnia, C. (2009). Enhancement of planning ability by transcranial direct current stimulation. *The Journal of Neuroscience, 29*(22), 7271–7. doi:10.1523/JNEUROSCI.0065-09.2009

Dodd, M. D., Van der Stigchel, S., Adil Leghari, M., Fung, G., & Kingstone, A. (2008). Attentional SNARC: There's something special about numbers (let us count the ways). *Cognition, 108*(3), 810–818. doi:10.1016/j.cognition.2008.04.006

Dolscheid, S., & Casasanto, D. (2015). Spatial congruity effects reveal metaphorical thinking, not polarity correspondence. *Frontiers in Psychology*, *6*(NOV), 1–11. doi:10.3389/fpsyg.2015.01836

Domahs, F., Krinzinger, H., & Willmes, K. (2008). Mind the gap between both hands: Evidence for internal finger-based number representations in children's mental calculation. *Cortex, 44*(4), 359–367. doi:10.1016/j.cortex.2007.08.001

Domahs, F., Moeller, K., Huber, S., Willmes, K., & Nuerk, H.-C. (2010). Embodied numerosity: implicit hand-based representations influence symbolic number processing across cultures. *Cognition, 116*(2), 251–66. doi:10.1016/j.cognition.2010.05.007

Doricchi, F., Guariglia, P., Gasparini, M., & Tomaiuolo, F. (2005). Dissociation between physical and mental number line bisection in right hemisphere brain damage. *Nature neuroscience, 8*(12), 1663–5. doi:10.1038/nn1563

Driver, J., Blankenburg, F., Bestmann, S., Vanduffel, W., & Ruff, C. C. (2009). Concurrent brain-stimulation and neuroimaging for studies of cognition. *Trends in Cognitive Sciences*, *13*(7), 319–327. doi:10.1016/j.tics.2009.04.007

Duecker, F., & Sack, A. T. (2015) Rethinking the role of sham TMS. *Frontiers in Psychology,* 6, 1–5. doi: 10.3389/fpsyg.2015.00210

Edwards, D., Cortes, M., Datta, A., Minhas, P., Wassermann, E. M., & Bikson, M. (2013). Physiological and modeling evidence for focal transcranial electrical brain stimulation in humans: A basis for high-definition tDCS. *NeuroImage, 74,* 266–275. doi:10.1016/j.neuroimage.2013.01.042

Eger, E., Sterzer, P., Russ, M. O., Giraud, A.-L., & Kleinschmidt, A. (2003). A supramodal number representation in human intraparietal cortex. *Neuron*, *37*(4), 719–725.

Egner, T., & Hirsch, J. (2005). Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. *Nature Neuroscience, 8*, 1784–1790.

Egner, T., Etkin, A., Gale, S., & Hirsch, J. (2008). Dissociable neural systems resolve conflict from emotional versus nonemotional distracters. *Cerebral Cortex*, *18*(6), 1475–1484. doi:10.1093/cercor/bhm179

Ehlis, A. C., Haeussinger, F. B., Gastel, A., Fallgatter, A. J., & Plewnia, C. (2016). Task-dependent and polarity-specific effects of prefrontal transcranial direct current stimulation on cortical activation during word fluency. *Neuroimage, 140,* 134-140. doi:10.1016/j.neuroimage.2015.12.047

Elliot, A. J., & Maier, M. A. (2014). Color psychology: effects of perceiving color on psychological functioning in humans. *Annual Review of Psychology, 65,* 95–120. doi:10.1146/annurev-psych-010213-115035

Fertonani, A., & Miniussi, C. (2017). Transcranial Electrical Stimulation: What We Know and Do Not Know About Mechanisms. *The Neuroscientist, 23(2), 109-123.* doi:10.1177/1073858416631966

Fias, W., Brysbaert, M., Geypens, F., & D'Ydewalle, G. (1996). The Importance of Magnitude Information in Numerical Processing: Evidence from the SNARC Effect. *Mathematical Cognition*, *2*(1), 95–110. doi:10.1080/135467996387552

Fias, W., & Fischer, M. H. (2005). Spatial representation of numbers. *Handbook of Mathematical Cognition*.

Fias, W., Lammertyn, J., Reynvoet, B., Dupont, P., & Orban, G. A. (2003). Parietal representation of symbolic and nonsymbolic magnitude. *Journal of Cognitive Neuroscience*, *15*(1), 47–56. doi:10.1162/089892903321107819

Fias, W., Lauwereyns, J., & Lammertyn, J. (2001). Irrelevant digits affect feature-based attention depending on the overlap of neural circuits. *Cognitive Brain Research*, *12*(3), 415–423. doi:10.1016/S0926-6410(01)00078-7

Fiedler, K., Messner, C., & Bluemke, M. (2006). Unresolved problems with the "I", the "A", and the "T": A logical and psychometric critique of the Implicit Association Test (IAT). *European Review of Social Psychology*, *17*(1), 74–147. doi:10.1080/10463280600681248

Fischer, M. H. (2008). Finger counting habits modulate spatial-numerical associations. *Cortex*, *44*(4), 386–92. doi:10.1016/j.cortex.2007.08.004

Fischer, M. H. (2012). A hierarchical view of grounded, embodied, and situated numerical cognition. *Cognitive processing, 13,* S161-4. doi:10.1007/s10339-012-0477-5

Fischer, M. H., Castel, A. D., Dodd, M. D., & Pratt, J. (2003). Perceiving numbers causes spatial shifts of attention. *Nature Neuroscience*, *6*(6), 555–556. doi:10.1038/nn1066

Fischer, M. H., Mills, R. A., & Shaki, S. (2010). How to cook a SNARC: number placement in text rapidly changes spatial-numerical associations. *Brain and cognition*, *72*(3), 333–6. doi:10.1016/j.bandc.2009.10.010

Fischer, M. H., & Shaki, S. (2016). Measuring spatial-numerical associations: evidence for a purely conceptual link. *Psychological Research*, *80*(1), 109–112. doi:10.1007/s00426-015-0646-0

Fischer, M. H., & Shaki, S. (2017). Implicit Spatial-Numerical Associations: Negative Numbers and the Role of Counting Direction. *Journal of Experimental Psychology: Human Perception and Performance*, *43*(4), 639–643. doi:10.1037/xhp0000369

Fischer, U., Moeller, K., Class, F., Huber, S., Cress, U., & Nuerk, H.-C. (2016). Dancing with the SNARC: Measuring spatial-numerical associations on a digital dance mat. *Canadian Journal of Experimental Psychology*, 70(4), 306. doi:10.1037/cep0000084

Francis, G. (2012). Too good to be true: Publication bias in two prominent studies from experimental psychology. *Psychonomic Bulletin & Review*, *19*(2), 151–156. doi:10.3758/s13423-012-0227-9

Fregni, F., Boggio, P. S., Nitsche, M. A., Bermpohl, F., Antal, A., Feredoes, E., Marcolin, M. A., … Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research*, *166*(1), 23–30. doi:10.1007/s00221-005-2334-6

Friese, M., Hofmann, W., & Wiers, R. W. (2011). On taming horses and strengthening riders: Recent developments in research on interventions to improve self-control in health behaviors. *Self and Identity*, *10*(3), 336–351. doi:10.1080/15298868.2010.536417

Gamer, J., Schmukle, S. C., Luka-Krausgrill, U., & Egloff, B. (2008). Examining the dynamics of the implicit and the explicit self-concept in social anxiety: changes in the Implicit Association Test-Anxiety and the Social Phobia Anxiety Inventory following treatment. *Journal of personality assessment*, *90*(5), 476–480. doi:10.1080/00223890802248786

Gandiga, P. C., Hummel, F. C., & Cohen, L. G. (2006). Transcranial DC stimulation (tDCS): a tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology*, *117*(4), 845–50. doi:10.1016/j.clinph.2005.12.003

Gawronski, B., & De Houwer, J. (2014). Implicit measures in social and personality psychology. *Social and Personality Psychology*, *1*(519), 1–28.

Gazes, R. P., Diamond, R. F. L., Hope, J. M., Caillaud, D., Stoinski, T. S., & Hampton, R. R. (2017). Spatial representation of magnitude in gorillas and orangutans. *Cognition*, *168*, 312–319. doi:10.1016/j.cognition.2017.07.010

Gbadeyan, O., McMahon, K., Steinhauser, M., & Meinzer, M. (2016). Stimulation of Dorsolateral Prefrontal Cortex Enhances Adaptive Cognitive Control: A High-Definition Transcranial Direct Current Stimulation Study. *Journal of Neuroscience, 36*(50), 12530–12536. doi:10.1523/JNEUROSCI.2450-16.2016

Georges, C., Hoffmann, D., & Schiltz, C. (2017). How and Why Do Number-Space Associations Co-Vary in Implicit and Explicit Magnitude Processing Tasks? *Journal of Numerical Cognition, 3*(2), 182-211. doi:10.5964/jnc.v3i2.46

Georges, C., Hoffmann, D., & Schiltz, C. (2016). How math anxiety relates to number-space associations. *Frontiers in Psychology, 7*, 1401. doi:10.3389/fpsyg.2016.01401

Georges, C., Schiltz, C., & Hoffmann, D. (2014). Task instructions determine the visuo-spatial and verbal-spatial nature of number-space associations. *Quarterly Journal of Experimental Psychology (2006), 0218*, 1–37. doi:10.1080/17470218.2014.997764

Gernsbacher, M. A. (1984). Resolving 20 years of inconsistent interactions between lexical familiarity and orthography, concreteness, and polysemy. *Journal of Experimental Psychology: General, 113*(2), 256-281.

Gevers, W., Caessens, B., & Fias, W. (2005). Towards a common processing architecture underlying Simon and SNARC effects. *European Journal of Cognitive Psychology, 17*(5), 659–673. doi:10.1080/09541440540000112

Gevers, W., Lammertyn, J., Notebaert, W., Verguts, T., & Fias, W. (2006). Automatic response activation of implicit spatial information: Evidence from the SNARC effect. *Acta Psychologica*, *122*(3), 221–233.doi:/10.1016/j.actpsy.2005.11.004

Gevers, W., & Notebaert, W. (2008). Two orienting mechanisms, one architecture: a comment on Rusconi, Turatto and Umiltà (2007). *Cognitive Neuropsychology*, *25*(1), 118–24. doi:10.1080/02643290701763977

Gevers, W., Reynvoet, B., & Fias, W. (2003). The mental representation of ordinal sequences is spatially organized. *Cognition*, *87*. doi:10.1016/S0010-0277(02)00234-2

Gevers, W., Reynvoet, B., & Fias, W. (2004). The Mental Representation of Ordinal Sequences is Spatially Organised: Evidence from Days of the Week. *Cortex, 40*(1), 171–172. doi:10.1016/S0010-9452(08)70938-9

Gevers, W., Santens, S., Dhooge, E., Chen, Q., Van den Bossche, L., Fias, W., & Verguts, T. (2010). Verbal-spatial and visuospatial coding of number-space interactions. *Journal of experimental psychology. General, 139*(1), 180–190. doi:10.1037/a0017688

Gevers, W., Verguts, T., Reynvoet, B., Caessens, B., & Fias, W. (2006). Numbers and space: A computational model of the SNARC effect. *Journal of Experimental Psychology: Human Perception and Performance*, *32*(1), 32–44. doi:10.1037/0096-1523.32.1.32

Gigerenzer, G., & Gaissmaier, W. (2011). Heuristic decision making. *Annual Review of Psychology*, *62*, 451–482. doi:10.1146/annurev-psych-120709-145346

Gill, J., Shah-basak, P. P., & Hamilton, R. (2015) It's the Thought That Counts: Examining the Task-dependent Effects of Transcranial Direct Current Stimulation on Executive Function. *Brain Stimulation* 8, 253–259. doi: 10.1016/j.brs.2014.10.018

Ginsburg, V., & Gevers, W. (2015). Spatial coding of ordinal information in short- and long-term memory. *Frontiers in Human Neuroscience*, *9*(5), 1–10. doi:10.3389/fnhum.2015.00008

Ginsburg, V., van Dijck, J.-P., Previtali, P., Fias, W., & Gevers, W. (2014). The impact of verbal working memory on number-space associations. *Journal of experimental psychology. Learning, memory, and cognition*, *40*(4), 976–86. doi:10.1037/a0036378

Gladwin, T. E., den Uyl, T. E., Fregni, F. F., & Wiers, R. W. (2012). Enhancement of selective attention by tDCS: interaction with interference in a Sternberg task. *Neuroscience letters*, *512*(1), 33–7. doi:10.1016/j.neulet.2012.01.056

Gladwin, T. E., den Uyl, T. E., & Wiers, R. W. (2012). Anodal tDCS of dorsolateral prefontal cortex during an Implicit Association Test. *Neuroscience Letters*, *517*, 82–86. doi:10.1016/j.neulet.2012.04.025

Göbel, S. M., Johansen-Berg, H., Behrens, T., & Rushworth, M. F. S. (2004). Response-selection-related parietal activation during number comparison. *Journal of Cognitive Neuroscience*, *16*, 1536–1551. doi:10.1162/0898929042568442

Göbel, S. M., Walsh, V., & Rushworth, M. F. (2001). The mental number line and the human angular gyrus. *NeuroImage*, *14*(6), 1278–89. doi:10.1006/nimg.2001.0927

Grabner, R. H., Rütsche, B., Ruff, C. C., & Hauser, T. U. (2015) Transcranial direct current stimulation of the posterior parietal cortex modulates arithmetic learning. *European Journal of Neuroscience* 42:1667–1674. doi:10.1111/ejn.12947

Gray, N.S., Brown, A.S., MacCulloch, M.J., Smith, J., & Snowden, R.J. (2005). An Implicit Test of the Associations Between Children and Sex in Pedophiles. *Journal of Abnormal Psychology*, 114(2), 304–8. doi:10.1037/0021-843X.114.2.304

Greenwald, A. G., Greenwald, A. G., Mcghee, D. E., Mcghee, D. E., Schwartz, J. L. K., & Schwartz, J. L. K. (1998). Measuring Individual Differences in Implicit Cognition: The Implicit Association Test. *Journal of Personality and Soclal Psychology, 74*(6), 1464–1480. doi:10.1037/0022-3514.74.6.1464

Greenwald, A.G., Nosek, B.A., & Banaji, M.R. (2003). Understanding and using the Implicit Association Test: An improved scoring algorithm. *Journal of Personality and Social Psychology, 85*(2), 197–216. doi:10.1037/0022-3514.85.2.197

Greenwald, A. G., Poehlman, T. A., Uhlmann, E., & Banaji, M. R. (2009). Understanding and using the Implicit Association Test: III. Meta-analysis of predictive validity. *Journal of Personality and Social Psychology, 97*(1), 17–41. doi:10.1037/a0015575

van der Groen, O., & Wenderoth, N. (2016). Transcranial Random Noise Stimulation of Visual Cortex: Stochastic Resonance Enhances Central Mechanisms of Perception. *Journal of Neuroscience, 36*(19), 5289–5298. doi: 10.1523/JNEUROSCI.4519-15.2016

Grundey, J., Thirugnanasambandam, N., Kaminsky, K., Drees, A., Skwirba, A. C., Lang, N., Paulus, W., ... Nitsche, M. A. (2012). Neuroplasticity in cigarette smokers is altered under withdrawal and partially restituted by nicotine exposition. *Journal of Neuroscience, 32*(12), 4156–4162. doi:10.1523/JNEUROSCI.3660-11.2012

Guida, A., Leroux, A., Lavielle-Guida, M., & Noël, Y. (2016). A SPoARC in the Dark: Spatialization in Verbal Immediate Memory. Cognitive Science, 40, 2108–2121. doi:10.1111/cogs.12316

Harty, S., Sella, F., & Cohen Kadosh, R. (2017). Mind the Brain: The mediating and moderating role of neurophysiology. *Trends in Cognitive Sciences,* 21(1), 2-5. doi:10.1016/j.tics.2016.11.002

Harvey, B. M., & Dumoulin, S. O. (2017). A network of topographic numerosity maps in human association cortex. *Nature Human Behaviour*, *1*(2), 36. doi:10.1038/s41562-016-0036

Haspelmath, M. (2006). Against Markedness (And What to Replace It With). *Journal of Linguistics*, *42*(1), 25–70.

Hauser, T. U., Rotzer, S., Grabner, R. H., Mérillat, S., & Jäncke, L. (2013) Enhancing performance in numerical magnitude processing and mental arithmetic using transcranial Direct Current Stimulation (tDCS). *Frontiers in Human Neuroscience* 7, 244. doi: 10.3389/fnhum.2013.00244

Hauser, T. U., Rütsche, B., Wurmitzer, K., Brem, S., Ruff, C. C., & Grabner, R. H. (2016). Neurocognitive Effects of Transcranial Direct Current Stimulation in Arithmetic Learning and Performance: a Simultaneous tDCS-fMRI Study. *Brain Stimulation*, *9*(6), 850-858. doi:10.1016/j.brs.2016.07.007

Heinemann, A., Pfister, R., & Janczyk, M. (2013). Manipulating number generation: Loud+long=large? *Consciousness and Cognition*, *22*(4), 1332–1339. doi:10.1016/j.concog.2013.08.014

Herrera, A., Macizo, P., & Semenza, C. (2008). The role of working memory in the association between number magnitude and space. *Acta Psychologica*, *128*(2), 225–237. doi:10.1016/j.actpsy.2008.01.002

Hesse, P. N., & Bremmer, F. (2016). SNARC Effect in Different Effectors. *Perception*, *45*(1–2), 180–195. doi:10.1177/0301006615614453

Hilgard, J., Bartholow, B.D., Dickter, C.L., & Blanton, H. (2015). Characterizing switching and congruency effects in the implicit association test as reactive and proactive cognitive control. *Social Cognitive and Affective Neuroscience*, *10*(3), 381–88. doi:10.1093/scan/nsu060

Hines, T. M. (1990). An odd effect: Lengthened reaction times for judgments about odd digits. *Memory & Cognition*, *18*(1), 40–46. doi:10.3758/BF03202644

Ho, K. A., Taylor, J. L., Chew, T., Gálvez, V., Alonzo, A., Bai, S., Dokos, S., & Loo, C. K. (2016) The Effect of Transcranial Direct Current Stimulation (tDCS) Electrode Size and Current Intensity on Motor Cortical Excitability: Evidence from Single and Repeated Sessions. *Brain Stimulation*, 9(1), 1–7. doi: 10.1016/j.brs.2015.08.003

Hoffmann, D., Hornung, C., Martin, R., & Schiltz, C. (2013). Developing number-space associations: SNARC effects using a color discrimination task in 5-year-olds. *Journal of experimental child psychology*, *116*(4), 775–91. doi:10.1016/j.jecp.2013.07.013

Hoffmann, D., Mussolin, C., Martin, R., & Schiltz, C. (2014). The impact of mathematical proficiency on the number-space association. *PloS One*, 9, e85048.

Hoffmann, D., Pigat, D., & Schiltz, C. (2014). The impact of inhibition capacities and age on number-space associations. *Cognitive Processing*, *15*(3), 329–342. doi:10.1007/s10339-014-0601-9

Hofmann, W., Rauch, W., & Gawronski, B. (2007). And deplete us not into temptation: Automatic attitudes, dietary restraint, and self-regulatory resources as determinants of eating behavior. *Journal of Experimental Social Psychology*, 43, 497–504. doi:10.1016/j.jesp.2006.05.004

Holmes, J., Byrne, E. M., Gathercole, S. E., & Ewbank, M. P. (2016) Transcranial Random Noise Stimulation Does Not Enhance the Effects of Working Memory Training. *Journal of Cognitive Neuroscience*, 28, 1471-1483. doi:10.1162/jocn_a_00993

Holloway, I. D., & Ansari, D. (2009). Mapping numerical magnitudes onto symbols: The numerical distance effect and individual differences in children's mathematics achievement. *Journal of Experimental Child Psychology*, *103*(1), 17–29. doi:10.1016/j.jecp.2008.04.001

Hommel, B. (2011). The Simon effect as tool and heuristic. *Acta Psychologica*, *136*(2), 189–202. doi:10.1016/j.actpsy.2010.04.011

Horvath, J. C., Carter, O., & Forte, J. D. (2014). Transcranial direct current stimulation: five important issues we aren't discussing (but probably should be). *Frontiers in systems neuroscience*, *8*(January), 2. doi:10.3389/fnsys.2014.00002

Horvath, J. C., Forte, J. D., & Carter, O. (2015). Quantitative review finds no evidence of cognitive effects in healthy populations from single-session transcranial direct current stimulation (tDCS). *Brain Stimulation*, *8*(3), 535–550. doi:10.1016/j.brs.2015.01.400

Houben, K., & Wiers, R.W. (2006). A test of the salience asymmetry interpretation of the alcohol-IAT. *Experimental Psychology*, *53*(4), 292–300. doi:10.1027/1618-3169.53.4.292

Houser, R., Thoma, S., Fonseca, D., O’Conner, E., & Stanton, M. (2015). Enhancing statistical calculation with transcranial direct current stimulation (tDCS) to the left intra-parietal sulcus (IPS). *Trends in Neuroscience and Education,* 4(4), 98–101. doi: 10.1016/j.tine.2015.07.002

Houser, R., Thoma, S., & Stanton, M. (2014). The effect of transcranial direct current stimulation (tDCS) on learning and performing statistical calculations. *Journal of Articles in Support of the Null Hypothesis,* 11, 1–10.

Hubbard, E. M., Piazza, M., Pinel, P., & Dehaene, S. (2005). Interactions between number and space in parietal cortex. *Nature reviews Neuroscience, 6*(6), 435–48. doi:10.1038/nrn1684

Huber, S., Klein, E., Graf, M., Nuerk, H.-C., Moeller, K., & Willmes, K. (2014). Embodied markedness of parity? Examining handedness effects on parity judgments. *Psychological research*. doi:10.1007/s00426-014-0626-9

Huber, S., Klein, E., Moeller, K., & Willmes, K. (2016). Spatial-numerical and ordinal positional associations coexist in parallel. *Frontiers in Psychology*, *7*(438). doi:10.3389/fpsyg.2016.00438

Huijding, J., De Jong, P. J., Wiers, R. W., & Verkooijen, K. (2005). Implicit and explicit attitudes toward smoking in a smoking and a nonsmoking setting. *Addictive Behaviors, 30*(5), 949–961. doi:10.1016/j.addbeh.2004.09.014

Hunt, S., Low, J., & Burns, K. C. (2008). Adaptive numerical competency in a food-hoarding songbird. *Proceedings of the Royal Society B: Biological Sciences*, *275*(1649), 2373–9. doi:10.1098/rspb.2008.0702

Hurlstone, M. J., Hitch, G. J., & Baddeley, A. D. (2014). Memory for serial order across domains: An overview of the literature and directions for future research. *Psychological Bulletin*, *140*(2), 339–373. doi:10.1037/a0034221

Hussey, I. (2017). Open Source Implicit Association Test

Imbo, I., Brauwer, J. De, Fias, W., & Gevers, W. (2012). The development of the SNARC effect: evidence for early verbal coding. *Journal of Experimental Child Psychology, 111*(4), 671–80. doi:10.1016/j.jecp.2011.09.002

Ishihara, M., Keller, P. E., Rossetti, Y., & Prinz, W. (2008). Horizontal spatial representations of time: Evidence for the STEARC effect. *Cortex*, *44*(4), 454–461. doi:10.1016/j.cortex.2007.08.010

Ishihara, S. (1917). *Test for Colour-Blindness.* Tokyo: Hongo Harukicho.

Iuculano, T., & Cohen Kadosh, R. (2013). The Mental Cost of Cognitive Enhancement. *Journal of Neuroscience*, *33*(10), 4482–4486. doi:10.1523/JNEUROSCI.4927-12.2013

Iuculano, T., & Cohen Kadosh, R. (2014). Preliminary evidence for performance enhancement following parietal lobe stimulation in Developmental Dyscalculia. *Frontiers in Human Neuroscience*, 8, 38. doi: 10.3389/fnhum.2014.00038

Iversen, W., Nuerk, H.-C., Jäger, L., & Willmes, K. (2006). The influence of an external symbol system on number parity representation, or What's odd about 6? *Psychonomic bulletin & review*, *13*(4), 730–736. doi:10.3758/BF03193988

Iversen, W., Nuerk, H.-C., & Willmes, K. (2004). Do signers think differently? The processing of number parity in deaf participants. *Cortex*, *40*(1), 176–178. doi:10.1016/S0010-9452(08)70940-7

Iversen, W., Nuerk, H., & Willmes, K. (2006). The influence of an external symbol system on number parity representation, or What's odd about 6? *Psychonomic Bulletin & Review*, *13*(4), 730–736.

Jacobson, L., Koslowsky, M., & Lavidor, M. (2012). tDCS polarity effects in motor and cognitive domains: a meta-analytical review. *Experimental brain research*, *216*(1), 1–10. doi:10.1007/s00221-011-2891-9

Jakobson, R. (1932; 1984). The structure of the Russian verb. In *Russian and Slavic Grammar: Studies 1931-1981* (pp. 1–14).

Jakobson, R. (1968). *Child Language, Aphasia, and Universals of Language.* (Vol. 72). The Hague: Mouton.

Jamil, A., Batsikadze, G., Kuo, H.-I., Labruna, L., Hasan, A., Paulus, W., & Nitsche, M. A. (2017). Systematic evaluation of the impact of stimulation intensity on neuroplastic after-effects induced by transcranial direct current stimulation. *The Journal of Physiology*, *595*(4), 1273–1288. doi:10.1113/JP272738

Jarick, M., Dixon, M. J., Stewart, M. T., Maxwell, E. C., & Smilek, D. (2009). A different outlook on time: Visual and auditory month names elicit different mental vantage points for a time-space synaesthete. *Cortex*, *45*(10), 1217–1228. doi:10.1016/j.cortex.2009.05.014

Jung, Y., Kim, J., & Im, C. (2013). COMETS: A MATLAB toolbox for simulating local electric fields generated by transcranial direct current stimulation (tDCS). *Biomedical Engineering Letters*, 3(1), 39-46. doi:10.1007/s13534-013-0087-x

Kanouse, D. E., & Hanson, L. (1972). *Negativity in evaluations*. In & B. W. E. E. Jones, D. E. Kanouse, S. Valins, H. H. Kelley, R. E. Nisbett (Ed.), Attribution: Perceiving the causes of behavior (pp. 47–62). Morristown, NJ: General Learning Press.

Kaufmann, L., Mazzocco, M. M., Dowker, A., ... Nuerk, H.-C. (2013). Dyscalculia from a developmental and differential perspective. *Frontiers in Psychology*, 4, 516. doi:10.3389/fpsyg.2013.00516

Keeser, D., Meindl, T., Bor, J., Palm, U., Pogarell, O., Mulert, C., Brunelin, J., ... Padberg, F. (2011). Prefrontal Transcranial Direct Current Stimulation Changes Connectivity of Resting-State Networks during fMRI. *Journal of Neuroscience*, *31*(43), 15284–15293. doi:10.1523/JNEUROSCI.0542-11.2011

Kemps, E., & Tiggemann, M. (2015). Approach Bias for Food Cues in Obese Individuals. *Psychology & Health*, *30*(3), 370–380. doi:10.1080/08870446.2014.974605

Keus, I. M., Jenks, K. M., & Schwarz, W. (2005). Psychophysiological evidence that the SNARC effect has its functional locus in a response selection stage. *Cognitive Brain Research*, *24*(1), 48–56. doi:10.1016/j.cogbrainres.2004.12.005

Keus, I. M., & Schwarz, W. (2005). Searching for the functional locus of the SNARC effect: evidence for a response-related origin. *Memory & Cognition*, *33*(4), 681–695. doi:10.3758/BF03195335

Kinoshita, S., & Peek-O’Leary, M. (2006). Two bases of the compatibility effect in the Implicit Association Test (IAT). *Quarterly Journal of Experimental Psychology*, *59*(12), 2102–20. doi:10.1080/17470210500451141

Klein, E., Mann, A., Huber, S., Bloechle, J., Willmes, K., Karim, A. A., Nuerk, H.-C., & Mueller, K. (2013). Bilateral Bi-Cephalic tDCS with Two Active Electrodes of the Same Polarity Modulates Bilateral Cognitive Processes Differentially. *PLoS One,* 8(8), e71607. doi: 10.1371/journal.pone.0071607

Klein, E., Moeller, K., Glauche, V., Weiller, C., & Willmes, K. (2013). Processing pathways in mental arithmetic--evidence from probabilistic fiber tracking. *PloS One*, *8*(1), e55455. doi:10.1371/journal.pone.0055455

Klein, E., Moeller, K., Willmes, K., Nuerk, H. C., & Domahs, F. (2011). The influence of implicit hand-based representations on mental arithmetic. *Frontiers in Psychology, 2*(SEP), 1–7. doi:10.3389/fpsyg.2011.00197

Klein, E., Suchan, J., Moeller, K., Karnath, H.-O., Knops, A., Wood, G., Nuerk, H.-C., … Willmes, K. (2016). Considering structural connectivity in the triple code model of numerical cognition: differential connectivity for magnitude processing and arithmetic facts. *Brain Structure and Function*, *221*(2), 979–95. doi:10.1007/s00429-014-0951-1

Knops, A., Nuerk, H.-C., Sparing, R., Foltys, H., & Willmes, K. (2006). On the Functional Role of Human Parietal Cortex in Number Processing: How Gender Mediates the Impact of a Virtual Lesion Induced by rTMS. *Neuropsychologia,* 44, 2270-2283.

Knops, A., Thirion, B., Hubbard, E. M., Michel, V., Knops, A., Thirion, B., … Dehaene, S. (2015). Recruitment Movements of an Area Involved in Eye Arithmetic During Mental, *324*(5934), 1583–1585.

Krause, B., & Cohen Kadosh, R. (2013). Can transcranial electrical stimulation improve learning difficulties in atypical brain development? A future possibility for cognitive training. *Developmental Cognitive Neuroscience,* 6, 176–194. doi: 10.1016/j.dcn.2013.04.001

Krause, F., Lindemann, O., Toni, I., & Bekkering, H. (2014). Different brains process numbers differently: structural bases of individual differences in spatial and nonspatial number representations. *Journal of Cognitive Neuroscience, 26,* 768–776. doi:10.1162/jocn_a_00518

Kuo, H.-I. I., Bikson, M., Datta, A., Minhas, P., Paulus, W., Kuo, M.-F. F., & Nitsche, M. A. (2013). Comparing Cortical Plasticity Induced by Conventional and High-Definition 4 × 1 Ring tDCS: A Neurophysiological Study. *Brain Stimulation*, *6*(4), 644–648. doi:10.1016/j.brs.2012.09.010

Lakens, D. (2012). Polarity Correspondence in Metaphor Congruency Effects: Structural Overlap Predicts Categorization Times for Bipolar Concepts Presented in Vertical Space. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *38*, 726–723. doi:10.1037/a0024955

Lee, D., Chun, J., & Cho, S. (2015). The Instructional Dependency of SNARC Effects Reveals Flexibility of the Space-Magnitude Association of Nonsymbolic and Symbolic Magnitudes. *Perception*, *45*(5), 552–567. doi:10.1177/0301006616629027

Leibovich, T., Katzin, N., Harel, M., & Henik, A. (2017). From "sense of number" to "sense of magnitude" - The role of continuous magnitudes in numerical cognition. *Behavioral and brain sciences*, *40*, e164. doi:10.1017/S0140525X16000960

Leite, J., Gonçalves, Ó. F., Pereira, P., Khadka, N., Bikson, M., Fregni, F., & Carvalho, S. (in press). The differential effects of unihemispheric and bihemispheric tDCS over the inferior frontal gyrus on proactive control. *Neuroscience Research.* http://doi.org/10.1016/j.neures.2017.08.005

Leth-Steensen, C., & Citta, R. (2016). Bad-good constraints on a polarity correspondence account for the spatial-numerical association of response codes (SNARC) and markedness association of response codes (MARC) effects. *Quarterly journal of experimental psychology*, *69*(3), 482–94. doi:10.1080/17470218.2015.1055283

Li, L. M., Leech, R., Scott, G., Malhotra, P., Seemungal, B., & Sharp, D. J. (2015) The effect of oppositional parietal transcranial direct current stimulation on lateralized brain functions. *European Journal of Neuroscience*, *42*(11), 2904–2914. doi: 10.1111/ejn.13086

Lidji, P., Kolinsky, R., Lochy, A., & Morais, J. (2007). Spatial associations for musical stimuli: a piano in the head? *Journal of Experimental Psychology. Human Perception and Performance*, *33*(5), 1189–1207. doi:10.1037/0096-1523.33.5.1189

Lindemann, O., Abolafia, J. M., Pratt, J., & Bekkering, H. (2008). Coding strategies in number space: Memory requirements influence spatial–numerical associations. *The Quarterly Journal of Experimental Psychology*, *61*(4), 515–524. doi:10.1080/17470210701728677

Lindgren, K. P., Neighbors, C., Teachman, B. A., Gasser, M. L., Kaysen, D., Norris, J., & Wiers, R. W. (2015). Habit doesn't make the predictions stronger: Implicit alcohol associations and habitualness predict drinking uniquely. *Addictive Behaviors*, *45*, 139–145. doi:10.1016/j.addbeh.2015.01.003

Lippold, O., & Redfearn, J. W. (1964). Mental changes resulting from the passage of small direct currents through the human brain. *The British journal of psychiatry*, *110*, 768–72.

Liu, X., Banich, M. T., Jacobson, B. L., & Tanabe, J. L. (2004). Common and distinct neural substrates of attentional control in an integrated Simon and spatial Stroop task as assessed by event-related fMRI. *NeuroImage*, *22*(3), 1097–106. doi:10.1016/j.neuroimage.2004.02.033

Loetscher, T., Bockisch, C. J., Nicholls, M. E. R., & Brugger, P. (2010). Eye position predicts what number you have in mind. *Current Biology*, *20*(6), R264-5. doi:10.1016/j.cub.2010.01.015

Loetscher, T., Schwarz, U., Schubiger, M., & Brugger, P. (2008). Head turns bias the brain's internal random generator. *Current Biology*, *18*(2), R60-2. doi:10.1016/j.cub.2007.11.015

Looi, C. Y., Cohen Kadosh, R. (2016). Brain stimulation, mathematical and numerical training: Contribution of core and non-core skills. *Progress in brain research*, *227*, 353–388. doi:10.1016/bs.pbr.2016.04.009.

Looi, C. Y., Duta, M., Brem, A.-K., Huber, S., Nuerk, H.-C., & Cohen Kadosh, R. (2016). Combining brain stimulation and video game to promote long-term transfer of learning and cognitive enhancement. *Scientific Reports*, *6*(August 2015), 22003. doi:10.1038/srep22003

Looi, C. Y., Thompson, J., Krause, B. & Cohen Kadosh, R. (2016). The Neuroscience of Mathematical Cognition and Learning. *OECD Education Working Papers*, *136*, 1-68. doi:0.1787/5jlwmn3ntbr7-en

Lorch, R. F., & Myers, J. L. (1990). Regression analyses of repeated measures data in cognitive research. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 16*(1), 149–157.

Lyons, J. (1977). *Semantics*. London: Cambridge University Press.

Mapelli, D., Rusconi, E., & Umiltà, C. (2003). The SNARC effect: an instance of the Simon effect? *Cognition, 88*(3), B1–B10. doi:10.1016/S0010-0277(03)00042-8

Matejko, A. A., & Ansari, D. (2015). Drawing connections between white matter and numerical and mathematical cognition: A literature review. *Neuroscience and Biobehavioral Reviews, 48,* 35–52. doi: 10.1016/j.neubiorev.2014.11.006

McCrink, K., Dehaene, S., & Dehaene-Lambertz, G. (2007). Moving along the number line: operational momentum in nonsymbolic arithmetic. *Perception & psychophysics, 69*(8), 1324–33.

Medina, J., & Cason, S. (2017). No Evidential Value in Samples of Transcranial Direct Current Stimulation (tDCS) Studies of Cognition and Working Memory in Healthy Populations. *Cortex, 94,* 131-141. http://doi.org/10.1016/j.cortex.2017.06.021

Meissner, F., & Rothermund, K. (2013). Estimating the Contributions of Associations and Recoding in the Implicit Association Test: The ReAL Model for the IAT. *Journal of Personality and Social Psychology, 104*(1), 45–69. doi:10.1037/a0030734.

Meissner, F., & Rothermund, K. (2015). The insect-nonword IAT revisited: Dissociating between evaluative associations and recoding. *Social Psychology, 46*(1), 46–54. doi:10.1027/1864-9335/a000220

Mierke, J., & Klauer, K.C. (2001). Implicit association measurement with the IAT: Evidence for effects of executive control processes. *Experimental Psychology, 48*(2), 107–22. doi:10.1026//0949-3946.48.2.107

Mihulowicz, U., Klein, E., Nuerk, H.-C., Willmes, K., & Karnath, H.-O. (2015). Spatial displacement of numbers on a vertical number line in spatial neglect. *Frontiers in Human Neuroscience, 9*(April), 1–10. doi:10.3389/fnhum.2015.00240

Milhau, A., Brouillet, T., & Brouillet, D. (2014). Valence-space compatibility effects depend on situated motor fluency in both right- and left-handers. *Quarterly Journal of Experimental Psychology (2006), 218*(November), 1–13.doi:10.1080/17470218.2014.967256

Milhau, A., Brouillet, T., Dru, V., Coello, Y., & Brouillet, D. (2017). Valence activates motor fluency simulation and biases perceptual judgment. *Psychological Research, 81*(4), 795-805. doi:10.1007/s00426-016-0788-8

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual review of neuroscience*, *24*, 167–202. doi:10.1146/annurev.neuro.24.1.167

Miller, J., & Ulrich, R. (2013). Mental chronometry and individual differences: modeling reliabilities and correlations of reaction time means and effect sizes. *Psychonomic Bulletin & Review*, *20*(5), 819–58. doi:10.3758/s13423-013-0404-5

Miniussi, C., Harris, J. A., & Ruzzoli, M. (2013). Modelling non-invasive brain stimulation in cognitive neuroscience. *Neuroscience and biobehavioral reviews*, *37*(8), 1702–12. doi:10.1016/j.neubiorev.2013.06.014

Miranda, P. C., Faria, P., & Hallett, M. (2009). What does the ratio of injected current to electrode area tell us about current density in the brain during tDCS? *Clinical Neurophysiology, 120,* 1183–1187. doi: 10.1016/j.clinph.2009.03.023

Mitchell, T., Bull, R., & Cleland, A. A. (2012). Implicit response-irrelevant number information triggers the SNARC effect: Evidence using a neural overlap paradigm. *The Quarterly Journal of Experimental Psychology*, *65*(10), 1945–1961. doi:10.1080/17470218.2012.673631

Moliadze, V., Antal, A., & Paulus, W. (2010). Electrode-distance dependent after-effects of transcranial direct and random noise stimulation with extracephalic reference electrodes. *Clinical neurophysiology*, *121*(12), 2165–71. doi:10.1016/j.clinph.2010.04.033

Moliadze, V., Fritzsche, G., & Antal, A. (2014). Comparing the efficacy of excitatory transcranial stimulation methods measuring motor evoked potentials. *Neural Plasticity*, Article ID 837141. doi: 10.1155/2014/837141

Monte-Silva, K., Kuo, M. F., Liebetanz, D., Paulus, W., & Nitsche, M. A. (2010). Shaping the Optimal Repetition Interval for Cathodal Transcranial Direct Current Stimulation. *Journal of Neurophysiology*, *103*, 1735–1740. doi:10.1152/jn.00924.2009

Monte-Silva, K., Kuo, M. F., Hessenthaler, S., Fresnoza, S., Liebetanz, D., Paulus, W., & Nitsche, M. A. (2013). Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. *Brain Stimulation*, *6*(3), 424–432. doi:10.1016/j.brs.2012.04.011

Moyer, R. S., & Landauer, T. K. (1967). Time required for Judgements of Numerical Inequality. *Nature*, *215*(5109), 1519–1520. doi:10.1038/2151519a0

Mulquiney, P. G., Hoy, K. E., Daskalakis, Z. J., & Fitzgerald, P. B. (2011). Improving working memory: Exploring the effect of transcranial random noise stimulation and transcranial direct current stimulation on the dorsolateral prefrontal cortex. *Clinical Neurophysiology, 122*, 2384–2389. doi: 10.1016/j.clinph.2011.05.009

Nasseri, P., Nitsche, M. A., & Ekhtiari, H. (2015). A framework for categorizing electrode montages in transcranial direct current stimulation. *Frontiers in Human Neuroscience, 9,* 1–5. doi: 10.3389/fnhum.2015.00054

Nieder, A. (2016). The neuronal code for number. *Nature Reviews Neuroscience*, 17, 366-382. doi:10.1038/nrn.2016.40

Nieder, A. (2017). Number Faculty Is Rooted in Our Biological Heritage. *Trends in Cognitive Sciences*, 21(6), 403–404. doi:10.1016/j.tics.2017.03.014

Nieder, A., & Dehaene, S. (2009). Representation of Number in the Brain. *Annual Review of Neuroscience*, 32(1), 185–208. http://doi.org/10.1146/annurev.neuro.051508.135550

Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., Paulus, W., … Pascual-Leone, A. (2008). Transcranial direct current stimulation: State of the art 2008. *Brain stimulation*, *1*(3), 206–23. doi:10.1016/j.brs.2008.06.004

Nitsche, M. A., Nitsche, M. S., Klein, C. C., Tergau, F., Rothwell, J. C., & Paulus, W. (2003). Level of action of cathodal DC polarisation induced inhibition of the human motor cortex. *Clinical Neurophysiology*, *114*(4), 600–604. doi:10.1016/S1388-2457(02)00412-1

Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology*, *527 Pt 3*(2000), 633–9. doi:10.1111/j.1469-7793.2000.t01-1-00633.x

Nitsche, M. A., Schauenburg, A., Lang, N., Liebetanz, D., Exner, C., Paulus, W., & Tergau, F. (2003). Facilitation of implicit motor learning by weak transcranial direct current stimulation of the primary motor cortex in the human. *Journal of cognitive neuroscience, 15*(4), 619–626. doi:10.1162/089892903321662994

Noetscher, G. M., Member, S., Yanamadala, J., & Makarov, S. N. (2014). Comparison of Cephalic and Extracephalic Montages for Transcranial Direct Current Stimulation – A Numerical Study. *IEEE Transactions on Biomedical Engineering*, *61*(9). doi:10.1109/TBME.2014.2322774

Nosek, B. A., Alter, G., Banks, G. C., Borsboom, D., Bowman, S. D., Breckler, S. J., Buck, S., … Yarkoni, T. (2015). Promoting an open research culture. *Science*, 348(6242), 1422–1425. doi:10.1126/science.aab2374

Nosek, B.A., Banaji, M.R., & Greenwald, A.G. (2002). Harvesting implicit group attitudes and beliefs from a demonstration web site. *Group Dynamics: Theory, Research, and Practice, 6*(1), 101–15.

Nosek, B.A., Greenwald, A.G., & Banaji, M.R. (2007). *The Implicit Association Test at Age 7: A Methodological and Conceptual Review* (pp. 265-292). In J. A. Bargh (Ed.), Automatic Processes in Social Thinking and Behavior. Psychology Press.

Notebaert, W., Gevers, W., Verguts, T., & Fias, W. (2006). Shared spatial representations for numbers and space: the reversal of the SNARC and the Simon effects. *Journal of Experimental Psychology. Human Perception and Performance*, *32*(5), 1197–207. doi:10.1037/0096-1523.32.5.1197

Nozari, N., Woodard, K., & Thompson-Schill, S. L. (2014). Consequences of cathodal stimulation for behavior: when does it help and when does it hurt performance? *PloS one*, *9*(1), e84338. doi:10.1371/journal.pone.0084338

Nuerk, H.-C., Bauer, F., Krummenacher, J., Heller, D., & Willmes, K. (2005). The power of the mental number line: how the magnitude of unattended numbers affects performance in an Eriksen task. *Psychology Science*, *47*(1), 34–50.

Nuerk, H.-C., Iversen, W., & Willmes, K. (2004). Notational modulation of the SNARC and the MARC (linguistic markedness of response codes) effect. *The Quarterly Journal of Experimental Psychology*, *57*(5), 835–63. doi:10.1080/02724980343000512

Nuerk, H.-C., Patro, K., Cress, U., Schild, U., Friedrich, C. K., & Göbel, S. M. (2015). How space-number associations may be created in preliterate children: six distinct mechanisms. *Frontiers in psychology*, *6*(March), 215. doi:10.3389/fpsyg.2015.00215

Nuerk, H.-C., Wood, G., & Willmes, K. (2005). The universal SNARC effect: the association between number magnitude and space is amodal. *Experimental Psychology, 52*(3), 187–94. doi:10.1027/1618-3169.52.3.187

Núñez, R. E. (2011). No Innate Number Line in the Human Brain. *Journal of Cross-Cultural Psychology, 42*(4), 651–668. doi:10.1177/0022022111406097

Núñez, R. E. (2017). Number – Biological Enculturation Beyond Natural Selection. *Trends in Cognitive Sciences, 21*(6), 404–405. doi:10.1016/j.tics.2017.03.013

Núñez, R., & Fias, W. (2017). Ancestral Mental Number Lines: What Is the Evidence? *Cognitive Science, 41*(8), 2262–2266. doi:10.1111/cogs.12296

Oberauer, K. (2002). Access to information in working memory: Exploring the focus of attention. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 28*(3), 411–421. http://doi.org/10.1037//0278-7393.28.3.411

Ochsner, K. N., & Gross, J. J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences*, *9*(5), 242–249. doi:10.1016/j.tics.2005.03.010

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, *9*, 97–113. doi:10.1016/0028-3932(71)90067-4

Open Science Collaboration. (2015). Estimating the reproducibility of psychological science. *Science, 349*(6251). doi:10.1126/science.aac4716

Opfer, J. E., Thompson, C. A., & Furlong, E. E. (2010). Early development of spatial-numeric associations: evidence from spatial and quantitative performance of preschoolers. *Developmental Science, 13*(5), 761–771. doi:10.1111/j.1467-7687.2009.00934.x

Opitz, A., Falchier, A., Yan, C., Yeagle, E., & Linn, G. (2016). Spatiotemporal structure of intracranial electric fields induced by transcranial electric stimulation in human and nonhuman primates. *Scientific Reports, 6*, 1–11. doi:10.1101/053892

Ozen, S., Sirota, A., Belluscio, M. A., Anastassiou, C. A., Stark, E., Koch, C., & Buzsáki, G. (2010). Transcranial Electric Stimulation Entrains Cortical Neuronal Populations in Rats. *Journal of Neuroscience, 30*(34), 11476–11485. doi: 10.1523/JNEUROSCI.5252-09.2010

Pagel, M., & Meade, A. (2018). The Deep History of the Number Words. *Philosophical Transactions of the Royal Society B, 373*(1740), 20160517. doi:10.1098/rstb.2016.0517

Paivio, A. (1986). *Mental Representations: A Dual-Coding Approach*. New York: Oxford University Press.

Pansky, A., & Algom, D. (1999). Stroop and Garner effects in comparative judgment of numerals: The role of attention. *Journal of Experimental Psychology: Human Perception and Performance, 25*(1), 39–58. doi:10.1037/0096-1523.25.1.39

Parkin, B. L., Ekhtiari, H., & Walsh, V. F. (2015). Non-invasive human brain stimulation in cognitive neuroscience: a primer. *Neuron, 87*(5), 932-945. doi:10.1016/j.neuron.2015.07.032

Pasqualotto, A. (2016). Transcranial random noise stimulation benefits arithmetic skills. Neurobiology of Learning and Memory, 133, 7–12. doi: 10.1016/j.nlm.2016.05.004

Patro, K., Fischer, U., Nuerk, H.-C., & Cress, U. (2015). How to rapidly construct a spatial-numerical representation in preliterate children (at least temporarily). *Developmental Science*, *19*(1), 126–144. doi:10.1111/desc.12296

Patro, K., & Haman, M. (2018). Playing reading, using hands: Which activities are linked to number-space processing in preschool children? *Psychology of Language and Communication, 22.*

Patro, K., & Nuerk, H. C. (2016). Limitations of Trans-Species Inferences: The Case of Spatial-Numerical Associations in Chicks and Humans. *Cognitive Science,* 1–8. doi:10.1111/cogs.12432

Patro, K., Nuerk, H.-C., Cress, U., & Haman, M. (2014). How number-space relationships are assessed before formal schooling: A taxonomy proposal. *Frontiers in Psychology*, *5*, 419. doi:10.3389/fpsyg.2014.00419

Patro, K., Nuerk, H. C., & Cress, U. (2016). Mental Number Line in the Preliterate Brain: The Role of Early Directional Experiences. *Child Development Perspectives, 10*(3), 172–177. doi:10.1111/cdep.12179

Peirce, J. W. (2007). PsychoPy--Psychophysics software in Python. *Journal of Neuroscience Methods*, *162*(1-2), 8–13. doi:10.1016/j.jneumeth.2006.11.017

Piazza, M., Izard, V., Pinel, P., Le Bihan, D., & Dehaene, S. (2004). Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron*, *44*(3), 547–555. doi:10.1016/j.neuron.2004.10.014

Pfister, R., & Janczyk, M. (2013). Confidence intervals for two sample means: Calculation, interpretation, and a few simple rules. *Advances in Cognitive Psychology, 9*(2), 74–80. doi:10.2478/v10053-008-0133-x

Pfister, R., Schroeder, P. A., & Kunde, W. (2013). SNARC struggles: Instant control over spatial-numerical associations. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *39*(6), 1953–8. doi:10.1037/a0032991

Pinhas, M., Tzelgov, J., & Ganor-Stern, D. (2012). Estimating linear effects in ANOVA designs: the easy way. *Behavior Research Methods*, *44*(3), 788–94. doi:10.3758/s13428-011-0172-y

Pirulli, C., Fertonani, A., & Miniussi, C. (2014). Is neural hyperpolarization by cathodal stimulation always detrimental at the behavioral level? *Frontiers in Behavioral Neuroscience*, *8*(June), 226. doi:10.3389/fnbeh.2014.00226

Plewnia, C., Schroeder, P. A., Kunze, R., Faehling, F., & Wolkenstein, L. (2015). Keep Calm and Carry On: Improved Frustration Tolerance and Processing Speed by Transcranial Direct Current Stimulation (tDCS). *Plos One*, *10*(4), e0122578. doi:10.1371/journal.pone.0122578

Plewnia, C., Schroeder, P. A., & Wolkenstein, L. (2015). Targeting the biased brain: non-invasive brain stimulation to ameliorate cognitive control. *The Lancet Psychiatry*, *2*(4), 351–356. doi:10.1016/S2215-0366(15)00056-5

Polanía, R., Paulus, W., & Nitsche, M. A. (2012). Modulating cortico-striatal and thalamo-cortical functional connectivity with transcranial direct current stimulation. *Human Brain Mapping, 33*(10), 2499–2508. http://doi.org/10.1002/hbm.21380

Pope, P. A., Brenton, J. W., & Miall, R. C. (2015). Task-Specific Facilitation of Cognition by Anodal Transcranial Direct Current Stimulation of the Prefrontal Cortex. *Cerebral Cortex*, *11*(1), 4551-4558. doi: 10.1093/cercor/bhv094

Pope, P. A., & Miall, R. C. (2012). Task-specific facilitation of cognition by cathodal transcranial direct current stimulation of the cerebellum. *Brain Stimulation, 5*(1), 84–94. doi: 10.1016/j.brs.2012.03.006

Popescu, T., Krause, B., Terhune, D. B., Twose, O., Page, T., Humphreys, G., & Cohen Kadosh, R. (2016). Transcranial random noise stimulation mitigates increased difficulty in an arithmetic learning task. *Neuropsychologia, 81*, 255–264. doi: 10.1016/j.neuropsychologia.2015.12.028

Previtali, P., De Hevia, M. D., & Girelli, L. (2010). Placing order in space: The SNARC effect in serial learning. *Experimental Brain Research*, *201*(3), 599–605. doi:10.1007/s00221-009-2063-3

Price, A. R., & Hamilton, R. H. (2015). A Re-evaluation of the Cognitive Effects From Single-session Transcranial Direct Current Stimulation. *Brain Stimulation*, *8*(3), 663–665.

Priftis, K., Zorzi, M., Meneghello, F., Marenzi, R., & Umiltà, C. (2006). Explicit versus Implicit Processing of Representational Space in Neglect: Dissociations in Accessing the Mental Number Line. *Journal of Cognitive Neuroscience*, *18*(4), 680–688. doi:10.1162/jocn.2006.18.4.680

Priori, A., Berardelli, A., Rona, S., Accornero, N., & Manfredi, M. (1998). Polarization of the human motor cortex through the scalp. *Neuroreport*, *9*(10), 2257–60.

Proctor, R. W., & Cho, Y. S. (2003). Effects of response eccentricity and relative position on orthogonal stimulus-response compatibility with joystick and keypress responses. *The Quarterly Journal of Experimental Psychology Section A*, *56 A*(2), 309–327. doi:10.1080/02724980244000350

Proctor, R. W., & Cho, Y. S. (2006). Polarity correspondence: A general principle for performance of speeded binary classification tasks. *Psychological Bulletin*, *132*(3), 416–42. doi:10.1037/0033-2909.132.3.416

Proctor, R. W., & Xiong, A. (2015). Polarity Correspondence as a General Compatibility Principle. *Current Directions in Psychological Science*, *24*(6), 446–451. doi:10.1177/0963721415607305

Rabbitt, P. (1979). How old and young subjects monitor and control responses for accuracy and speed. *British Journal of Psychology*, *70*(2), 305–311. doi:10.1111/j.2044-8295.1979.tb01687.x

Radman, T., Ramos, R., Brumberg, J., & Bikson, M. (2009). Role of Cortical Cell Type and Morphology in Sub- and Suprathreshold Uniform Electric Field Stimulation. *Brain stimulation*, *2*(4), 215–228. doi:10.1016/j.brs.2009.03.007

Rahman, A., Reato, D., Arlotti, M., Gasca, F., Datta, A., Parra, L. C., & Bikson, M. (2013). Cellular effects of acute direct current stimulation: somatic and synaptic terminal effects. *The Journal of Physiology*, *591*(Pt 10), 2563–78. doi:10.1113/jphysiol.2012.247171

Ramirez-Cardenas, A., Moskaleva, M., & Nieder, A. (2016). Neuronal Representation of Numerosity Zero in the Primate Parieto-Frontal Number Network. *Current Biology*, *26*(10), 1285-1294. doi:10.1016/j.cub.2016.03.052

Rawji, V., Ciocca, M., Zacharia, A., Soares, D., Truong, D., Rothwell, J., & Bestmann, S. (2017). tDCS changes in motor excitability are specific to orientation of current flow. *bioRxiv*. doi:10.1101/149633 doi:

Redfearn, W. T., Lippold, O. C., & Costain, R. (1964). A Preliminary Account of the Clinical Effects of Polarizing the Brain in Certain Psychiatric Disorders By. *British Journal of Psychiatry*, *110*, 773–785.

Riva, G. (2014). Out of my real body: cognitive neuroscience meets eating disorders. *Frontiers in human neuroscience*, *8*(May), 236. doi:10.3389/fnhum.2014.00236

Rogalewski, A., Breitenstein, C., Nitsche, M. a, Paulus, W., & Knecht, S. (2004). Transcranial direct current stimulation disrupts tactile perception. *European Journal of Neuroscience*, *20*(1), 2001–2004. doi:10.1111/j.1460-9568.2004.03450.x

Roefs, A., Huijding, J., Smulders, F. T. Y., MacLeod, C. M., de Jong, P. J., Wiers, R. W., & Jansen, A. T. M. (2011). Implicit measures of association in psychopathology research. *Psychological Bulletin*, *137*(1), 149–193. doi:10.1037/a0021729

Roettger, T. B., & Domahs, F. (2015). Grammatical number elicits SNARC and MARC effects as a function of task demands. *The Quarterly Journal of Experimental Psychology*, *68*(6), 1231–1248. http://doi.org/10.1080/17470218.2014.979843

Di Rosa, E., Bardi, L., Umiltà, C., Masina, F., Forgione, M., & Mapelli, D. (2017). Transcranial direct current stimulation (tDCS) reveals a dissociation between SNARC and MARC effects: implication for the polarity correspondence account. *Cortex*, *93*, 68-78. doi:10.1016/j.cortex.2017.05.002

Rosenberg-Lee, M., Ashkenazi, S., Chen, T., Young, C. B., Geary, D. C., & Menon, V. (2014). Brain hyper-connectivity and operation-specific deficits during arithmetic problem solving in children with developmental dyscalculia. *Developmental Science*. doi:10.1111/desc.12216

Rothermund, K., & Wentura, D. (2001). Figure-ground asymmetries in the Implicit Association Test (IAT). *Experimental Psychology, 48*(2), 94–106. doi: 10.1026//0949-3946.48.2.94

Rothermund, K., & Wentura, D. (2004). Underlying processes in the implicit association test: dissociating salience from associations. *Journal of experimental psychology: General, 133*(2), 139–165. doi:10.1037/0096-3445.133.2.139

Rubinsten, O., Dana, S., Lavro, D., & Berger, A. (2013). Processing ordinality and quantity: ERP evidence of separate mechanisms. *Brain and Cognition*, *82*(2), 201–212. doi:10.1016/j.bandc.2013.04.008

Rubinsten, O., & Sury, D. (2011). Processing Ordinality and Quantity: The Case of Developmental Dyscalculia. *Plos One*, *6*(9). doi:10.1371/journal.pone.0024079

Ruf, S. P., Fallgatter, A. J., & Plewnia, C. (2017). Augmentation of working memory training by transcranial direct current stimulation (tDCS). *Scientific Reports*, *7*(1), 876. doi:10.1038/s41598-017-01055-1

Rugani, R., & de Hevia, M.-D. (2017). Number-space associations without language: Evidence from preverbal human infants and non-human animal species. *Psychonomic Bulletin & Review*, *24*(2), 352–369. Psychonomic Bulletin & Review. doi:10.3758/s13423-016-1126-2

Rugani, R., Vallortigara, G., Priftis, K., & Regolin, L. (2015). Number-space mapping in the newborn chick resembles humans' mental number line. *Science*, *347*(6221), 534–536.

Rugani, R., Vallortigara, G., & Regolin, L. (2016). Mapping number to space in the two hemispheres of the avian brain. *Neurobiology of Learning and Memory*, *133*(8), 13–18. doi:10.1016/j.nlm.2016.05.010

Ruiz Fernández, S., Rahona, J. J., Hervás, G., Vázquez, C., & Ulrich, R. (2011). Number magnitude determines gaze direction: Spatial-numerical association in a free-choice task. *Cortex*, *47*(5), 617–20. doi:10.1016/j.cortex.2010.10.006

Rusconi, E., Bueti, D., Walsh, V., & Butterworth, B. (2011). Contribution of frontal cortex to the spatial representation of number. *Cortex*, *47*(1), 2–13. doi:10.1016/j.cortex.2009.08.005

Rusconi, E., Dervinis, M., Verbruggen, F., & Chambers, C. D. (2013). Critical time course of right frontoparietal involvement in mental number space. *Journal of cognitive neuroscience*, *25*(3), 465–83. doi:10.1162/jocn_a_00330

Rusconi, E., Turatto, M., & Umiltà, C. (2007). Two orienting mechanisms in posterior parietal lobule: an rTMS study of the Simon and SNARC effects. *Cognitive Neuropsychology*, *24*(4), 373–92. doi:10.1080/02643290701309425

Rütsche, B., Hauser, T. U., Jäncke, L., & Grabner, R. H. (2015) When problem size matters: Differential effects of brain stimulation on arithmetic problem solving and neural oscillations. *PLoS One*, *10*(3), e0120665. doi: 10.1371/journal.pone.0120665

Salillas, E., & Semenza, C. (2015). *Mapping the Brain for Math: Reversible inactivation by direct cortical electrostimulation and transcranial magnetic stimulation*. In: Cohen Kadosh R, Dowker A (eds) The Oxford Handbook of Numerical Cognition (pp 583–611). Oxford University Press, New York, USA.

Santiago, J., & Lakens, D. (2015). Can conceptual congruency effects between number, time, and space be accounted for by polarity correspondence? *Acta psychologica*, *156*, 179-91. doi: 10.1016/j.actpsy.2014.09.016

Santiago, J., Román, A., & Ouellet, M. (2011). *Flexible foundations of abstract thouight: A review and a theory*. In T. W. Schubert & A. Maass (Eds.), Spatial dimensions of social thought (pp. 41–109). De Gruyter Mouton.

Santens, S., & Gevers, W. (2008). The SNARC effect does not imply a mental number line. *Cognition*, 108(1), 263-270.

Sarkar, A., Dowker, A., & Cohen Kadosh, R. (2014). Cognitive Enhancement or Cognitive Cost: Trait-Specific Outcomes of Brain Stimulation in the Case of Mathematics Anxiety. *Journal of Neuroscience*, *34*(50), 16605–16610. doi:10.1523/JNEUROSCI.3129-14.2014

Sarkar, A., & Cohen Kadosh, R. (2016). Transcranial electrical stimulation and numerical cognition. *Canadian Journal of Experimental Psychology*, *70*(1), 41–58. doi:10.1037/cep0000064

Schestatsky, P., Simis, M., Freeman, R., Pascual-Leone, A., & Fregni, F. (2013). Non-invasive brain stimulation and the autonomic nervous system. *Clinical Neurophysiology*, *124*(9), 1716–1728. doi:10.1016/j.clinph.2013.03.020

Schiller, F., Eloka, O., & Franz, V. H. (2016). Using Key Distance to Clarify a Theory on the SNARC. *Perception*, *45*(1–2), 196–221. doi:10.1177/0301006615616754

Schroeder, P.A., Dresler, T., Bahnmueller, J., Artemenko, C., Cohen Kadosh, R., & Nuerk, H.-C. (2017). Cognitive Enhancement of Numerical and Arithmetic Capabilities: a Mini-Review of Available Transcranial Electric Stimulation Studies. *Journal of Cognitive Enhancement, 1*(1), 39-47.

Schroeder, P. A., Ehlis, A.-C., Wolkenstein, L., Fallgatter, A. J., & Plewnia, C. (2015). Emotional Distraction and Bodily Reaction: Modulation of Autonomous Responses by Anodal tDCS to the Prefrontal Cortex. *Frontiers in Cellular Neuroscience, 9*, 1–8. doi:10.3389/fncel.2015.00482

Schroeder, P. A., Nuerk, H.-C., & Plewnia, C. (2017). Prefrontal neuromodulation reverses spatial associations of non-numerical sequences, but not numbers. *Biological Psychology*, 128, 39–49. doi:10.1016/j.biopsycho.2017.07.008

Schroeder, P.A., Nuerk, H.-C., Plewnia, C. (2017). Space in Numerical and Ordinal Information: A common construct? Journal of Numerical Cognition, 3(2), 164-181. doi:10.5964/jnc.v3i2.40

Schroeder, P. A., & Pfister, R. (2015). Arbitrary numbers counter fair decisions: trails of markedness in card distribution. *Frontiers in Psychology, 6*(240). doi:10.3389/fpsyg.2015.00240

Schroeder, P. A., Pfister, R., Kunde, W., Nuerk, H.-C., & Plewnia, C. (2016). Counteracting Implicit Conflicts by Electrical Inhibition of the Prefrontal Cortex. *Journal of cognitive neuroscience, 28*(11), 1737–1748. doi:10.1162/jocn

Schroeder, P. A., & Plewnia, C. (2016). Beneficial Effects of Cathodal Transcranial Direct Current Stimulation (tDCS) on Cognitive Performance. *Journal of Cognitive Enhancement*, *1*(1), 5–9. Journal of Cognitive Enhancement. doi:10.1007/s41465-016-0005-0

Schwippel, T., Wasserka, B., Fallgatter, A. J., & Plewnia, C. (2017). Safety and efficacy of long-term home treatment with transcranial direct current stimulation (tDCS) in a case of multimodal hallucinations. *Brain Stimulation*, (April), 1–2. doi:10.1016/j.brs.2017.04.124

Sedlmeier, P., & Gigerenzer, G. (1989). Do Studies of Statistical Power Have an Effect on the Power of Studies? *Psychological bulletin*, 105(2), 309–316.

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation*, *7*(2), 325–331. doi:10.1016/j.brs.2013.12.008

Sella, F., Tressoldi, P., Lucangeli, D., & Zorzi, M. (2016). Training numerical skills with the adaptive videogame “The Number Race”: A randomized controlled trial on preschoolers. *Trends in Neuroscience and Education*, *5*(1), 20–29. doi:10.1016/j.tine.2016.02.002

Sellaro, R., Derks, B., Nitsche, M. A., Hommel, B., van den Wildenberg, W. P. M., van Dam, K., & Colzato, L. S. (2015). Reducing prejudice through brain stimulation. *Brain Stimulation*, *8*(5), 1–7. doi:10.1016/j.brs.2015.04.003

Shaki, S., & Fischer, M. H. (2014). Random walks on the mental number line. *Experimental Brain Research*, *232*(1), 43–9. doi:10.1007/s00221-013-3718-7

Shaki, S., Fischer, M. H., & Petrusic, W. M. (2009). Reading habits for both words and numbers contribute to the SNARC effect. *Psychonomic Bulletin & Review*, *16*(2), 328–31. doi:10.3758/PBR.16.2.328

Shaki, S., & Gevers, W. (2011). Cultural characteristics dissociate magnitude and ordinal information processing. *Journal of Cross-Cultural Psychology, 42*(4), 639–650. doi:10.1177/0022022111406100

Sheeran, P., Bosch, J. A., Crombez, G., Hall, P. A., Harris, J. L., Papies, E. K., & Wiers, R. W. (2016). Implicit processes in health psychology: Diversity and promise. *Health Psychology*, 35(8), 761. doi:10.1037/hea0000409

Silberzahn, R., Uhlmann, E. L., Martin, D., Aust, F., Awtrey, E. C., Bahník, Š., ... & Cheung, F. (2017). Many analysts, one dataset: Making transparent how variations in analytical choices affect results. *PsyArxiv*, September 21. doi:10.17605/OSF.IO/QKWST

Silvanto, J., & Pascual-Leone, A. (2008). State-dependency of transcranial magnetic stimulation. *Brain topography*, *21*(1), 1–10. doi:10.1007/s10548-008-0067-0

Simonsohn, U., Nelson, L. D., & Simmons, J. P. (2014). P-curve: A key to the file-drawer. *Journal of Experimental Psychology: General*, *143*(2), 534–547. http://doi.org/10.1037/a0033242

Simon, J. R., & Rudell, A. P. (1967). Auditory S-R compatibility: The effect of an irrelevant cue on information processing. *Journal of Applied Psychology*, *51*(3), 300.

Smirni, D., Turriziani, P., Mangano, G. R., Cipolotti, L., & Oliveri, M. (2015). Modulating Memory Performance in Healthy Subjects with Transcranial Direct Current Stimulation Over the Right Dorsolateral Prefrontal Cortex. *Plos One, 10*(12), e0144838. doi:10.1371/journal.pone.0144838

Smith, E. E., & Jonides, J. (1997). Working memory: a view from neuroimaging. *Cognitive Psychology, 33*(1), 5–42. http://doi.org/10.1006/cogp.1997.0658

Snowball, A., Tachtsidis, I., Popescu, T., Thompson, J., Delazer, M., Zamarian, L., …, & Cohen Kadosh, R. (2013). Long-term enhancement of brain function and cognition using cognitive training and brain stimulation. *Current Biology, 23*(11), 987–92. doi:10.1016/j.cub.2013.04.045

Soltanlou, M., Pixner, S., & Nuerk, H.-C. (2015). Contribution of working memory in multiplication fact network in children may shift from verbal to visuo-spatial: a longitudinal investigation. *Frontiers in Psychology*, *6*(July), 1–10. doi:10.3389/fpsyg.2015.01062

Stagg, C. J., Best, J. G., Stephenson, M. C., O'Shea, J., Wylezinska, M., Kincses, Z. T., … Johansen-Berg, H. (2009). Polarity-sensitive modulation of cortical neurotransmitters by transcranial stimulation. *The Journal of Neuroscience, 29*(16), 5202–6. http://doi.org/10.1523/JNEUROSCI.4432-08.2009

Steenbergen, L., Sellaro, R., Hommel, B., Lindenberger, U., Kühn, S., & Colzato, L. S. (2015). "Unfocus" on foc.us: commercial tDCS headset impairs working memory. *Experimental Brain Research, 234*(3), 637-643. doi:10.1007/s00221-015-4391-9

Stillings, D. (1975). A survey of the history of electrical stimulation for pain to 1900. *Medical instrumentation*, *9*(6), 255–9.

Strack, F., & Deutsch, R. (2004). Reflective and impulsive determinants of social behavior. *Personality and social psychology review*, *8*(3), 220–247. doi:10.1207/s15327957pspr0803_1

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology: General*, *121*(1), 15–23.

Strube, W., Bunse, T., Nitsche, M. A., Nikolaeva, A., Palm, U., Padberg, F., Falkai, P., … Hasan, A. (2016). Bidirectional variability in motor cortex excitability modulation following 1 mA transcranial direct current stimulation in healthy participants. *Physiological reports, 4*(15), 307–321. doi:10.14814/phy2.12884

Suárez-Pellicioni, M., Núñez-Peña, M. I., & Colomé, À. (2016). Math anxiety: A review of its cognitive consequences, psychophysiological correlates, and brain bases. *Cognitive Affective and Behavioral Neuroscience, 16,* 3–22. doi: 10.3758/s13415-015-0370-7

Tan, S., & Dixon, P. (2011). Repetition and the SNARC effect with one- and two-digit numbers. *Canadian Journal of Experimental Psychology*, *65*(2), 84–97. doi:10.1037/a0022368

Teachman, B. A., Marker, C. D., & Smith-Janik, S. B. (2009). Automatic associations and panic disorder: Trajectories of change over the course of treatment. *Journal of Consulting and Clinical Psychology, 76*(6), 988–1002. doi:10.1037/a0013113.

Terney, D., Chaieb, L., Moliadze, V., Antal, A., & Paulus, W. (2008). Increasing human brain excitability by transcranial high-frequency random noise stimulation. *Journal of Neuroscience 28*(52),14147–14155. doi: 10.1523/JNEUROSCI.4248-08.2008

Tremblay, S., Lepage, J.-F., Latulipe-Loiselle, A., Fregni, F., Pascual-Leone, A., & Théoret, H. (2014). The uncertain outcome of prefrontal tDCS. *Brain Stimulation*, *7*(6), 773–783. doi:10.1016/j.brs.2014.10.003

Truong, D. Q., Hüber, M., Xie, X., Datta, A., Rahman, A., Parra, L. C., Dmochowski, J. P., & Bikson, M. (2014). Clinician accessible tools for GUI computational models of transcranial electrical stimulation: BONSAI and SPHERES. *Brain Stimulation, 7*(4), 521–524. doi: 10.1016/j.brs.2014.03.009.

Tsushima, Y., Sasaki, Y., & Watanabe, T. (2006). Greater Disruption Due to Failure of Inhibitory Control on an Ambiguous Distractor. *Science*, *314*, 1786–1788.

Tudusciuc, O., & Nieder, A. (2009). Contributions of primate prefrontal and posterior parietal cortices to length and numerosity representation. *Journal of neurophysiology*, *101*(6), 2984–94. doi:10.1152/jn.90713.2008

Tversky, A., & Kahneman, D. (1974). Judgment under Uncertainty: Heuristics and Biases. *Science (New York, N.Y.), 185*(4157), 1124–31. doi:10.1126/science.185.4157.1124

Tzelgov, J., Meyer, J., & Henik, A. (1992). Automatic and Intentional Processing of Numerical Information. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *18*(1), 166–179. doi:10.1037/0278-7393.18.1.166

Tzelgov, J., Yehene, V., Kotler, L., & Alon, A. (2000). Automatic comparisons of artificial digits never compared: learning linear ordering relations. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *26*(1), 103–120. doi: 10.1037/0278-7393.26.1.103

Tzelgov, J., Zohar-Shai, B., & Nuerk, H.-C. (2013). On defining quantifying and measuring the SNARC effect. *Frontiers in Psychology*, *4*, 302. doi:10.3389/fpsyg.2013.00302

Umiltà, C. (1991). Problems of the Salient-Features Coding Hypothesis: Comment on Weeks and Proctor. *Journal of Experimental Psychology: General*, *120*(1), 83–86.

Umiltà, C., Priftis, K., & Zorzi, M. (2009). The spatial representation of numbers: Evidence from neglect and pseudoneglect. *Experimental Brain Research*, *192*, 561–569. doi:10.1007/s00221-008-1623-2

Vahey, N. A., Nicholson, E., & Barnes-Holmes, D. (2015). A meta-analysis of criterion effects for the Implicit Relational Assessment Procedure (IRAP) in the clinical domain. *Journal of Behavior Therapy and Experimental Psychiatry*, *48*, 59–65. doi:10.1016/j.jbtep.2015.01.004

Vallesi, A., Binns, M. A., & Shallice, T. (2008). An effect of spatial-temporal association of response codes: Understanding the cognitive representations of time. *Cognition*, *107*(2), 501–527. doi:10.1016/j.cognition.2007.10.011

Van Beek, L., Ghesquière, P., Lagae, L., & De Smedt, B. (2015). Mathematical Difficulties and White Matter Abnormalities in Subacute Pediatric Mild Traumatic Brain Injury. *Journal of Neurotrauma*, *32*(20), 1567-1578 . doi:10.1089/neu.2014.3809

van Dijck, J. P., Abrahamse, E. L., Acar, F., Ketels, B., & Fias, W. (2014). A working memory account of the interaction between numbers and spatial attention. *Quarterly Journal of Experimental Psychology (2006)*, *67*(8), 1500–13. doi:10.1080/17470218.2014.903984

van Dijck, J. P., & Fias, W. (2011). A working memory account for spatial-numerical associations. *Cognition*, *119*(1), 114–9. doi:10.1016/j.cognition.2010.12.013

van Dijck, J. P., Gevers, W., & Fias, W. (2009). Numbers are associated with different types of spatial information depending on the task. *Cognition, 113*(2), 248–253. doi:10.1016/j.cognition.2009.08.005

Vanderhasselt, M. A., De Raedt, R., Namur, V., Lotufo, P. A., Bensenor, I. M., Boggio, P. S., & Brunoni, A. R. (2015). Transcranial electric stimulation and neurocognitive training in clinically depressed patients: A pilot study of the effects on rumination. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 57,* 93–99. doi: 10.1016/j.pnpbp.2014.09.015

Vandermeeren, Y., Jamart, J., & Ossemann, M. (2010). Effect of tDCS with an extracephalic reference electrode on cardio-respiratory and autonomic functions. *BMC neuroscience, 11*(1), 38. doi:10.1186/1471-2202-11-38

Viarouge, A., Hubbard, E. M., & McCandliss, B. D. (2014). The cognitive mechanisms of the SNARC effect: An individual differences approach. *PLoS ONE, 9*(4). doi:10.1371/journal.pone.0095756

Vierck, E., & Kiesel, A. (2010). Congruency effects between number magnitude and response force. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *36*(1), 204–9. doi:10.1037/a0018105

Vöröslakos, M., Takeuchi, Y., Brinyiczki, K., Zombori, T., Oliva, A., Fernández-Ruiz, A., ... & Berényi, A. (2018). Direct effects of transcranial electric stimulation on brain circuits in rats and humans. *Nature communications*, 9(1), 483. doi:10.1038/s41467-018-02928-3

Wager, T., & Smith, E. E. (2003). Neuroimaging studies of working memory: a meta-analysis. *Cognitive, Affective & Behavioral Neuroscience, 3*(4), 255–74.

Walsh, V. (2003). A theory of magnitude: common cortical metrics of time, space and quantity. *Trends in Cognitive Sciences*, *7*(11), 483–8.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063–1070. doi:10.1037/0022-3514.54.6.1063

Weeks, D. J., & Proctor, R. W. (1990). Salient-features coding in the translation between orthogonal stimulus and response dimensions. *Journal of Experimental Psychology: General*, *119*(4), 355–366. doi:10.1037//0096-3445.119.4.355

Weidacker, K., Weidemann, C. T., Boy, F., & Johnston, S. J. (2016). Cathodal tDCS improves task performance in participants high in Coldheartedness. *Clinical Neurophysiology*, *127*(9), 3102–3109. doi:10.1016/j.clinph.2016.05.274

Weis, T., Estner, B., van Leeuwen, C., & Lachmann, T. (2015). SNARC meets SPARC: Automaticity and Interdependency in Compatibility Effects. *Quarterly Journal of Experimental Psychology (2006)*, 1–37. doi:10.1080/17470218.2015.1082142

Weiss, M., Lavidor, M., O'Neil, I., & Adamson, D. (2012). When Less Is More: Evidence for a Facilitative Cathodal tDCS Effect in Attentional Abilities. *Journal of Cognitive Neuroscience*, *24*(9), 1–8. doi:10.1162/jocn_a_00248

Wiegand, A., Nieratschker, V., & Plewnia, C. (2016). Genetic Modulation of Transcranial Direct Current Stimulation Effects on Cognition. *Frontiers in Human Neuroscience*, *10*(December), 651. doi:10.3389/fnhum.2016.00651

Wiers, R. W., Van Woerden, N., Smulders, F. T. Y., & De Jong, P. J. (2002). Implicit and explicit alcohol-related cognitions in heavy and light drinkers. *Journal of Abnormal Psychology*, *111*(4), 648–658. doi:10.1037/0021-843X.111.4.648

Wiethoff, S., Hamada, M., & Rothwell, J. C. (2014). Variability in response to transcranial direct current stimulation of the motor cortex. *Brain Stimulation*, *7*(3), 468–475. doi:10.1016/j.brs.2014.02.003

Wolkenstein, L., & Plewnia, C. (2013). Amelioration of cognitive control in depression by transcranial direct current stimulation. *Biological Psychiatry*, *73*(7), 646–51. doi:10.1016/j.biopsych.2012.10.010

Wolkenstein, L., Zeiller, M., Kanske, P., & Plewnia, C. (2014). Induction of a depression-like negativity bias by cathodal transcranial direct current stimulation. *Cortex*, *59*, 103–112. doi:10.1016/j.cortex.2014.07.011

Wood, G., Nuerk, H.-C., & Willmes, K. (2006a). Crossed hands and the SNARC effect: A failure to replicate Dehaene, Bossini and Giraux (1993). *Cortex*, *42*(8), 1069–1079. doi:10.1016/S0010-9452(08)70219-3

Wood, G., Nuerk, H.-C., & Willmes, K. (2006b). Variability of the SNARC effect: Systematic interindividual differences or just random error? *Cortex*, *3*, 1–5. doi:10.1016/S0010-9452(08)70223-5

Wood, G., Nuerk, H. C., Moeller, K., Geppert, B., Schnitker, R., Weber, J., & Willmes, K. (2008). All for one but not one for all: How multiple number representations are recruited in one numerical task. *Brain Research*, *1187*(1), 154–166. doi:10.1016/j.brainres.2007.09.094

Wood, G., Willmes, K., Nuerk, H.-C., & Fischer, R. (2008). On the cognitive link between space and number: A meta-analysis of the SNARC effect. *Psychology Science Quarterly*, *50*(4), 489–525.

Zaehle, T., Sandmann, P., Thorne, J. D., Jäncke, L., & Herrmann, C. S. (2011). Transcranial direct current stimulation of the prefrontal cortex modulates working memory performance: combined behavioural and electrophysiological evidence. *BMC neuroscience*, *12*, 2. doi:10.1186/1471-2202-12-2

Zago, S., Ferrucci, R., Fregni, F., & Priori, A. (2007). Bartholow, Sciamanna, Alberti: Pioneers in the Electrical Stimulation of the Exposed Human Cerebral Cortex. *The Neuroscientist*, *14*(5), 521–528. doi:10.1177/1073858407311101

Zago, S., Priori, A., & Ferrucci, R. (2016). Historical Aspects of Transcranial Electric Stimulation. In A. R. Brunoni, M. A. Nitsche, & C. Loo (Eds.), *Transcranial Direct Current Stimulation in Neuropsychiatric Disorders* (pp. 3–19). doi:10.1007/978-3-319-33967-2

Zamarian, L., Ischebeck, A., & Delazer, M. (2009). Neuroscience of learning arithmetic-Evidence from brain imaging studies. *Neuroscience & Biobehavioral Review, 33*(6), 909–925. doi: 10.1016/j.neubiorev.2009.03.005

Zamarian, L., Egger, C., & Delazer, M. (2007). The mental representation of ordered sequences in visual neglect. *Cortex*, *43*(4), 542–550. doi:10.1016/S0010-9452(08)70248-X

Zanolie, K., & Pecher, D. (2014). Number-induced shifts in spatial attention: A replication study. *Frontiers in Psychology, 5*(AUG), 1–10. doi:10.3389/fpsyg.2014.00987

Zhou, X., Chen, C., Chen, L., & Dong, Q. (2008). Holistic or compositional representation of two-digit numbers? Evidence from the distance, magnitude, and SNARC effects in a number-matching task. Cognition, 106, 1525–36. doi:10.1016/j.cognition.2007.06.003

Ziemann, U., Paulus, W., Nitsche, M. A., Pascual-Leone, A., Byblow, W. D., Berardelli, A., Siebner, H. R., … Rothwell, J. C. (2008). Consensus: Motor cortex plasticity protocols. *Brain Stimulation*, *1*(3), 164–182. doi:10.1016/j.brs.2008.06.006

Zmigrod, S., Zmigrod, L., & Hommel, B. (2016). Transcranial direct current stimulation (tDCS) over the right dorsolateral prefrontal cortex affects stimulus conflict but not response conflict. *Neuroscience*. doi:10.1016/j.neuroscience.2016.02.046

Zohar-Shai, B., Tzelgov, J., Karni, A., & Rubinsten, O. (2017). It does exist! A left-to-right spatial–numerical association of response codes (SNARC) effect among native Hebrew speakers.. *Journal of Experimental Psychology: Human Perception and Performance*, *43*(4), 719–728. doi:10.1037/xhp0000336

Zorzi, M., Di Bono, M. G., & Fias, W. (2011). Distinct representations of numerical and non-numerical order in the human intraparietal sulcus revealed by multivariate pattern recognition. *NeuroImage*, *56*(2), 674–680. doi:10.1016/j.neuroimage.2010.06.035

Zorzi, M., Priftis, K., Meneghello, F., Marenzi, R., & Umiltá, C. (2006). The spatial representation of numerical and non-numerical sequences: Evidence from neglect. *Neuropsychologia*, *44*(7), 1061–1067. doi:10.1016/j.neuropsychologia.2005.10.025

Zorzi, M., Priftis, K., & Umiltà, C. (2002). Neglect disrupts the mental number line. *Nature*, *417*, 138–140. doi:10.1038/417138a

Zwissler, B., Sperber, C., Aigeldinger, S., Schindler, S., Kissler, J., & Plewnia, C. (2014). Shaping Memory Accuracy by Left Prefrontal Transcranial Direct Current Stimulation. *The Journal of Neuroscience*, *34*(11), 4022–6. doi:10.1523/JNEUROSCI.5407-13.2014

FURTHER PUBLICATIONS

1) **Schroeder, P.A.,** Nuerk, H.-C., Plewnia, C. (Stage I Preregistered Report). Prefrontal representations of serial-order working memory: Modulation of SNARC-like positional effects with cathodal tDCS.

2) Holcombe, A., …, **Schroeder, P.A.**, et al. (forthcoming). Registered Replication Report: Fischer, Castel, Dodd, & Pratt (2003). *Advances in Psychological Research.*

3) Cipora, K., **Schroeder, P.A.**, Soltanlou, M., & Nuerk, H.-C. (in press). More space, better math: Is space a powerful tool or a cornerstone for understanding arithmetic? In M. Battista & K. S. Mix (Ed.), *Visualizing Mathematics* (working title).

4) **Schroeder, P.A.,** Collantoni, E., Lohmann, J., Butz, M. V., & Plewnia, C. (in preparation). Interaction Intention Directs Behavioral Bias for Unhealthy Food: Evidence from Virtual Reality.

5) Lohmann, J., **Schroeder, P.A.**, Plewnia, C., Nuerk, H.-C., & Butz, M.V. (in preparation). How Deep is your SNARC: Nonlinear Interactions Between Numerical Magnitude and Reachability in Peripersonal Space.

6) **Schroeder, P.A.,** Dignath, D., Janczyk, M. (revision invited). Individual differences in uncertainty tolerance are not associated with cognitive control functions (in the flanker task).

7) Hesse, K., **Schroeder, P.A**., Scheef, J., Klingberg, S., Plewnia, C. (2017). Investigating models of psychotic disorders by manipulating social feedback in virtual reality: Feasibility and first results. *Journal of Behavior Therapy and Experimental Psychiatry, 59*, 129-136.

8) **Schroeder, P.A.,** & Plewnia, C. (2016). Beneficial effects of cathodal transcranial direct current stimulation (tDCS) on cognitive performance. *Journal of Cognitive Enhancement, 1*(1), 5-9.

9) **Schroeder, P. A.,** Lohmann, J., Butz, M. V., & Plewnia, C. (2016). Behavioral Bias for Food Reflected in Hand Movements: A Preliminary Study with Healthy Subjects. *Cyberpsychology, Behavior, and Social Networking*, 19(2), 120-6.

10) **Schroeder, P.A**., Ehlis, A.-C., Wolkenstein, L., Fallgatter, A.J., Plewnia, C. (2015). Emotional distraction and bodily reaction: Modulation of autonomous responses by anodal tDCS to the prefrontal cortex. *Frontiers in Cellular Neuroscience,* 9:482.

11) Plewnia, C., **Schroeder, P.A.,** & Wolkenstein, L. (2015). Targeting the biased brain: non-invasive brain stimulation to ameliorate cognitive control. *The Lancet Psychiatry*, 2(4), 351-356.

12) **Schroeder, P.A.,** & Pfister, R. (2015). Arbitrary numbers counter fair decisions: trails of markedness in card distribution. *Frontiers in Psychology,* 6, 240.

13) Plewnia, C., **Schroeder, P.A.,** Kunze, R., Faehling, F., & Wolkenstein, L. (2015). Keep Calm and Carry On: Improved Frustration Tolerance and Processing Speed by Transcranial Direct Current Stimulation (tDCS). *PloS one*, 10(4), e0122578-e0122578.

14) **Schroeder, P.A.,** Mühlberger, A., & Plewnia, C. (2015) Virtuelle Welten für die psychiatrische Anwendung [*Virtual Realities for Psychiatric Applications*]. CME-certified article and e.Tutorial in the journal *Neurotransmitter*, 10, 45-52. doi:10.1007/s15016-015-0695-z

15) Pfister, R., **Schroeder, P.A.,** & Kunde, W. (2013). SNARC struggles: Instant control over spatial-numerical associations. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 39*(6), 1953-1958.

SHORT BIOGRAPHY

Philipp Alexander Schroeder was born on November 11, 1988 in Munich, Germany. From 2009-2013, he studied Psychology and Human-Computer Interaction at the University of Würzburg. In his diploma thesis, he investigated cognitive control processes in numerical cognition with a focus on experimental and general psychology. Mr. Schroeder was employed as student assistant and responsible for conductance of experiments, data preprocessing and analysis, as well as statistics teaching, at the Depts. of Psychology I and III for Cognitive and Experimental Clinical Psychology, respectively, and at the Dept. of Psychological Ergonomics (University of Würzburg). He has obtained further experience with virtual reality systems as research intern at the Center for Traffic Sciences in Veitshöchheim, and worked as student intern at the psychosomatic clinic Heiligenfeld in Bad Kissingen.

After completion of his diploma studies, Mr. Schroeder joined the Dept. of Psychiatry and Psychotherapy in Tübingen in 2013 to work on virtual reality and noninvasive brain stimulation under the guidance of Prof. Christian Plewnia. In parallel, he employed transcranial direct current stimulation methods to investigate the cognitive foundations of spatial-numerical processing and initiated his dissertation in cooperation with Prof. Hans-Christoph Nuerk and the Dept. of Psychology.

Mr. Schroeder is interested in the cognitive and psycholinguistic processes underlying the mental processing of abstract concepts, and in the utilization of modern technologies for addressing psychological and societal topics empirically. In 2016, he co-established and organized the VECTOR workshop series on psychological research prospects with Virtual Reality technologies. In his free time, Mr. Schroeder enjoys outdoor activities in the Swabian Mountains and engages in rock music projects.

EIDESSTATTLICHE ERKLÄRUNG

Ich erkläre hiermit, dass ich die zur Promotion eingereichte Arbeit mit dem Titel: „*Neuromodulation of Spatial Associations: Evidence from Choice Reaction Tasks During Transcranial Direct Current Stimulation*“ selbständig verfasst, nur die angegebenen Quellen und Hilfsmittel benutzt und wörtlich oder inhaltlich übernommene Stellen (alternativ: Zitate) als solche gekennzeichnet habe. Ich erkläre, dass die Richtlinien zur Sicherung guter wissenschaftlicher Praxis der Universität Tübingen (Beschluss des Senats vom 25.5.2000) beachtet wurden. Ich versichere an Eides statt, dass diese Angaben wahr sind und dass ich nichts verschwiegen habe. Mir ist bekannt, dass die falsche Abgabe einer Versicherung an Eides statt mit Freiheitsstrafe bis zu drei Jahren oder mit Geldstrafe bestraft wird.

Tübingen, den 8.1.2018 Philipp A. Schröder