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

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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.

1. 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; Gevers, Reynvoet, & Fias, 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

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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, Verguts, Reynvoet, Caessens, & Fias, 2006; Gevers et al., 2010). Moreover, compatibility effects were observed between the parity concept and spatial responding in the MARC effect (Berch, Foley, Hill, & 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 depend 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