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RESEARCH ARTICLE

Searching for the inner self: evidence against a direct dependence of the self-prioritization effect on the ventro-medial prefrontal cortex

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Abstract

The processing of self-referential material is supposed to be located in the medial prefrontal cortex (MPFC) and in particular in the ventro-medial prefrontal cortex (VMPFC). A reliable method to assess effects of self-relevance is the so-called matching paradigm in which the prioritization of newly learned self-associations in comparison to non-self-relevant associations can be measured. To assess the connection of activation in the VMPFC and self-referential processing, we measured the self-prioritization effect (SPE) before and after experimentally manipulating activation in the VMPFC. We applied either excitatory or inhibitory stimulation to the VMPFC via transcranial direct current stimulation (tDCS). In a sample of $N = 65$ healthy adults, we found a significant SPE before and after both types of stimulation and, remarkably, no systematic change of the SPE due to the stimulation. These results are evidential against a direct dependence of the SPE from activation in the VMPFC, indicating either that the SPE differs from other, more elaborate self-effects, and thereby is processed in different brain areas, or that the connection of SPE and VMPFC is correlational rather than causal.

Keywords Transcranial direct current stimulation (tDCS) · Self · Attention · Self-prioritization

Introduction

It is a matter of fact that we are permanently influenced by the stimuli around us. They guide our attention, determine what we perceive and what we remember, and they can elicit specific behaviors. Yet, to predict and explain cognitive processes and behavior, it is essential to assess the systematic processing biases due to a stimulus' inherent valence, its match with current preferences and goals, and its self-relevance.

In the case of self-relevant stimuli, effects on different cognitive processes in different paradigms have been observed. Among others, an attention-grabbing effect of the participant's own name was demonstrated in different sensory modalities (for effects with auditory stimuli, see Moray 1959; for effects with visual stimuli, see Shapiro et al. 1997), different ways of associating stimuli with the self resulted in enhanced memory performance (see, e.g., Cunningham et al. 2008; Rogers et al. 1977), and a potentially perceptual advantage for self-relevant material was assumed based on studies using a perceptual matching task (Sui et al. 2012). However, those effects in studies using the participant's own name, the participant's own face, or other autobiographical material can be discussed in the sense of a higher familiarity of the self-relevant stimuli in comparison to the stimuli used in a non-self-relevant control condition (e.g., a friend's name or face; for a recap of the difficulties in the reported findings, see Humphreys and Sui 2016).

Aggregating these divergent interpretations of effects of self-relevance, there is an ongoing debate about the exact processes which underly self-effects in general. Valuable indications in this debate were revealed by the assessment of brain areas involved in self-referential processing. Taken together, this assessment of a 'self-brain area' revealed suggestive evidence for brain areas, which are selectively engaged in tasks involving self-referential processing. In particular, several studies demonstrated a constant association of self-referential processing with activation in the medial prefrontal cortex (MPFC; Wagner et al. 2012). In this context, a whole brain analysis in a study assessing brain activation during three different types of self-referential processing (i.e., thinking about one's own personality traits, current mental states, or physical attributes) revealed

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greatest responses in the MPFC (Jenkins and Mitchell 2011). An a priori region of interest (ROI) analysis confirmed this finding as the blood-oxygen-level dependent (BOLD) signal in the MPFC was increased for self-referential processing compared to other-referential processing (Jenkins and Mitchell 2011). Comparably, in a study in which participants had to rate trait adjectives according to whether they were self-descriptive or not, higher activation in the MPFC was found for adjectives, which were rated as self-descriptive, in comparison to adjectives, which were rated as non-self-descriptive (Macrae et al. 2004).

Beyond findings like that, the localization of the self-brain area can be further specified. When differentiating separate areas in the MPFC, studies found activation in particular in the ventral area of the MPFC. In this regard, summarizing a huge amount of findings about the neural representations of self and other, Wagner et al. (2012) concluded that the VMPFC is commonly associated with self-referential cognition, whereas the dorso-lateral prefrontal cortex (DLPFC) is more commonly associated with impression formation and thinking about the mental states of others (Figure 1 in Wagner et al. 2012). Correspondingly, a meta-analysis of 107 neuroimaging studies revealed self- and other-related activation significantly different from a baseline (Denny et al. 2012). A direct comparison of self- and other-related judgments indicated that the self-condition, relative to the other-condition, significantly activated the VMPFC, whereas the other-condition, relative to the self-condition, significantly activated dorsal regions of the MPFC (Figure 3 in Denny et al. 2012). A regression analysis confirmed the assumption of a spatial differentiation of self- and other-brain areas as increasing ventral or dorsal MPFC activation was significantly associated with either self- or other-related judgments.

Given the differentiation between self- and other-related processes and based on the finding that self-associations seem to be related to activity in the VMPFC, further specifications were postulated to understand the underlying processes of self-relevance. Recently, a framework was introduced, aiming at a structural overview of different self-effects and the related brain areas. This framework, the Self-Attention Network (Humphreys and Sui 2016), explains effects of self-relevant material on attentional processes by three components: a top-down attentional control network, a core self-representation, and a region involved in bottom-up orienting. Besides further explaining the interaction of these components, the framework provides a conceptualization of self-brain areas. In detail, research is summarized which shows that the postulated top-down component is associated with the DLPFC and the left intra-parietal sulcus, the bottom-up component with the posterior superior temporal sulcus (pSTS), and—most important in this context—the self-representation is associated with the VMPFC (Humphreys and Sui 2016). Confirmatively, in another review about neuroimaging studies examining social-cognitive effects, a differentiation between automatic and controlled self-effects was postulated and underpinned by different brain areas (Lieberman 2007). In that context, the VMPFC is categorized to be associated with the automatic, fast, and rather perceptual processes.

SPE and VMPFC

Taken together, reviews, meta-analyses, and theoretical frameworks suggest an association of effects of self-relevance with activation in the VMPFC. One method to assess effects of self-relevance is the so-called matching paradigm which was introduced by Sui et al. (2012) and which yields the self-prioritization effect (SPE). In this paradigm, formerly neutral stimuli are associated with the participant's self or with non-self-relevant others via instructions so that responses to newly learned self- and other-assignments can be measured independent of material confounds (like, as mentioned above, a higher familiarity of previously used self-relevant material). Thus, one participant might be instructed to learn: "I am a triangle. My friend is a square. And a stranger is a rectangle.". Subsequently, changing combinations of the shapes and labels are presented on the screen and the participant has to decide whether it is a matching or a non-matching combination according to the previously learned assignments. In this matching task, a robust prioritization of the self-associated combinations (in the given example, a combination of the label "I" and the triangle) in comparison to the non-self-relevant combinations (a combination of "friend" and square or "stranger" and rectangle) is indicated by faster and more accurate responses in the self-condition (for replications, generalizations and further assessments of the effect, see, e.g., Macrae et al. 2017; Schäfer et al. 2016a, b, 2017; Sui et al. 2012).

Meanwhile, there are several studies demonstrating that the SPE is associated with activation in the VMPFC. For instance, a study with participants working on the matching task in a functional magnetic resonance imaging (fMRI) scanner demonstrated significantly different activation in the VMPFC as a function of the self-relevance in each trial. In particular, when responding to self-combinations activation was measured mainly in the VMPFC (as well as in the left posterior superior temporal sulcus [LpSTS]). In contrast to that, when responding to other-combinations, activation was measured mainly in the DLPFC (Sui et al. 2013). Activation in the VMPFC significantly correlated with activation in the LpSTS, but did not correlate with activation in the DLPFC, suggesting a distinction between self- and other-associated brain areas. Above that, the SPE as a response benefit for self-relevant trials over other-relevant trials was positively

correlated with activation in the VMPFC and LpSTS, but negatively correlated with activation in the DLPFC (Sui et al. 2013, Figure 2D). Furthermore, a report about a patient with a lesion primarily in the left VMPFC supports the assumption of a connection between activation in the VMPFC and the SPE as it describes a significantly smaller SPE shown by the patient compared to the SPE shown by a gender- and age-matched control group (Sui et al. 2015).

The present study

The current literature converges on the assumption that self-relevant material is processed in the MPFC and in particular in the ventral area of the MPFC. Whereas some further brain regions might also be involved in the processing of specific types of self-relevant material, a robust activation of the VMPFC is reported for different types of material and in diverse studies (Jenkins and Mitchell 2011). Moreover, the activation of the VMPFC seems to be specific for self-relevant material in the sense that comparable, but non-self-relevant material activates different brain areas (i.e., the DLPFC; Sui et al. 2013; Wagner et al. 2012).

Thus, while it is clear that the VMPFC is correlated with the processing of self-relevant material this does by no means imply a causal connection of these two. Thus, to broaden the understanding of this particular connection, we set out to assess the influence of activation in the VMPFC on the SPE by experimentally manipulating the neural activity in this area. The manipulation of the neural activity was achieved by transcranial direct current stimulation (tDCS). tDCS is a non-invasive method of cortical stimulation. The applied direct current flows from an active to a reference electrode, partly being deflected by the scalp and the rest being delivered to the brain tissue (Miranda et al. 2006), thereby inducing diminutions or enhancements of cortical excitability (Nitsche et al. 2008). The underlying mechanism of single-session tDCS revolves around polarity specific modulation of membrane potentials and synaptic activity (Stagg and Nitsche 2011). The utilization of anodal (excitatory) and cathodal (inhibitory) stimulation can be used to clarify the role of different brain areas for specific processes.

In a pre-post design, participants underwent the matching paradigm so that the SPE was measured before and after a manipulation of the neural activity in the VMPFC via tDCS. To maximize primary variance due to tDCS stimulation, we compared anodal with cathodal conditions without a sham control (Frings et al. 2018; for arguments against a sham condition, see also; Ambrus et al. 2010; Roy et al. 2015). Electrode mounting was applied as to focus on the stimulation of the VMPFC. By applying excitatory or inhibitory stimulation of the neural activity in the VMPFC and measuring the SPE before and shortly after that, we assessed whether the occurrence of a basic self-effect like the SPE is influenced by activity in the VMPFC. If self-relevant material is inevitably processed in the VMPFC, then excitatory stimulation of this area could facilitate effects of self-related stimuli and, even more, inhibition of the same area should reduce or prevent effects of self-related stimuli. Hence, based on the findings reported above, we predict an increase of the SPE in the anodal condition and a decrease of the SPE in the cathodal condition.

Method

Participants Participants were excluded from the study if beforehand information suggested neurological, psychiatric or cardiovascular diseases. Additionally, participants were excluded if they reported to have consumed illegal drugs or large amounts of alcohol the previous night. The study was approved by the local ethics committee of the University of Trier. All participants provided written informed consent. Sixty-seven healthy participants (49 female) took part in the experiments receiving course credit. Their median age was 21 years (ranging from 18 to 27) and all participants had normal or corrected-to-normal vision. Two participants had to be excluded from the analyses because their overall responses were too erroneous (far outs compared to the mean error rates of the other participants due to the outlier criterion of Tukey 1977), resulting in a total sample size of $N = 65$.

Material and apparatus The experiment took place in an ordinarily lit room. The participants sat in front of a 19-inch color monitor with a viewing distance of about 65 cm. The computer used to present the stimuli was a standard PC and ran on Windows XP. Participants responded using a standard German QWERTZ keyboard in front of the computer. The experiment was run using E-Prime 2.0 software. The German word *Ich* [I] was used as the self-associated label, the German word *Fremder* [stranger] as a non-self-relevant other, and the German word *Stuhl* [chair] as a neutral instance. Note that each of these labels was used in the paradigm before and generated typical results (see, e.g., Frings and Wentura 2014; Schäfer et al. 2016). Each label was assigned either with a circle, a triangle, or a square (Latin-square balanced). Words were presented in black on white background, in Courier New, and in a visual angle of about 0.44°. All stimuli were presented at the (horizontally) screen center, the shape at a visual angle of 11.42° from the upper border of the screen, a fixation cross at 12.73° and the label at 14.03°. The geometric shapes were presented subtending approximately 2.6° × 2.6° visual angle.

Direct current was provided by a constant current stimulator (4-channel-DC-stimulator by NeuroConn, Ilmenau). To focalize the spatial excitability, a rather small stimulation

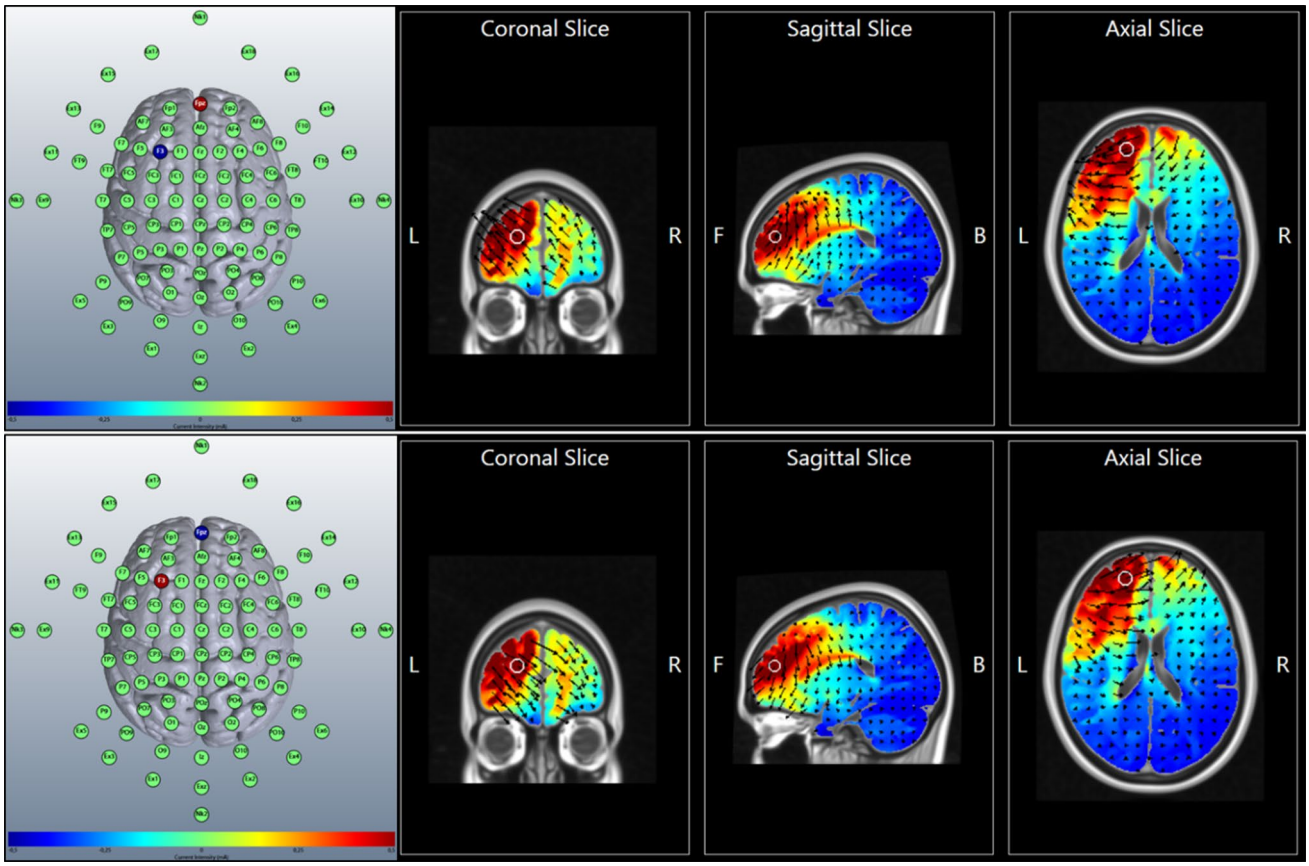

Fig. 1 Electrode placements and direct current flow during anodal (upper row) and cathodal (lower row) stimulation with the electrode positions Fpz and F3; anode depicted in red, cathode depicted in blue. Simulation by the HD-Explore software (version 3.0, Soterix Medical Inc, New York; the MNI 152 template was used for the MRI overlay)

electrode of 9 cm^2 (3 × 3 cm) was used. This electrode was positioned over the VMPFC (Fpz position according to the extended 10–20 electrode reference system; Chatrian et al. 1988). A reference electrode of 35 cm^2 (5 × 7 cm) was applied over the DLPFC (F3 position according to Chatrian et al. 1988). The contact between electrodes and scalp was made by electrode cream. Moreover, there was a ramp up/ramp down period of 30 s at the start and end of the direct current stimulation. In the anodal stimulation condition, a constant current of 0.5 mA was applied for 20 min on the active electrode which resulted in a current density of 0.056 mA/cm^2 at this electrode and of 0.014 mA/cm^2 at the reference electrode (due to the different sizes). Both, the relatively strong current density at the active electrode as well as the relatively long stimulation duration were implemented to maximize the effect of the stimulation because larger current densities are supposed to result in stronger tDCS effects and increasing stimulation durations also determine the occurrence and duration of tDCS-after effects (Nitsche et al. 2008). In this condition, the current flew from the reference electrode to the active electrode (placed over the VMPFC), resulting in a strong excitatory stimulation of the VMPFC (and potentially a weak inhibition of the DLPFC; Fig. 1 above). In the cathodal stimulation condition, the same procedure was applied, except that the constant current of 0.5 mA was applied on the reference electrode. Thus, the current flew from active to reference electrode, resulting in a strong inhibition of the VMPFC (and potentially a weak stimulation of the DLPFC; Fig. 1).

Design The experiment comprised a 2 (test: pre vs. post) × 2 (VMPFC stimulation: anodal vs. cathodal) repeated-measures design with the SPE as the dependent variable. Only the VMPFC stimulation was varied between participants. The assignment of label and shape was balanced across participants following a Latin-square design.

Procedure Participants were randomly assigned to one of two tDCS conditions: (a) anodal stimulation of the VMPFC or (2) cathodal stimulation (i.e., inhibition) of the VMPFC. After the exclusions due to the criteria mentioned above, 30 participants were in the cathodal condition and 35 participants in the anodal condition. They all were naive to the condition, which they were assigned to. Further, participants were tested individually and task instructions were given on the screen and summarized by the experimenter. Each

participant underwent the same standardized procedure: (1) fill out a questionnaire concerning the exclusion criteria and demographic data, (2) association phase of the matching paradigm, (3) pre-tDCS matching-task phase, (4) tDCS application, (5) post-tDCS matching-task phase (similar to the pre-tDCS phase), (6) side-effects questionnaire and hair cleaning. In whole, the experiment took the participant about 60 min.

In the association phase of the matching paradigm, the to-be-learned assignments (i.e., one self-relevant and two non-self-relevant assignments) were presented on the display for 60 s and in written form. For a particular participant, these assignments might read: "I am the triangle. A stranger is the circle. The chair is the square." The position of the labels in the text was balanced across participants (i.e., the self-relevant label could be in the first, the second, or the third assignment). Participants were instructed that varying combinations of these shapes and labels will be presented on the screen and to judge these displayed combinations according to its correspondence with the learned assignments. Further, they were instructed to place the index finger of the left hand on the S-key to indicate non-matching combinations and the index finger of the right hand on the L-key to indicate matching combinations. Subsequently, the matching task was applied. Here, each trial started with a 500 ms presentation of a black screen, followed by a fixation cross for 500 ms, a pairing of one label and one shape for 100 ms and another black screen until the participant responded or 1,500 ms had elapsed. Each phase of the matching task (pre and post) consisted of a practice phase and an experimental phase. The practice phase consisted of 48 trials and feedback was given after each trial. The experimental phase consisted of three blocks with 48 trials (resulting in 144 trials). Here, a feedback display was only presented when the participant did not respond within 1,500 ms. In both phases, each label was presented in one-third of the trials, half of it with matching and half with non-matching assignments. Trials were presented in random order.

Results

Only correct responses with RTs above 200 ms and below 1.5 interquartile ranges above the third quartile of the overall RT distribution (Tukey 1977) were used for the RT analysis. Averaged across participants, 88.2% of the trials were selected for RT analysis; 8.8% of the trials were excluded because of erroneous responses and 3.0% due to the RT-outlier criteria. Mean RTs and error rates are shown in Table 1 (Appendix 1).

The SPE is usually defined as better performance in self-associated matching trials compared to performance in non-self-associated matching trials (for a definition, see, e.g., Sui et al. 2012). Accordingly, we calculated the SPE in RTs as the difference between RTs in matching trials with the self-associated shape (i.e., the shape associated with the label "I") and the average of RTs in matching trials with one of the non-self-associated shapes (i.e., the average of trials either with the shape associated with the label ["friend"] or with the shape associated with the label ["chair"]). In a first step, an overall 2 (test: pre vs. post) × 2 (vmPFC stimulation: excitatory/anodal vs. inhibitory/cathodal) × 2 (matching condition: matching vs. non-matching) × 3 (shape association: I vs. friend vs. chair) repeated-measures MANOVA (for the use of MANOVA analyzing repeated-measures designs, see O'Brien and Kaiser 1985) with mean RTs (Table 1, Appendix 1) revealed a significant main effect of test, $F(1, 63) = 24.88$, $p < .001$, $\eta_p^2 = .28$, which indicates faster responses after the stimulation. To account for this difference, we adjusted the resulting difference scores to the mean RT in the particular condition. Therefore, we divided each difference score by the mean RT in the particular test condition (i.e., the SPE in the 'pre'-condition was divided by the mean RT in the 'pre'-condition and comparably for the 'post'-condition), resulting in a quotient (see Fig. 2). Overall, we found a significant SPE, $t(64) = 9.147$, $p < .001$, $d = 1.13$, indicating a strong prioritization of the self-associated stimuli.[1]

We then analyzed the adjusted SPE in RTs in a 2 (test: pre vs. post) × 2 (VMPFC stimulation: anodal vs. cathodal) repeated-measures MANOVA. Here, an influence of VMPFC stimulation on the SPE would be indicated by a significant interaction of test and VMPFC stimulation. However, none of the main effects was significant, $F(1, 63) = 3.98$, $p = .051$, $\eta_p^2 = .06$, for VMPFC stimulation, and $F < 1$, for test, and, most important for our hypothesis, no significant interaction was found, $F < 1$. Supporting this result, a direct comparison of the SPE before the stimulation (i.e., in the 'pre'-condition) with the SPE after the stimulation separate for the two stimulation conditions revealed that neither in the anodal, nor in the cathodal condition the SPE varied significantly, both ts < 1 (Fig. 2). Note that the power to detect a medium effect of the stimulation (d_z = 0.5 as defined by Cohen 1988) in one of these pair-wise comparisons, given $\alpha = 0.05$ and $N = 30$ (in the cathodal stimulation condition) or $N = 35$ (in the anodal stimulation condition), was $1 - \beta = 0.75$ and $1 - \beta = 0.82$, respectively (G*Power 3.1.9.2, Faul et al. 2007). For the sake of completeness, note that a corresponding analysis with the SPE

[1] Note that the corresponding analysis in the overall MANOVA indicated that the mean RTs in the two non-self-relevant conditions (i.e., with the label "friend" and with the label "chair") did not differ significantly, $F(1, 63) = 1.26$, $p = 0.267$ (second Helmert contrast of the factor 'shape association'), suggesting no performance differences between these two conditions.

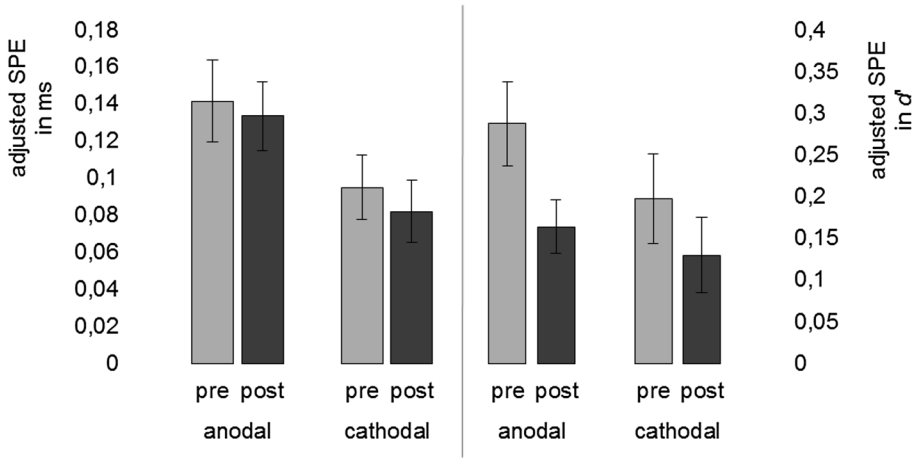

Fig. 2 The SPE as a difference score between mean RTs (left) or *d'* (right) in other- and self-relevant trials, adjusted to the mean RT or *d'* in the particular test condition (i.e., pre or post) and as a function of VMPFC stimulation and test. Error bars depict the standard error of the mean

as non-adjusted difference score reveals the same results (for details, see Appendix 2).

To provide further support for the conclusion of an independence of the SPE of the VMPFC, based on the absence of the interaction of test and VMPFC stimulation in the current study, we calculated a Bayes factor using the software program JASP (Love et al. 2015). A Bayesian repeated-measures ANOVA revealed that the data were about 3.7 times as likely to have occurred under a null hypothesis for the interaction than under an alternative hypothesis, $BF_{01} = 3.68$. According to the rules of thumb given by Jeffreys (1961; see also Wagenmakers et al. 2011), which give a suggestion for interpreting the evidential strength of a Bayes factor, this Bayes factor is considered "substantial evidence" for the null hypothesis.

Accuracy was analyzed computing signal-detection-sensitivity indices (*d'*) for each shape condition to consider the individual response criterion. Correct responses in matching trials were considered hits, while erroneous responses were considered missings. In non-matching trials, correct responses were considered correct rejections and erroneous responses were considered false alarms. Following the log-linear approach to account for cases with 100% hits or 0% false alarms (see Hautus 1995; Stanislaw and Todorov 1999), we then computed *d'* as a measure of sensitivity for each of the associated shapes. In accordance with the RT analysis, we calculated the SPE in *d'* as the difference between sensitivity in trials with the self-associated shape compared to sensitivity in trials with a non-self-associated shape (i.e., the shapes associated with "mother" or "friend"). Further, we adjusted the difference scores to the mean sensitivity in the particular test condition to analyze sensitivity consistent with RTs (see Appendix 2 for the analyses with the non-adjusted SPE). Overall, as in RTs, we found a significant SPE, $t(64) = 7.49$, $p < .001$, $d = 0.93$, indicating a strong prioritization of the self-associated stimuli in the sensitivity measures.

The SPE in *d'* was submitted to a 2 (test: pre vs. post) × 2 (VMPFC stimulation: anodal vs. cathodal) repeated-measures MANOVA which revealed a significant main effect of test, $F(1, 63) = 6.41$, $p = .014$, $\eta_p^2 = .09$, but no main effect of VMPFC stimulation, $F(1, 63) = 1.39$, $p = .243$, $\eta_p^2 = .02$, and, most important for our hypothesis as well as also comparable to the data pattern in RTs, no interaction, $F < 1$. The comparison of the SPE before the stimulation with the SPE after the stimulation separate for the two stimulation conditions revealed that the SPE did not vary significantly in the cathodal condition, $t(29) = 1.19$, $p = .244$, but, however, was reduced in the anodal condition, $t(34) = 2.41$, $p = .021$, $d = 0.36$ (Fig. 2). Note that, according to our predictions based on previous literature, the SPE should be stronger after anodal stimulation. Thus, this reduction of the SPE—solely in *d'*—was not predicted and will be discussed.

The corresponding Bayesian repeated-measures ANOVA revealed that the data were about 3.5 times as likely to have occurred under a null hypothesis for the interaction than under an alternative hypothesis, $BF_{01} = 3.45$ (JASP; Love et al. 2015). This finding again is interpreted as "substantial evidence" for the null hypothesis according to the rules of thumb given by Jeffreys (1961; see also Wagenmakers et al. 2011).

Discussion

In a pre-post design, we measured the prioritization due to self-relevance before and after the induction of either excitatory or inhibitory activation in the VMPFC via tDCS. The results indicate that there was no influence of the stimulation on the SPE in RTs, as neither after excitatory stimulating, nor after inhibiting the VMPFC the SPE changed. Only in the sensitivity measure, the SPE was significantly reduced after anodal stimulation. Note that this effect contradicts any hypotheses based on previous findings and can be explained

by simple group differences as the SPE in the anodal condition is rather large before the stimulation.

For the interpretation of this null effect of VMPFC stimulation on the SPE, two aspects are of importance. First, there was a significant SPE in both stimulation conditions as well as before and after the stimulation. Thus, the association of formerly neutral geometric shapes with the self resulted in a significant prioritization in comparison to associations with non-self-relevant instances (a stranger and a chair), depicting a typical effect of self-relevance (Humphreys and Sui 2016). Second, it is important to note that single-session tDCS has been reported to impact on cognitive processing previously. For example, an assessment of the effects of tDCS stimulation of the DLPFC on the Stroop effect (Stroop 1935) revealed a significant reduction of the effect after anodal tDCS stimulation, whereby there was no reduction in a control condition (sham; Jeon and Han 2012). In a subsequent study, a significant increase of the Stroop effect after cathodal stimulation of the DLPFC was reported (Frings et al. 2018). Moreover, the inhibition of a prepotent response was also shown to be influenced by anodal stimulation of the right DLPFC as the latency to inhibit a response in a stop-signal task was reduced after anodal stimulation while remaining unchanged in a sham condition (Friehs and Frings 2018). We chose a tDCS approach that maximizes the chance to observe an effect of stimulation as we directly compared anodal with cathodal stimulation that should elicit different effects on the SPE if the SPE depends on activation in the VMPFC. Given that the data suggest that there is no difference between these extreme conditions, we come to the conclusion that single-session tDCS of the VMPFC does not seem to affect the SPE.

Nonetheless, current interpretations are based on one experiment and thus of course need further clarification. Especially the assumption of an independence of the SPE from the VMPFC would be—considering previous findings as reported in the introduction—far too hasty. However, one arguable explanation for the conclusion that activation in the VMPFC does not affect the SPE is that the VMPFC is not at all involved in the prioritization of self-associations. Besides the indication of an association of the VMPFC with self-referential processing, studies assessing the self-brain area revealed further brain areas which are of importance. For example, the above mentioned full-brain analysis pointed out an involvement of brain areas like the insula, the medial parietal cortex, and the cerebellum (see Table 2–4 in Jenkins and Mitchell 2011). Appropriate to that, an analysis of brain activation during either self-relevant or non-self-relevant judgements of emotional pictures was interpreted as evidence for an involvement of the whole MPFC in self-referential processing. In particular, the authors postulate that not exclusively the ventral areas are involved, but also dorsal areas of the MPFC (Gusnard et al. 2001). Thus, even if most of the findings are interpreted in terms of an association of the VMPFC with self-referential processing, the current null-result might be an indication that the localization of self-effects in the ventral parts of the MPFC is questionable.

Another, potentially more plausible explanation for the conclusion that activation in the VMPFC does not affect the SPE provides further information about the connection of the SPE and the VMPFC, which was first assessed by Sui et al. (2013). In their study, participants worked on a matching task while in a fMRI scanner and a significant correlation of the SPE with activation in the VMPFC was indicated. However, in our study, an experimental manipulation of activation in the VMPFC did not reveal any systematic effect on the SPE. Combining these two findings, one can conclude that the connection of SPE and VMPFC is a *correlative* connection while the VMPFC does not causally influence the SPE. This assumption of a correlative rather than a causal connection of SPE and VMPFC is emphasized by the several times postulated synchronization of different brain areas during the processing of self-relevant material. In detail, activation in the VMPFC seems to be negatively correlated with activation in the dorsal MPFC (Gusnard et al. 2001) and positively correlated with activation in the LpSTS (Sui et al. 2013). On this basis, note that previous findings about the SPE suggest that the SPE is partly perceptual, indicating that it influences cognitive processes on a very early stage. Even if several empirical findings had been reported which either let to doubt any perceptual advantage of the SPE (Janczyk et al. 2018; Stein et al. 2016) or demonstrate a non-perceptual component of the SPE (Fuentes et al. 2015), other studies convincingly reveal a perceptual component of it (Macrae et al. 2017; Sui et al. 2013). In sum, research so far might be interpreted in terms of a perceptual as well as a non-perceptual component of the SPE (Sui et al. 2015). Possibly, the SPE can exactly by this perceptual component be differentiated from other self-effects. Then, while more elaborate self-effects—like for example thinking about one's own personality traits or one's own vs. others' mental states (as mentioned in the introduction)—might be processed in the VMPFC, the neural base of the SPE might be located in other brain areas. In further research, one could assess whether the SPE is correlated with activation in the VMPFC, but, in fact, is inevitably processed in for example one of the synchronized brain areas, but at any rate in a brain area other than the VMPFC.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Appendix 1

See Table 1.

Table 1 RTs in milliseconds and absolute error rates as well as the sensitivity measure *d'* are presented as a function of VMPFC stimulation condition, time of testing, matching condition, and shape association

Shape association	RTs		Error rates		
	Matching	Non-matching	Matching	Non-matching	*d'*
Anodal/excitatory					
Pre					
Self	526 (89)	664 (97)	1.0 (1.6)	1.5 (1.6)	3.22
Familiar other	612 (94)	646 (73)	3.1 (3.2)	2.9 (2.4)	2.42
Neutral instance	603 (79)	651 (90)	3.3 (3.2)	1.8 (1.6)	2.61
Post					
Self	498 (73)	625 (94)	0.9 (1.1)	1.7 (2.4)	3.23
Familiar other	570 (84)	633 (92)	2.2 (2.0)	2.2 (2.4)	2.74
Neutral instance	574 (88)	620 (88)	2.3 (2.1)	2.0 (2.8)	2.85
Cathodal/inhibitory					
Pre					
Self	531 (82)	634 (96)	1.7 (1.5)	1.9 (1.7)	2.86
Familiar other	591 (96)	636 (88)	3.3 (2.7)	2.9 (1.8)	2.29
Neutral instance	579 (87)	629 (98)	2.4 (2.6)	2.6 (2.0)	2.57
Post					
Self	515 (85)	610 (94)	1.2 (1.2)	1.6 (1.6)	3.10
Familiar other	565 (96)	606 (91)	1.9 (1.6)	2.0 (1.5)	2.78
Neutral instance	552 (78)	617 (84)	1.8 (1.7)	2.5 (2.0)	2.71

Standard deviationsare in parentheses

Appendix 2

Statistical analyses with the non-adjusted SPE score revealed results which are congruent with the results of the analysis of the adjusted SPE. In RTs, also the non-adjusted SPE was overall significant, $t(64) = 9.11$, $p < .001$, $d = 1.13$. Further, a 2 (test: pre vs. post) × 2 (VMPFC stimulation: anodal vs. cathodal) repeated-measures MANOVA with the non-adjusted SPE revealed a significant main effect of VMPFC stimulation, $F(1, 63) = 4.23$, $p = .044$, $\eta_p^2 = .06$, but no significant main effect of test, $F(1, 63) = 1.74$, $p = .192$, $\eta_p^2 = .03$. Most important for the hypothesis and comparable to the analysis with the adjusted SPE, no significant interaction was found, $F < 1$. Supporting this result, a direct comparisons of the SPE before the stimulation (i.e., in the 'pre'-condition) with the SPE after the stimulation separate for the two stimulation conditions revealed that neither in

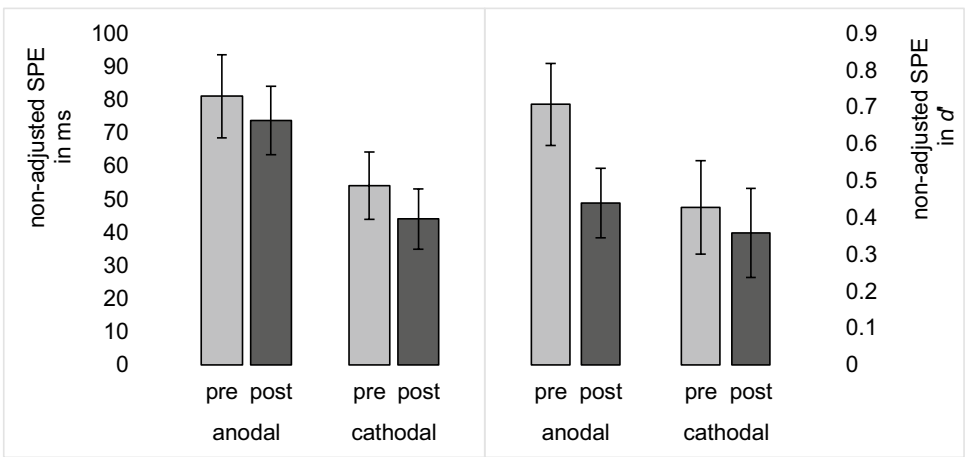

Fig. 3 The non-adjusted SPE as a difference score between mean RTs (left) or *d'* (right) in other- and self-relevant trials as a function of VMPFC stimulation and test. Error bars depict the standard error of the mean

the anodal, nor in the cathodal condition the SPE varied significantly, both *t*s < 1 (Fig. 3).

In sensitivity rates, the non-adjusted SPE was overall significant, $t(64) = 7.40$, $p < .001$, $d = 0.92$. Further, a 2 (test: pre vs. post) × 2 (VMPFC stimulation: anodal vs. cathodal) repeated-measures MANOVA revealed no significant main effect, $F(1, 63) = 1.87$, $p = .176$, $\eta_p^2 = 0.03$, for test, $F(1, 63) = 1.87$, $p = .176$, $\eta_p^2 = 0.03$, for VMPFC stimulation. There was also no significant interaction, $F(1, 63) = 1.22$, $p = 0.273$, $\eta_p^2 = 0.02$. The comparison of SPE before the stimulation with the SPE after the stimulation separate for the two stimulation conditions revealed—comparable to the results with the adjusted SPE—that the SPE did not vary significantly in the cathodal condition, $t < 1$, but, however, was reduced in the anodal condition, $t(34) = 2.41$, $p = .021$, $d = 0.41$ (Fig. 3). As with the adjusted SPE, this reduction of the SPE—solely in *d'*—was not predicted and thus is dicussed.

The corresponding Bayesian repeated-measures ANOVA revealed that, for RTs the data were about 3.9 times as likely to have occurred under a null hypothesis for the interaction than under an alternative hypothesis, $BF_{01} = 3.90$, and about 2.4 times as likely, $BF_{01} = 2.41$, for *d'* (JASP; Love et al. 2015). According to the rules of thumb given by Jeffreys (1961; see also Wagenmakers et al. 2011), this finding is interpreted as "substantial evidence" for the null hypothesis in RTs, and "anecdotal evidence" in *d'*.

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