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TDCS over the right inferior frontal gyrus disrupts control of interference in memory: A retrieval-induced forgetting study

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ABSTRACT

Retrieving information from episodic memory may result in later inaccessibility of related but task-irrelevant information. This phenomenon, known as retrieval-induced forgetting, is thought to represent a specific instance of broader cognitive control mechanisms, that would come into play during memory retrieval, whenever non-target competing memories interfere with recall of target items. Recent neuroimaging studies have shown an association between these mechanisms and the activity of the right Prefrontal Cortex. However, so far, few studies have attempted at establishing a causal relationship between this brain region and behavioural measures of cognitive control over memory. To address this missing link, we delivered transcranial Direct Current Stimulation (tDCS) over the right Inferior Frontal Gyrus (rIFG) during a standard retrieval-practice paradigm with category-exemplar word pairs. Across two experiments, tDCS abolished retrieval-induced forgetting to different degrees, compared to the sham control group whereas no effects of stimulation emerged in an ancillary measure of motor stopping ability. Moreover, influence analyses on specific subsets of the experimental material revealed diverging patterns of results, which depended upon the different categories employed in the retrieval-practice paradigm. Overall, the results support the view that rIFG has a causal role in the control of interference in memory retrieval and highlight the often underestimated role of stimulus material in affecting the effects. The present findings are therefore relevant in enriching our knowledge about memory functions from both a theoretical and methodological perspective.

1. Introduction

Cognitive control refers to a set of essential abilities that allow us to maintain an adaptive behaviour within an ever-changing environment. From abruptly stopping a course of action that is not optimal anymore (Verbruggen & Logan, 2008), to suppressing unwanted or irrelevant memories from coming to mind (Anderson & Hanslmayr, 2014; Storm & Levy, 2012), cognitive control is constantly recruited in our everyday life. Importantly, over the last thirty years, a set of cognitive models of memory has gained prominence, in which a role for cognitive control in both retrieval and forgetting is postulated. As a result, the concept of forgetting has also been profoundly revised, from a limitation or failure of our memory systems to an active process that benefits from cognitive control to allow for an adaptive and efficient functioning in every-day life (Nørby, 2015; Storm, 2011). In particular, it has been hypothesized that inhibitory mechanisms (putatively similar to those involved in response selection in perceptual and motor tasks and therefore sharing common neural substrates in the prefrontal cortex, PFC) may be responsible for a peculiar instance of forgetting that is detected when retrieving an information from our memory storage impairs later recall of related information, compared to unrelated ones. This finding, traditionally termed retrieval-induced forgetting (RIF), is thought to represent the mark that is left behind by inhibitory control mechanisms recruited to overcome interference during selective memory retrieval, i.e., when one actively engages in effortful retrieval from memory in the face of competing, irrelevant memory traces (Anderson, Björk, & Björk, 1994). The memory representation of these interfering memory traces would be weakened by inhibitory mechanisms that promote selection and emission of the correct,

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task-relevant response, so that their availability may be reduced on later attempts to retrieve the previously interfering memories.

According to some Authors, the inferior frontal gyrus (IFG) orchestrates inhibitory control across cognitive domains via top-down regulation of other cortical and subcortical areas depending on the task at hand (e.g., Aron, Robbins, & Poldrack, 2014). In this view, the IFG might represent a key node for the neural networks deputed to both motor stopping and memory suppression which, in turn, may constitute different but interrelated instances of inhibitory control. In the model put forward by Levy and Anderson (2002), response selection in both action and memory might be supported by inhibitory mechanisms that share similar neural substrates mainly located in the prefrontal cortices. In particular, the Authors pointed to the dorsolateral prefrontal cortex (DLPFC) as a putative central hub for the cognitive processes mediating inhibitory control in both domains, whereas the anterior cingulate cortex (ACC) would be deputed to the role of conflict detector and signaller to the DLPFC. Neuroimaging evidence suggests a role for both the DLPFC and the IFG during selective retrieval from episodic memory in the face of interference arising from competing memory traces (Wimber, Alink, Charest, Kriegeskorte, & Anderson, 2015; Wimber, Rutschmann, Greenlee, & Bäuml, 2009; Wimber et al., 2008). Moreover, these studies suggested a greater contribution of right prefrontal areas, similar to what has been reported in other work on related domains (e.g., Benoit & Anderson, 2012, in voluntary forgetting, and Goghari & MacDonald, 2009, in the go/no-go task).

In a previous study, Penolazzi, Stramaccia, Braga, Mondini, and Galfano (2014), used transcranial Direct Current Stimulation (tDCS) in the attempt to provide the first causal evidence for the involvement of right DLPFC in control over interfering memories, as indexed by RIF. Specifically, RIF was gradually reduced in two stimulation groups, which received anodal and cathodal tDCS respectively, compared to a sham control group. In particular, on average, participants receiving cathodal tDCS, which is thought to inhibit endogenous activation in the target area, showed the least amount of RIF, to the point of observing a reversed effect, compared to a sham stimulation (i.e., control) group, where a significant effect was observed.

Here, we focused on testing the involvement of the right IFG (rIFG) in RIF. We hypothesized that altering the activity of this particular brain region during a task that putatively relies on the ability to suppress interfering memories would affect later recall of these memories. To this end, we targeted the rIFG with tDCS in healthy volunteers performing a retrieval practice paradigm (RPP; Anderson et al., 1994; see Murayama, Miyatsu, Buchli, & Storm, 2014, for a recent meta-analysis), which is commonly used to assess the individual ability to overcome interference in memory. Importantly, many studies have already employed tDCS to modulate performance in behavioural tasks related to inhibitory control, with overall promising results (e.g., Ditye, Jacobson, Walsh, & Lavidor, 2012; Jacobson, Javitt, & Lavidor, 2011; Metzuyanim-Gorlick & Mashal, 2016; Penolazzi et al., 2014; Stramaccia et al., 2015).

In the RPP, participants first study a series of category-exemplar word pairs. Immediately after that, they repeatedly perform active retrieval practice on half the exemplars from half the categories. Finally, participants' memory for all the experimental material is tested. The RPP allows measuring two distinct effects. On the one hand, the well-known superiority of memory performance on subsequent recall of study material that underwent additional practice, compared to studied but unrehearsed material, typically referred to as facilitation (FAC) effect in the context of the RPP. On the other hand, the observation that selectively practicing retrieval of certain exemplars leads to impairment of unrehearsed exemplars that share the same category cue, compared to unrehearsed exemplars belonging to different unpracticed categories. The latter phenomenon is known as RIF, to highlight the fact that the very act of selectively retrieving memory traces is responsible for the later inaccessibility of related memory traces due to the need to overcome interference from related exemplars by weakening the memory traces associated to them. In the present study, in line with Penolazzi et al. (2014), tDCS was administered during the active retrieval practice phase of the RPP, i.e., when inhibitory mechanisms are thought to be implicitly recruited (e.g., Anderson, 2003).

If rIFG plays an important role in RIF, then we expected to observe a pattern similar to that reported by Penolazzi et al. (2014), with cathodal stimulation showing the greatest impact on the behavioural index of successful inhibition. On the contrary, the absence of major group differences could signify that rIFG may not primarily be involved in this internally directed instance of cognitive control, compared to the well-established contribution of the rDLPFC (Penolazzi et al., 2014). Moreover, in keeping with the inhibitory account of RIF, we did not expect to observe any stimulation effects on FAC, as the two phenomena would rely on distinct neural substrates and different cognitive processes.

2. Experiment 1

2.1. Methods

2.1.1. Participants

The ethical committee for psychological research of the University of Padua approved the study, which was performed in accordance with the principles of the Declaration of Helsinki. All participants underwent an eligibility screening for the tDCS procedure, and provided an informed consent prior to their participation and a final consent at the end of the experimental procedure. 53 healthy volunteers (18 males) aged between 21 and 27 years (*mean age* = 23.30, *SD* = 1.70; *mean years of education* = 17.43, *SD* = 1.64) took part in the experiment. All participants were Italian native speakers with no history of neurological disease, psychiatric disorders, heart conditions, severe head injury, seizures (personal or in first degree relatives), recurring syncope, or learning disability. Additional exclusion criteria included pregnancy, presence of metal in the face or the head (other than dental work), presence of skin conditions on the scalp or history of severe dermatitis, on-going or recent use of medical prescriptions other than contraceptives, and excessive use of alcohol on the day prior to the stimulation session.

2.1.2. Retrieval practice paradigm (RPP)

Participants sat approximately 57 cm from a 15-in. laptop monitor (1024 × 768 pixels, 60 Hz), on which stimuli (20-point Arial bold font) were shown in black against a gray background. Stimulus presentation and response collection were controlled using E-Prime 2.0.

A typical three-phase RPP was used, identical to that used by Penolazzi et al. (2014). The stimuli consisted of 96 category-exemplar word pairs (e.g. "FRUIT-cherry"), divided by eight semantic categories, with twelve exemplars for each category. We selected and adapted all the material from the categorical production norms for the Italian language by Boccardi and Cappa (1997), according to the following criteria: (i) within each category, we included seven exemplars with high taxonomic strength (strong exemplars) and five with low taxonomic strength (weak exemplars), according to the production norms; (ii) words within the same category always had a different initial letter; (iii) we tried to keep semantic associations between and within categories to a minimum, to avoid semantic integration (Goodmon & Anderson, 2011); (iv) we included only words that were no longer than ten or no shorter than four letters; (v) we chose only unambiguous, non-compound words for both exemplars and categories.

It is worth noting that participants were completely naïve to the procedure: participation to previous studies using this behavioural paradigm constituted an additional exclusion criterion. The RPP is schematically represented in Fig. 1.

In the study phase, we instructed the participants to memorize all of the 96 category-exemplar word pairs, by relating each exemplar to its category. We also informed them that they would have been tested later on the exemplars. Study trials began with a brief fixation point in the center of the screen for 500 ms, followed by a blank screen (500 ms); subsequently, one category-exemplar word pair was presented centered on screen for 2500 ms, followed by a blank screen (500 ms). The stimuli were delivered in a randomized blocked-by-category order.

In the practice phase, participants repeatedly practiced the weak exemplars of half the semantic categories (four repetitions of 20 exemplars, 80 trials in total). Importantly, practicing weak exemplars only should boost the RIF effect due to increased competition from the remaining strong exemplars (Anderson, 2003). In the practice trials, we provided the category and the first three letters of each exemplar (e.g. "FRUIT-che___") to the participants, and we instructed them to answer vocally with the name of the specific exemplar associated to the particular cue in full (4000 ms). Presentation of practice stimuli was randomized, and each practice item was preceded by a fixation cross for 1000 ms, followed by a blank screen lasting 1000 ms. The inter-trial interval consisted of a blank screen lasting 1000 ms. We labelled the practiced weak exemplars as RP+ items, the non-practiced strong items from practiced categories as RP– items, the weak non-practiced items from non-practiced categories NRP+ items, and the strong non-practiced items from non-practiced categories NRP– items. NRP+ and NRP– items served as controls for RP+ and RP– items, respectively. Four lists of categories were used to fully counterbalance the practiced categories across groups. As a result, all semantic categories contributed equally to all four types of items.

In the final test phase, we presented all the stimuli from the initial study phase (96 trials). Presentation format, timing, response modality, and instructions, were the same as in the practice phase, the only difference being that the participants were now shown the category plus the first letter of an exemplar only (e.g. "FRUIT-c____"). We presented the stimuli in randomized order, with the additional constraint that all RP– items were presented before all the NRP–, RP+, and NRP+ items, in order to control for output interference at test, which is known to inflate the RIF effect (Anderson, 2003).

2.1.3. Transcranial direct current stimulation (tDCS)

We used a battery-driven Direct Current stimulator (BrainStim, EMS, Italy) wired to a pair of surface 4 cm × 4 cm conductive rubber electrodes inserted in saline-soaked sponges, and secured to the scalp with rubber bands. Anodal, cathodal, or sham tDCS over the rIFG were delivered at 1.5 mA (current density of 0.09 mA/cm^2). The target area was located at the FC4 site of the EEG 10–20 system (Jasper, 1958) as the crossing point between

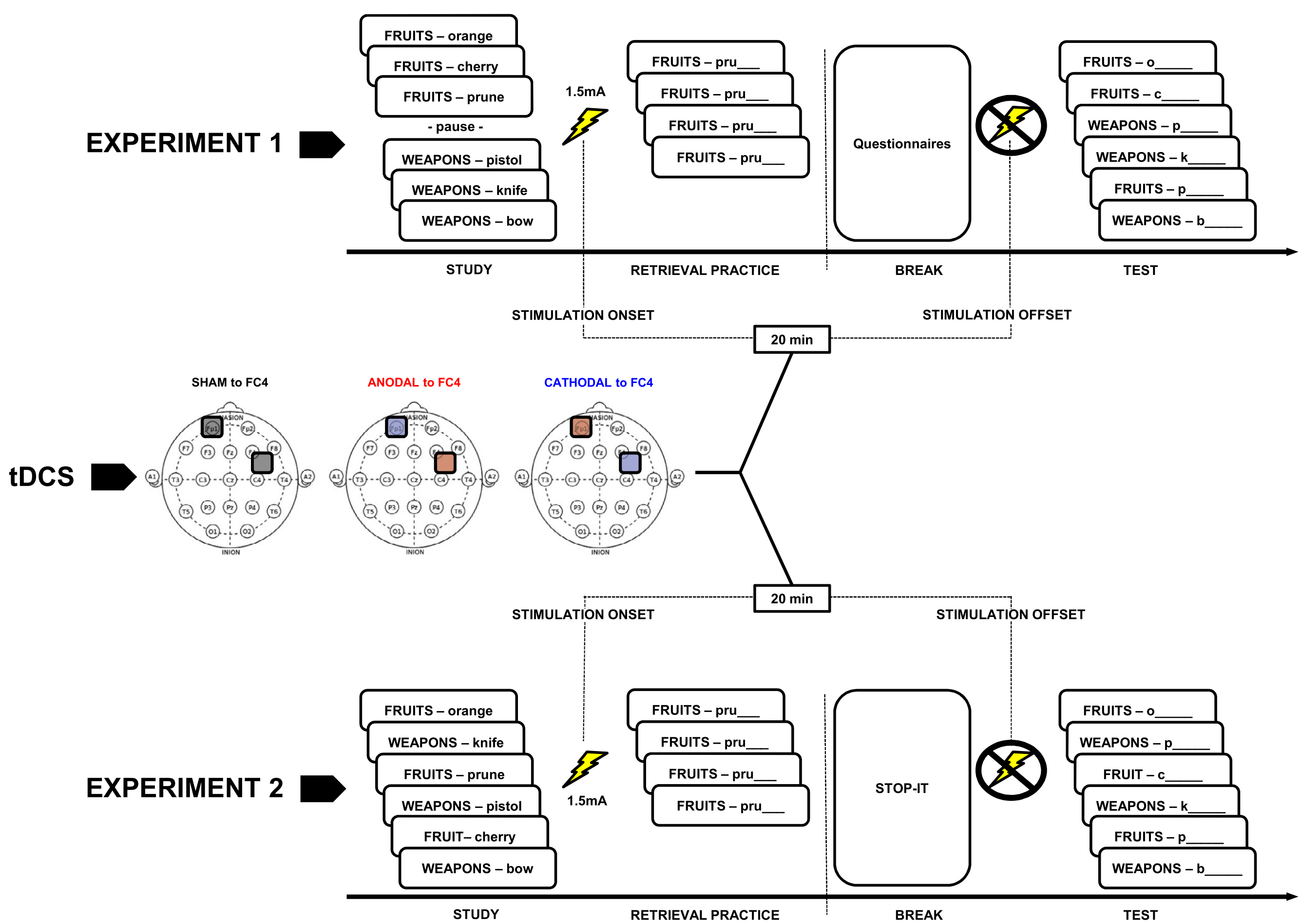

Fig. 1. Schematic representation of the RPP used in Experiment 1 (upper section) and Experiment 2 (lower section), and the tDCS montage employed across both experiments (middle section). See text for full details.

T4-Fz and F8-Cz (e.g., Jacobson et al., 2011), and the reference electrode was placed on the left supraorbital area (see Fig. 1, tDCS). The stimulation parameters were the same as in Penolazzi et al. (2014). A single blind, between group design was used: Participants were randomly assigned to anodal (N = 17, 6 males, *mean age* = 23.65, *SD* = 1.80), cathodal (N = 16, 6 males, *mean age* = 23.25, *SD* = 1.34), or sham tDCS (N = 20, 6 males, *mean age* = 23.05, *SD* = 1.90). Stimulation begun prior to the practice phase of the RPP, and lasted 20 min in total for all three groups, covering the entire practice phase. In the active tDCS conditions, we ramped up the stimulation to 1.5 mA over 30 s, maintained it for 19 min, and ramped it down over 30 s again at the end to minimize unpleasant sensations. In the Sham stimulation group, we ramped up and then immediately ramped down stimulation over 15 s at both the beginning and end of the protocol, an approach that is commonly used to blind participants in tDCS experiments (e.g., Brunoni et al., 2012; Gandiga, Hummel, & Cohen, 2006).

2.2. Procedure

As soon as participants completed the screening process for tDCS and gave their written consent, we prepared the montage for the tDCS, without starting the stimulation. Participants first performed the study phase of the RPP. After that, we checked the integrity of the montage, and turned the stimulation on. As soon as the participants felt comfortable with the stimulation (always within moment from the initial ramp up period), they performed the retrieval practice phase of the RPP, followed by filler questionnaires whose contents were unrelated to the experimental material. Stimulation ended shortly before completion of the questionnaires, and we removed the montage before proceeding with the final test phase of the RPP.

2.3. Data analysis

We analysed recall accuracy in the test phase of the RPP as the main dependent variable. Exact answers only were considered as correct, with the exception of occasional and obvious spelling mistakes. In keeping with the typical approach in the RIF literature, we analysed FAC-relevant items (RP+ and NRP+) separately from RIF-relevant items (NRP− and RP−). We analysed the data with R (R Core Team, 2016), and fitted logistic mixed effects models using the glmer procedure in the lme4 package (Bates, Maechler, Bolker, & Walker, 2015), which is more appropriate to examine accuracy data with respect to repeated measures ANOVA (e.g., Jaeger, 2008).

Following Baayen, Davidson, and Bates (2008), we entered item type, stimulation group, and the possible interaction term, as fixed effects, and participant and category as random intercept terms, in order to account for both participant- and item-related variability (type × group model). In particular, we entered category in the model as a random factor to counter the well-known *language-as-fixed-effect* fallacy (e.g., Clark, 1973), while keeping the stability of the model (i.e., avoiding convergence issues due to the relatively small number of observations per single item) and the experimental grouping of the stimuli within categories in mind. Using the same approach, we subsequently computed two additional models: a model without the interaction term (type + group model), and a model without the interaction term and the main effect of stimulation group (type model). We used the Akaike's information criterion (AIC; Akaike, 1973) transformed to conditional probabilities for each of the above models, i.e., AIC weights (*AICw*; Wagenmakers & Farrell, 2004) to select the model that more appropriately described our data. Indeed, AIC weights improve the interpretation and the accessibility of results for further analyses, provide a deeper insight on the features of the competing models, and quantify conclusions based on AIC (Wagenmakers & Farrell, 2004). Subsequently, we computed *ERs* (Evidence Ratios, e.g., Snipes & Taylor, 2014), i.e., the relative likelihood of a pair of models, to compare the best model in terms of *AICw* against other individual models. We then followed the framework proposed by Kass and Raftery (1995) to qualify the *LERs* (Log_{10}Evidence Ratios) between model probabilities, so that, *a priori*, *LERs* greater than 0, 0.5, 1, and 2, were described as yielding 'minimal', 'substantial', 'strong', or 'decisive' evidence against H_0, respectively.

The "qpcR" package (Spiess, 2014) was employed to compute *AICw*. Interaction effects for selected models were further investigated in terms of simple effects via multiple contrasts with the "testInteraction" function in the "phia" R package (De Rosario-Martinez, 2015), adjusting the false discovery rate with the method developed by Benjamini and Hochberg (1995). The "effects" R package (e.g., Fox & Hong, 2009) was used to investigate effects within specific models.

Finally, we computed Pearson's product-moment correlation to assess whether RIF and FAC were uncorrelated, as posited by the strength independence tenet of the inhibitory account of RIF (Anderson, 2003).

2.4. Results

Mean proportions of recall in the final test phase for each item type and FAC/RIF effects are reported in Table 1.

For the FAC effect, the type model best fit the data, yielding minimal to substantial evidence with respect to the competing models ($AICw_{(type \times group)} = 0.087$, $AICw_{(type+group)} = 0.287$, $AICw_{(type)} = 0.626$; $LER_{(type>type \times group)} = 0.857$, $LER_{(type>type+group)} = 0.339$). In line with our predictions, the FAC effect was significant in each group, as shown by group-wise multiple contrasts as a function of item type (all $ps < 0.0001$).

Concerning the RIF effect, in contrast with our predictions, the winning model was again the one that included only the main effect of item type, yielding substantial evidence against the competing models ($AICw_{(type \times group)} = 0.096$, $AICw_{(type+group)} = 0.195$, $AICw_{(type)} = 0.709$; $LER_{(type>type \times group)} = 0.868$, $LER_{(type>type+group)} = 0.561$). Detailed information on the model is reported in Table 2.

Furthermore, multiple contrasts did not reveal a significant RIF in any of the three stimulation groups (all $ps \geq 0.593$, see Fig. 2).

Finally, as expected, the correlational analysis did not show any evidence of a correlation between FAC and RIF effects across the whole sample ($r = -0.13$, $p > 0.250$).

2.5. Discussion

The results concerning the beneficial effect of retrieval practice were in line with our predictions, with a reliable FAC effect observed in all the experimental groups and no interaction with our tDCS protocol. Turning to RIF, the results observed in this first experiment were quite unexpected. As a matter of fact, in light of our previous work, upon which the present experiment capitalized, we were not surprised about the lack of RIF in the two real stimulation groups, in particular regarding the cathodal stimulation group. However, the absence of an interaction between item type and stimulation group, coupled with the lack of a significant RIF effect in the control group, does not allow either supporting or completely rejecting our initial hypotheses. Therefore, results from this first experiment appeared to be inconclusive on whether interfering with rIFG during a RPP has any effects on inhibitory performance as indexed by RIF.

It is important to note that the RPP variant used in this experiment suffered from a few limitations, which also affected and were partially addressed in our previous work (Penolazzi et al., 2014), and which could have influenced the current results nonetheless:

Table 1
Mean proportion of recall accuracy in the final test phase of Experiment 1 as a function of item type/effect and stimulation group.

		Final test phase																	
		Item type								Effect									
		RP+		NRP+		RP−		NRP−		FAC					RIF				
Stimulation group	*N*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*95% CI*	g_{av}	*CL*	*M*	*SD*	*95% CI*	g_{av}	*CL*
Sham tDCS	20	0.538	±0.174	0.212	±0.142	0.246	±0.131	0.279	±0.139	0.325	±0.169	0.248, 0.404	1.970	98%	0.033	±0.096	−0.012, 0.078	0.235	63%
Anodal tDCS	17	0.626	±0.134	0.241	±0.119	0.313	±0.118	0.296	±0.147	0.385	±0.140	0.314, 0.455	2.893	99%	−0.017	±0.085	−0.027, 0.060	0.121	58%
Cathodal tDCS	16	0.566	±0.141	0.250	±0.108	0.292	±0.122	0.261	±0.092	0.316	±0.133	0.245, 0.387	2.388	99%	−0.031	±0.163	0.056, 0.118	0.272	58%

Note. *N*: sample size. *RP+*: practiced items; *RP+* non-practiced items from practiced categories; *RP−*: non-practiced items from practiced categories; *NRP+* and *NRP−*: non-practiced items acting as control for *RP+* and *RP−* items respectively. *FAC*: facilitation effect ((*RP+*)-(*NRP+*)); *RIF*: Retrieval-induced forgetting effect ((*NRP−*)-(*RP−*)). *M*: mean. *SD*: standard deviation. *95% CI*: confidence intervals at 95%. g_{av}: Hedges' g_{av} (absolute values), where 0.20 is considered a small effect, 0.50 a medium effect, and 0.80 a large effect (Cohen, 1988). *CL*: *common language effect size* (McGraw & Wong, 1992), an intuitively understandable statistic derived from Cohen's *d*, expresses the probability than an individual has a higher recall accuracy for one item type than the other. Choice and computation of effect sizes were performed according to recommendations by Lakens (2013, spreadsheet version 3.4).

(i) We employed a blocked-by-category study format that could have facilitated encoding strategies based on grouping the exemplars together under the category label, thus favouring integration in our participants, which is known to reduce RIF (Anderson & McCulloch, 1999); (ii) The study material consisted of a standard number of categories (eight) compared to the literature on RIF (e.g., Anderson et al., 1994), but quite a large number of exemplars (twelve) by the same standards. Therefore, interference during retrieval practice in our paradigm may have been more diluted among the many competing items (seven), thus potentially limiting the inhibitory demands, and/or the subsequent inhibitory effort may have been less effective at reducing the competing items' representation in memory to a point that later recall would suffer from such impairment; (iii) While the test format allowed to rule out output interference on RP− items (Anderson, 2003), it could have caused NRP− items to undergo more interference than the RP− items, since the former items were mixed together with the RP+ and NRP+ items. It should be noted that such bias was held constant across participants and hence is unlikely to have influenced the results as a function of stimulation (see also Penolazzi et al., 2014). In addition to that, this particular test order could have likely been more susceptible to persisting, non-specific effects of tDCS, which in turn would have differentially affected RP− compared to NRP− items given their higher proximity to stimulation offset. In consideration of all these critical points, and because the results provided by this experiment did not lend themselves to a straightforward interpretation, we carried out a second experiment in which we employed a similar rationale and improved upon the behavioural procedure and neuromodulation parameters. Moreover, sample size was increased in all stimulation groups.

3. Experiment 2

This new experiment was not just a refined replication of the previous one, but also included an important element of novelty. In fact, we took the chance to replace the filler questionnaires acting as a buffer between the retrieval practice and test phases of the RPP with an additional task aimed at measuring the individual ability to override an initiated course of action. Specifically, we employed a stop-signal task (SST; Verbruggen & Logan, 2008) that participants performed immediately after the retrieval practice phase, while tDCS was still active. In the SST, participants perform a choice RT task and withhold response when a stop signal is presented shortly after the target stimulus. In order to push participants into committing mistakes, trials that require stopping are infrequent (often 25%) compared to go trials, and the delay between the target and stop signal (stop-signal delay, SSD) is adaptively adjusted by a staircase procedure aimed at keeping participants' accuracy at about 50%. The horse-race model of inhibition in the SST (e.g., Logan & Cowan, 1984) posits that whenever a stop trial occurs, the inhibitory process triggered by the stop signal competes with the response process elicited by the target. Consequently, longer SSDs make it harder to inhibit response to stop trials, as the response process will be closer to translate into action and further "out of reach" for the inhibitory process. The main index of the efficiency of inhibitory performance in the SST at the individual level is the stop-signal reaction time (SSRT), which can be computed as the difference between mean RTs in the go trials (no-signal RTs, NSRTs) and the mean SSD in the stop-trials, for a given participant. Given that the SSRT is interpreted as the covert latency of the inhibitory process that overrides motor action, shorter SSRTs indicate a more efficient stopping process.

Many tDCS studies have shown that stimulation of prefrontal areas significantly modulates control abilities in different tasks

Table 2
Results of logistic mixed effects model with recall accuracy from Experiment 1 as dependent variable.

	Recall accuracy					
Parameters	*B (SE)*	*z*	*p*	Omnibus χ^2	*df*	*p*
Intercept	−1.022 (0.179)	−5.709	<0.001			
Item type				0.002	1	0.967
RP−	−0.181 (0.140)	−1.288	0.198			
Stimulation group				1.415	2	0.493
Anodal tDCS	0.103 (0.217)	0.485	0.627			
Cathodal tDCS	−0.052 (0.216)	−0.244	0.807			
Interaction				2.605	2	0.272
RP− × *Anodal tDCS*	0.244 (0.202)	1.206	0.228			
RP− × *Cathodal tDCS*	0.314 (0.207)	1.515	0.130			

Note: Number of subjects = 53. Number of observations = 2968. Number of semantic categories = 8. Baseline level for Item Type was *NRP−*. Baseline level for Stimulation Group was *Sham tDCS*. Random effects were Subject and Category. χ^2 values were computed with the "Anova" function in the "car" package (Fox & Weisberg, 2011). *RP−*: non-practiced items from practiced categories.

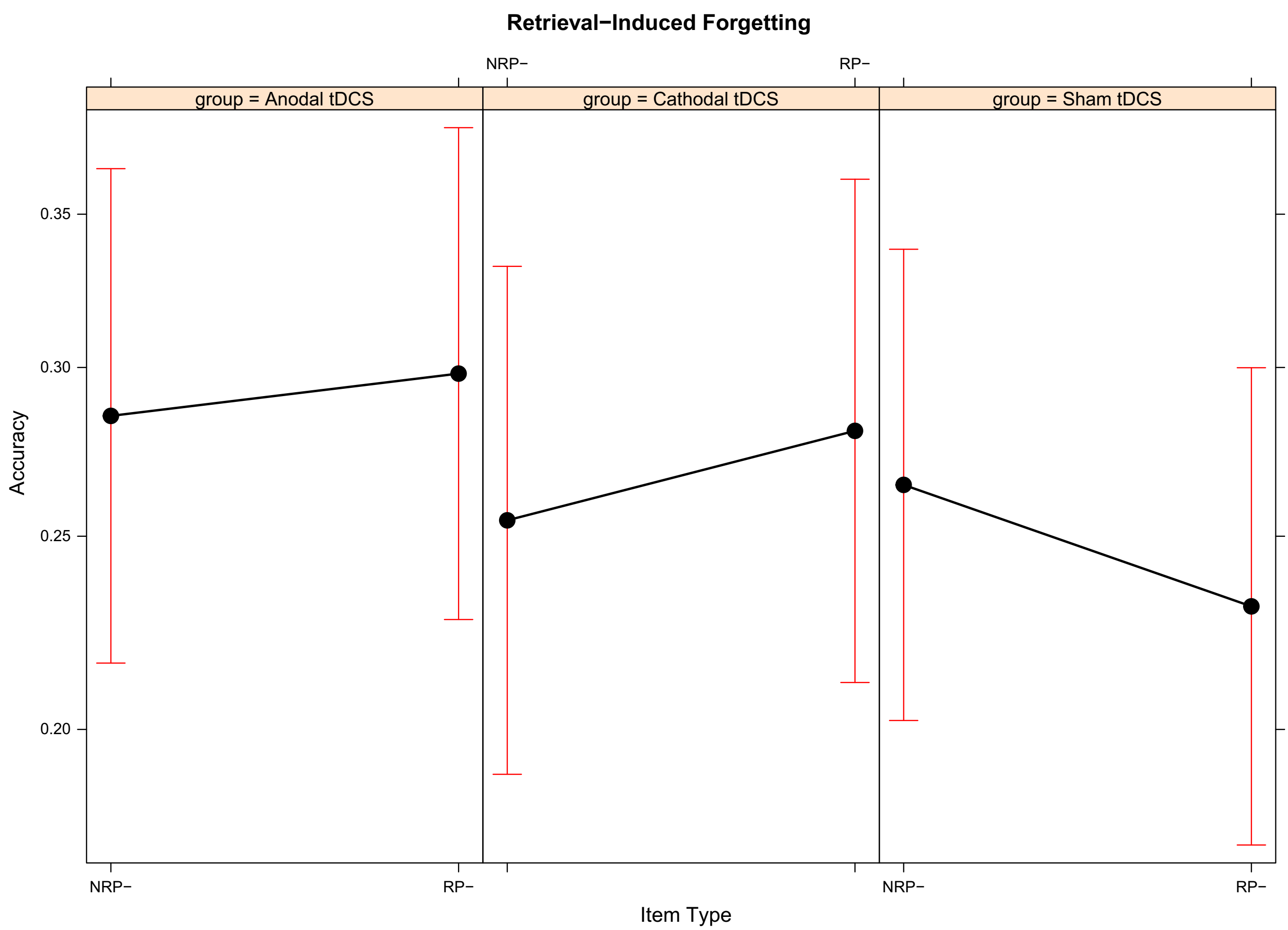

Fig. 2. Interaction plot showing recall accuracy in Experiment 1 as a function of item type in RIF (NRP− vs. RP−) for each stimulation group.

spanning both memory and action; however, they all investigated a single inhibitory measure at a time (see Brevet-Aeby, Brunelin, Iceta, Padovan, & Poulet, 2016, for a review on PFC involvement in inhibitory control as revealed by non-invasive brain stimulation). Moreover, although a few works have investigated the relationship between motor inhibition and suppression of competing memories (e.g., Schilling, Storm, & Anderson, 2014; Storm & Bui, 2016), none of them has implemented tES as a method of concurrent modulations of the two mechanisms, and correlational results have been inconsistent (see also Noreen & MacLeod, 2015). Hence, to further our understanding of tDCS effects over memory and action control, as well as the relationship between the two cognitive mechanisms, in Experiment 2 we first combined multiple behavioural methods typically used for measuring inhibitory control in episodic memory and motor action within a PFC-tDCS study. We tested whether active tDCS over the rIFG would modulate suppression of competing memories, i.e., RIF, compared to sham stimulation, but also affect the ability to override a prepotent motor

Table 3
Mean proportion of recall accuracy in the final test phase of Experiment 2 as a function of item type/effect and stimulation group.

Stimulation group	N	Final test phase																	
		Item type								Effect									
		RP+		NRP+		RP−		NRP−		FAC					RIF				
		M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*95% CI*	g_{av}	*CL*	*M*	*SD*	*95% CI*	g_{av}	*CL*
Sham tDCS	24	0.449	±0.149	0.213	±0.144	0.354	±0.117	0.436	±0.110	0.236	±0.167	0.166, 0.307	1.558	92%	0.082	±0.169	0.011, 0.173	0.698	69%
Anodal tDCS	24	0.447	±0.163	0.227	±0.133	0.385	±0.154	0.408	±0.101	0.220	±0.118	0.170, 0.270	1.430	97%	0.023	±0.140	−0.036, 0.082	0.171	57%
Cathodal tDCS	24	0.447	±0.204	0.185	±0.096	0.354	±0.120	0.366	±0.099	0.262	±0.211	0.173, 0.351	1.589	89%	0.012	±0.130	−0.043, 0.067	0.105	54%

Note. *N*: sample size. *RP+*: practiced items; *RP+* non-practiced items from practiced categories; *RP−*: non-practiced items from practiced categories; *NRP+* and *NRP−*: non-practiced items acting as control for *RP+* and *RP−* items respectively. *FAC*: facilitation effect ((*RP+*)-(*NRP+*)); *RIF*: Retrieval-induced forgetting effect ((*NRP−*)-(*RP−*)). *M*: mean. *SD*: standard deviation. *95% CI*: confidence intervals at 95%. g_{av}: Hedges' g_{av} (absolute values), where 0.20 is considered a small effect, 0.50 a medium effect, and 0.80 a large effect (Cohen, 1988). *CL*: *common language effect size* (McGraw & Wong, 1992), an intuitively understandable statistic derived from Cohen's *d*, expresses the probability than an individual has a higher recall accuracy for one item type than the other. Choice and computation of effect sizes were performed according to recommendations by Lakens (2013, spreadsheet version 3.4).

response, as indexed by SSRTs, because of the importance of this brain region for motor stopping (e.g., Aron et al., 2014; Stramaccia et al., 2015). Concerning the latter hypothesis, we expected to find a better inhibitory performance in the anodal stimulation group, compared to the sham and cathodal stimulation groups, based on results from previous work that investigated the effects of tDCS to the rIFG in the SST (e.g., Ditye et al., 2012; Jacobson et al., 2011; Stramaccia et al., 2015). Finally, we sought to explore the relationship between measures of motor stopping and memory suppression.

3.1. Methods

3.1.1. Participants

The ethical committee for psychological research of the University of Padua approved the study, which was performed in accordance with the principles of the Declaration of Helsinki. All participants, none of which had taken part in the previous experiment, underwent an eligibility screening for the tDCS procedure, and provided written informed consents. With respect to the previous experiment, sample size was increased to 72 healthy volunteers (28 males) aged between 20 and 40 years (*mean age* = 23.57, *SD* = 2.86; *mean years of education* = 17.43, *SD* = 1.28). All participants were screened for possible exclusion criteria identical to Experiment 1.

3.1.2. Retrieval practice paradigm (RPP)

The apparatus was the same as in the previous experiment. There were several changes in the RPP paradigm with respect to that used in Experiment 1. Our revised paradigm included 84 category-exemplar word pairs (e.g. "FRUIT-prune"), divided by 12 semantic categories, with seven exemplars for each category. We reasoned that to observe a stronger RIF in the control group, it would have been better to include more semantic categories with fewer exemplars each, rather than relatively few categories with many exemplars each, because competition under the latter circumstances could be more diluted among the exemplars, and subsequent inhibitory efforts less effective. Moreover, having more exemplars in each category increased the risk of unwanted semantic associations (Goodmon & Anderson, 2011). We selected and adapted all the material from the categorical production norm for the Italian language by Boccardi and Cappa (1997), according to the same criteria used in Experiment 1, with the exception that in all categories, four out of seven items were strong exemplars, whereas the other three items were weak exemplars.

In the study phase, the only change with respect to Experiment 1 was that category-exemplar word pairs were now visible for 3500 ms.

In the practice phase, participants repeatedly practiced the weak exemplars of half the semantic categories (four repetitions of 18 exemplars, 72 trials in total). Also at variance with Experiment 1, in the practice trials, we provided the category and only the first two letters of each exemplar (e.g. "FRUIT-pr____") to the participants. Moreover, the participants were now given 8000 ms to answer with the name of the specific exemplar associated to the particular cue in full. Similar to Experiment 1, four lists of categories were used to fully counterbalance the practiced categories across groups.

In the final test phase, format, response modality, and instructions were the same as in Experiment 1, the only change being that stimuli were now presented with the additional constraint that all RP− and NRP− items came before all the RP+ and NRP+ items. In so doing, we not only controlled for output interference at test, but also prevented the imbalance in the amount of interference received by NRP− items, compared to RP− items, that likely affected the data of Experiment 1 by reducing the chance to observe RIF.

3.1.3. Stop-signal task (SST)

Between the retrieval practice phase and the test phase of the RPP, participants performed the SST provided within the STOP-IT software (Verbruggen, Logan, & Stevens, 2008), which probes the individual efficiency of the covert motor stopping process (i.e., SSRTs). The task begun with a short practice block (32 trials) allowing the participants to familiarize with the task, followed by two experimental blocks of 64 trials each (128 total trials). In the primary task, participants performed a choice reaction time test, with the instruction to prioritize both speed and accuracy of responses. Each trial began with a 250-ms central fixation (+), followed by a visual stimulus (either a circle or a square) that stayed centrally on screen until the participants responded, with the constraint that participants had up to 1250 ms to respond. The central fixation and stimuli were presented in white on a black background. The ISI was 2000 ms, irrespective of RTs. The participants used a keyboard to respond, and they had to press "A" for squares or "L" for circles. On 25% of the trials, shortly after stimulus onset, a sound (750 Hz, 75 ms) signalling to hold back the response (i.e., a stop-signal) was presented through loudspeakers. The stop-signal delay was 250 ms at the beginning of the task, and subsequently increased or decreased by 50 ms after each successful or unsuccessful stopping trial, respectively. Under this tracking procedure, participants correctly withheld approximately half the responses, meeting the requirements of the method used to calculate SSRT. In keeping with the horse-race model (e.g., Logan & Cowan, 1984), SSRT was calculated as the difference between mean RT in the trials where participants must respond and mean SSD in the trials where they must hold back the response.

3.1.4. Transcranial direct current stimulation (tDCS)

The apparatus, stimulation parameters, montages, and overall procedure, were identical to Experiment 1. A single blind, between group design was adopted: The participants were randomly assigned to anodal ($N = 24$, 9 males, *mean age* = 23.96, $SD = 3.74$), cathodal ($N = 24$, 12 males, *mean age* = 23.33, $SD = 2.28$), or sham stimulation ($N = 24$, 7 males, *mean age* = 23.42, $SD = 2.43$). Stimulation begun prior to the practice phase of the RPP, and lasted 20 min in total for all three groups, covering the entire practice phase and the subsequent SST. In the active tDCS conditions, we ramped up the stimulation to 1.5 mA over 30 s, maintained it for 19 min, and ramped it down over 30 s again at the end to minimize unpleasant sensations. In the Sham stimulation group, we ramped up and then immediately ramped down stimulation over 60 s at both the beginning and end of the protocol.

3.2. Procedure

This was the same as in Experiment 1 except that after completing the retrieval practice phase of the RPP, participants performed the SST (see Fig. 1). Stimulation ended shortly before completion of the SST, and the montage was removed before proceeding with the final test phase of the RPP.

3.3. Data analysis

We performed identical treatment and subsequent analysis of RPP data were processed and analysed as in Experiment 1.

As for the SST, to assess whether tDCS selectively modulated motor stopping, individual SSRTs and NSRTs were computed using the ANALYZE-IT software (Verbruggen et al., 2008). With respect to individual SSRTs, ANALYZE-IT computes the mean RTs for all successful go trials and then subtracts the mean stop-signal delay from this value.

3.4. Results

3.4.1. Retrieval practice paradigm (RPP)

Mean proportions of recall in the final test phase for each item type and FAC/RIF effects are reported in Table 3.

For the FAC effect, the type model yielded minimal to strong evidence against the competing models ($AICw_{(type \times group)} = 0.037$, $AICw_{(type+group)} = 0.264$, $AICw_{(type)} = 0.698$; $LER_{(type>type \times group)} = 1.276$, $LER_{(type>type+group)} = 0.422$). The FAC effect was significant in each group, as confirmed by group-wise multiple contrasts as a function of item type (all $ps < 0.0001$):

As for the RIF effect, in contrast with our predictions, the best fitting model was again the one that included only the main effect of item type, which yielded minimal evidence in respect to the alternative models ($AICw_{(type \times group)} = 0.193$, $AICw_{(type+group)} = 0.253$, $AICw_{(type)} = 0.554$; $LER_{(type>type \times group)} = 0.458$, $LER_{(type>type+group)} = 0.340$). Detailed information on the model is reported in Table 4.

Multiple contrasts driven by our initial hypothesis revealed a significant RIF in the Sham tDCS group only ($p = 0.011$, see Fig. 3), whose magnitude was numerically similar to that observed by Penolazzi et al. (2014). Neither the Anodal tDCS, nor the Cathodal tDCS groups exhibited a significant RIF effect (all $ps \geq 0.844$).

As for the correlational analysis, we did not find any evidence for a correlation between FAC and RIF effects across the whole sample ($r < 0.01$, $p > 0.250$).

At a first glance, these results seemed to merely suggest a similar pattern with respect to our previous work (Penolazzi et al., 2014), though with little statistical support behind it. At the same time, it should be noted that, when compared directly, the interac-

Table 4
Results of logistic mixed effects model with recall accuracy from Experiment 2 as dependent variable.

Parameters	Recall accuracy					
	B (SE)	*z*	*p*	Omnibus χ^2	*df*	*p*
Intercept	−0.269 (0.141)	−1.903	0.057			
Item type				5.695	1	<0.01
RP−	−0.356 (0.123)	−2.884	<0.001			
Stimulation group				2.473	2	0.290
Anodal tDCS	−0.120 (0.144)	−0.836	0.403			
Cathodal tDCS	−0.303 (0.144)	−2.096	<0.05			
Interaction				3.458	2	0.178
RP− × Anodal tDCS	0.257 (0.174)	1.475	0.140			
RP− × Cathodal tDCS	0.302 (0.176)	1.716	0.086			

Note: Number of subjects = 72. Number of observations = 3456. Number of semantic categories = 12. *RP−*: non-practiced items from practiced categories. Baseline level for Item Type was *NRP−*. Baseline level for Stimulation Group was *Sham tDCS*. Random effects were Subject and Category. χ^2 values were computed with the "Anova" function in the "car" package (Fox & Weisberg, 2011).

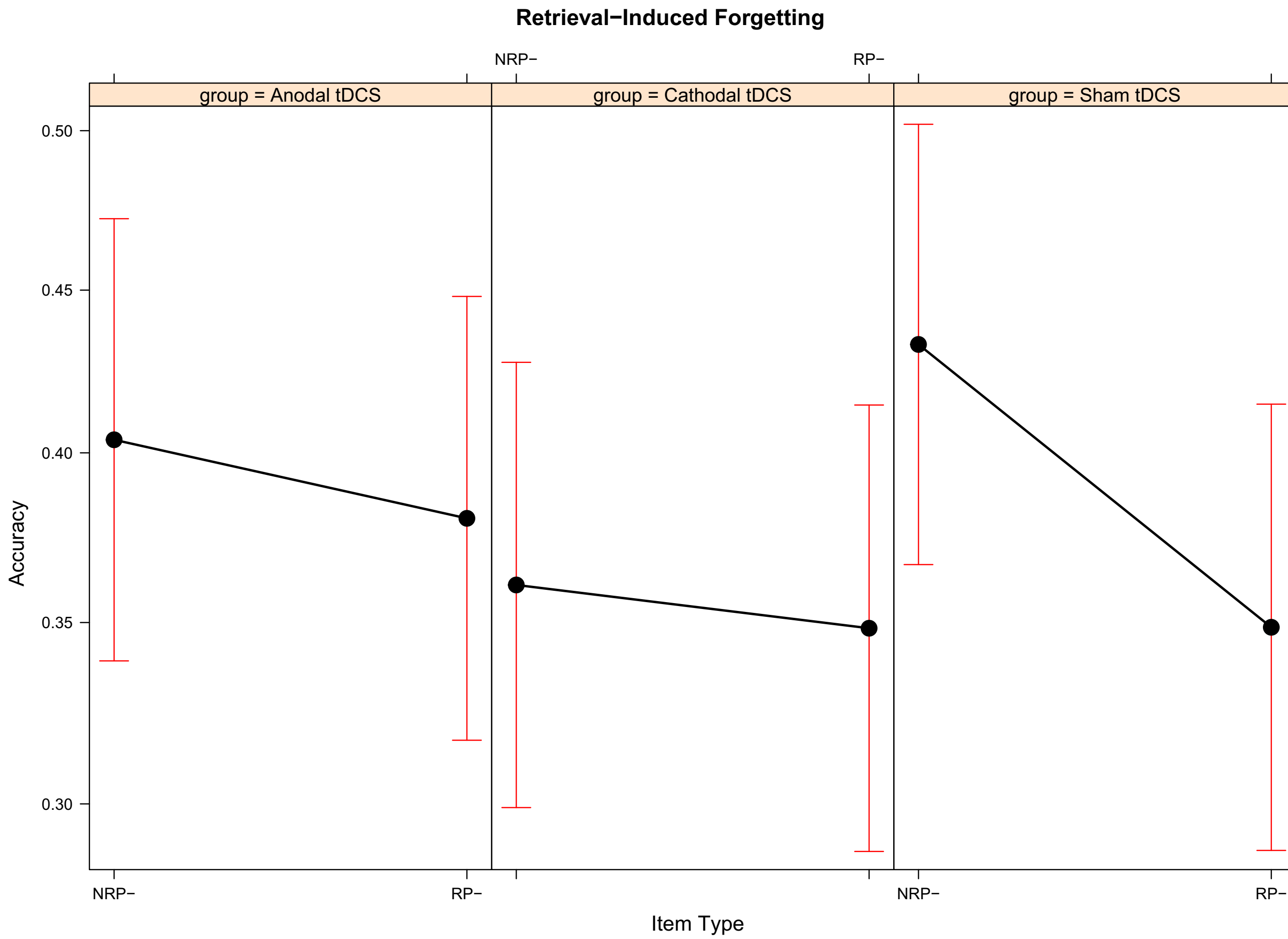

Fig. 3. Interaction plot showing recall accuracy in Experiment 2 as a function of item type in RIF (NRP− vs. RP−) for each stimulation group.

tion model and the main effects model did not show a large difference in *AICw*, as further confirmed by direct model comparisons as revealed by *LERs* values for both the type > type × group and type > type + group comparisons. Interestingly, further visual inspection of the data suggested large differences in the amount of RIF elicited by the different semantic categories employed here. To shed light on the contribution of the individual categories to the overall results, we carried out exploratory analyses aimed at quantifying the amount of evidence in favour of a main effect of item type within each category taken separately in the sham (control) group only, so that additional predicted effects due to the neuromodulatory manipulations could be ruled out.

This procedure revealed that few categories showed a particularly weak or reversed RIF effect in the control group (i.e., "BIRDS", "FLOWERS", "FRUITS", "SPORTS"). Because of that, we performed new model comparisons between the full model (type × group) and the model without interaction (type + group), gradually excluding the categories that showed the least support for the presence of RIF in the control group (hereafter referred to as 'null-RIF' categories), in order to assess whether the inability of these categories to elicit RIF in the control group was responsible for the lack of evidence in support of the interaction model. Surprisingly, removing the two null-RIF categories that showed the least amount of (or even reversed) RIF in the control group (i.e., "SPORTS" and "BIRDS", respectively) improved the amount of RIF in the control group to a magnitude that was unparalleled in the experimental groups, resulting in the new analysis now showing substantial evidence in favouring the type × group model over the type + group model ($AICw_{(\text{type}\times\text{group})} = 0.773$, $AICw_{(\text{type+group})} = 0.227$; $LER_{(\text{type}\times\text{group>type+group})} = 0.532$; see Fig. 4).

In keeping with the same logic, further removal of the two remaining null-RIF categories (i.e., "FLOWERS" and "FRUITS") resulted in the type × group model now yielding strong evidence against the type + group model ($AICw_{(type\times group)} = 0.931$, $AICw_{(type+group)} = 0.069$; $LER_{(\text{type}\times\text{group>type+group})} = 1.130$; see Fig. 5).

It is worth noting that the procedure employed in this additional category-wise influence analysis allowed looking into the contribution of each category to the effect of interest (i.e., RIF) in the control group, and subsequently to the item type × stimulation group interaction, while keeping the random effect of item into account. Because of the valuable information provided by these additional analyses, we decided to reanalyse RPP data from Experiment 1, in order to ascertain whether specific semantic categories had a similar impact on the results, and more specifically whether the same categories behaved similarly across the two experiments.

3.4.2. Re-analysis of Experiment 1 data

We carried out category-wise analyses to assess the contribution of each category to RIF in the control group. These new analyses revealed that different categories impacted differently on RIF in the control group. More specifically, four out of the eight semantic categories employed in the first experiment exhibited none to reversed RIF, with "BIRDS", "FRUITS", "JOBS", and "WEAPONS", being the categories showing the least amount of forgetting for RP− items compared to the NRP−. Interestingly, two of them overlapped with the null-RIF categories detected in the previous

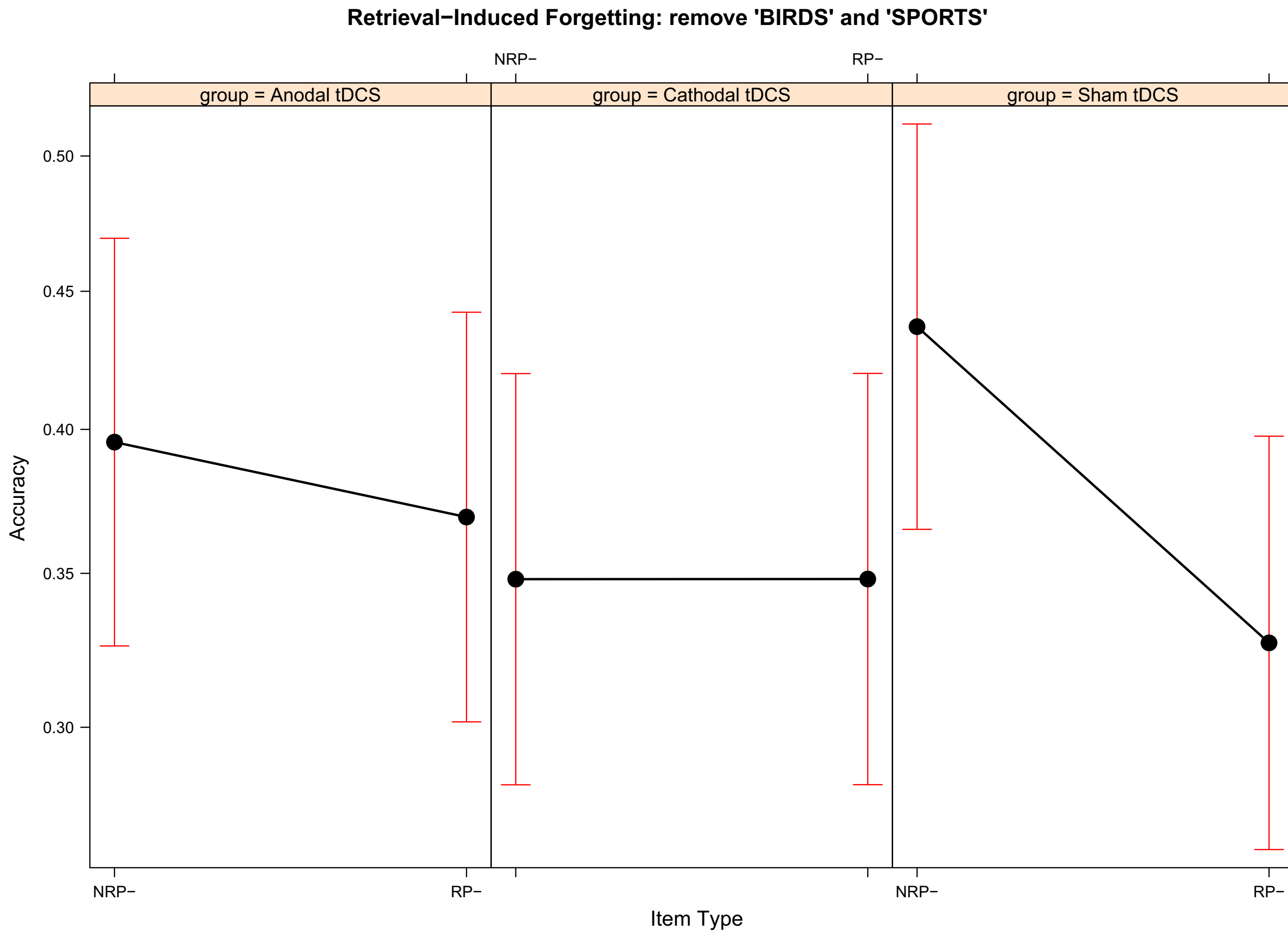

Fig. 4. Interaction plot showing recall accuracy in Experiment 2 as a function of item type in RIF (NRP− vs. RP−) for each stimulation group after removal of "BIRDS" and "SPORTS" categories.

re-ANALYSIS of Experiment 2 (i.e., "BIRDS" and "FRUITS"), although it should be noted that there were some differences in the exemplars contributing to the same category in the two experiments. We then proceeded to compare the interaction model with the main effects model by excluding an increasing number of null-RIF categories. This procedure yielded a pattern that was similar but weaker to that observed in Experiment 2. Indeed, when we removed the two categories that showed the least amount of RIF in the control group (i.e., "BIRDS" and "WEAPONS"), the available evidence favoured the type × group model over the type + group model although by a minimal extent only ($AICw_{(\text{type}\times\text{group})} = 0.517$, $AICw_{(\text{type+group})} = 0.483$; $LER_{(\text{type}\times\text{group}>\text{type+group})} = 0.053$; see Fig. 6).

Further excision of the remaining null-RIF categories (i.e., "FRUITS" and "JOBS") yielded an increase in the evidence, though still minimal, in favour of the type×group model over the type + group model ($AICw_{(type\times group)} = 0.629$, $AICw_{(type+group)} = 0.371$; $LER_{(\text{type}\times\text{group}>\text{type+group})} = 0.229$; see Fig. 7).

Once again, the interaction was mainly dependent on the increased RIF observed in the control group, whereas removing the categories yielding no RIF did not affect RIF in the stimulated groups as much as in the sham group.

3.4.3. Stop-signal task (SST)

Data from one participant in Cathodal tDCS group were discarded because of a technical failure of the software. No differences were found between groups for either SSRTs, $F_{(2,68)} = 1.13$, $p > 0.250$ ($M_{SHAM\text{-}SSRT} = 286.025$, $SD_{SHAM\text{-}SSRT} = 38.906$; $M_{ANODAL\text{-}SSRT} = 287.186$, $SD_{ANODAL\text{-}SSRT} = 47.616$; $M_{CATHODAL\text{-}SSRT} = 269.370$, $SD_{CATHODAL\text{-}SSRT} = 48.851$), or NSRTs, $F_{(2,68)} = 0.03$, $p > 0.250$ ($M_{SHAM\text{-}NSRT} = 564.688$, $SD_{SHAM\text{-}NSRT} = 148.073$; $M_{ANODAL\text{-}NSRT} = 566.913$, $SD_{ANODAL\text{-}NSRT} = 131.117$; $M_{CATHODAL\text{-}NSRT} = 567.861$, $SD_{CATHODAL\text{-}NSRT} = 132.007$). The correlation between SSRTs and RIF was not significant (all $ps > 0.05$) neither across the whole sample ($r = 0.038$) nor in each group separately ($r_{SHAM} = 0.124$, $r_{ANODAL} = -0.266$, $r_{CATHODAL} = 0.211$).

3.5. Discussion

The results from Experiment 2 closely resembled the pattern reported by Penolazzi et al. (2014). In particular, constraining the analysis to the subset of the experimental material that better expressed RIF in the control group yielded results that were highly similar to those reported by Penolazzi et al. (2014), even though the detrimental effect of tDCS on the cathodal group was not as strong as in that study. There are several reasons that support the rationale for looking at category-specific patterns in our data. In particular, possible different baseline levels of relevant psycholinguistic variables such as memorability and imageability, might have very well led to various degree of uncontrolled semantic integration (Goodmon & Anderson, 2011) whose effects would not just be ruled out by counterbalancing the categories across participants and groups, and which may have partially jeopardized our attempt to separate high- from low-interfering exemplars. These features may have the potential to specifically affect the

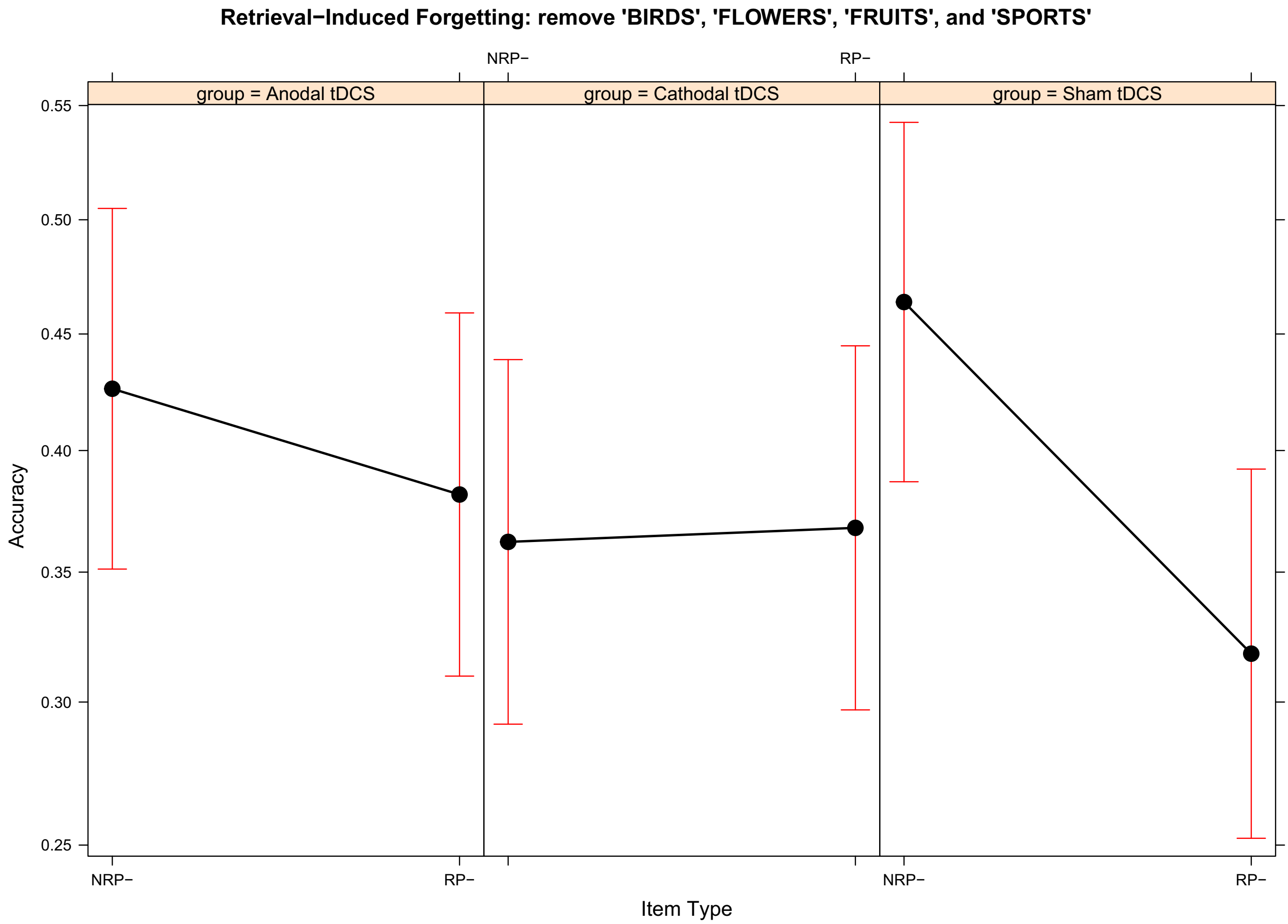

Fig. 5. Interaction plot showing recall accuracy in Experiment 2 as a function of item type in RIF (NRP− vs. RP−) for each stimulation group after removal of "BIRDS", "FLOWERS", "FRUITS", and "SPORTS" categories.

amount of forgetting due to competition resolution (i.e., RIF), while not affecting the magnitude of the benefit from additional study (i.e., FAC) at all. Critical to our argument, across the new analyses the control group steadily constituted the main drive behind the interaction, showing a gradual increase in the detected RIF effect as we removed more "negative" categories, whose magnitude was not mirrored in the stimulation groups. Interestingly enough, there was some overlapping between the categories that negatively affected RIF (in the control group considered in isolation) in Experiment 1 and 2. For example, "BIRDS" consistently showed a reversed RIF pattern, with higher recall for RP− than NRP− items. Unfortunately, indexes pertaining the specific features of the semantic categories that we hypothesized may have had a negative impact on RIF in the control group were not readily available to us, therefore we cannot directly quantify the potential contributions of these factors toward the observed pattern of results.

Turning to the results concerning the motor stopping task, Experiment 2 failed to show any difference of modulation as a function of tDCS, as opposed to what has been reported by previous studies (e.g., Cunillera, Fuentemilla, Brignani, Cucurell, & Miniussi, 2014; Jacobson et al., 2011; Stramaccia et al., 2015). Moreover, we did not find a correlation between the individual ability to suppress competing memories as indexed by RIF, and the individual efficiency of the motor stopping process as indexed by SSRTs. We will address these null findings in the following section.

4. General discussion

In recent years, non-invasive brain stimulation has been extensively applied to investigate various aspects of memory (e.g., Manenti, Cotelli, Robertson, & Miniussi, 2012; Sandrini, Cohen, & Censor, 2015; Smirni, Turriziani, Mangano, Cipolotti, & Oliveri, 2015). However, in sharp contrast, only a handful of studies examined the potential of tDCS to modulate behavioural performance in tasks addressing memory control, i.e., the ability to exert cognitive control to overcome interference from competing memory traces during memory retrieval (e.g., Anderson, Davis, Fitzgerald, & Hoy, 2015; Penolazzi et al., 2014; see also Oldrati, Patricelli, Colombo, & Antonietti, 2016, and Silas & Brandt, 2016, for relevant results in different but related domains). In particular, the emerging pattern from this relatively scarce literature points to consistent, detrimental effects of prefrontal cathodal tDCS on suppression of competing memories and related abilities, across a range of slightly different stimulation parameters. In this view, our study presents a set of findings that support this prefrontal cathodal tDCS impairing effect, with a varying degree of generalizability of our results across the two experiments. Specifically, we delivered anodal, cathodal, or sham (control) tDCS to healthy volunteers in order to modulate memory control as indexed by RIF, which reflects the negative effects of selective memory retrieval in the face of competition on subsequent recall of competing memory traces.

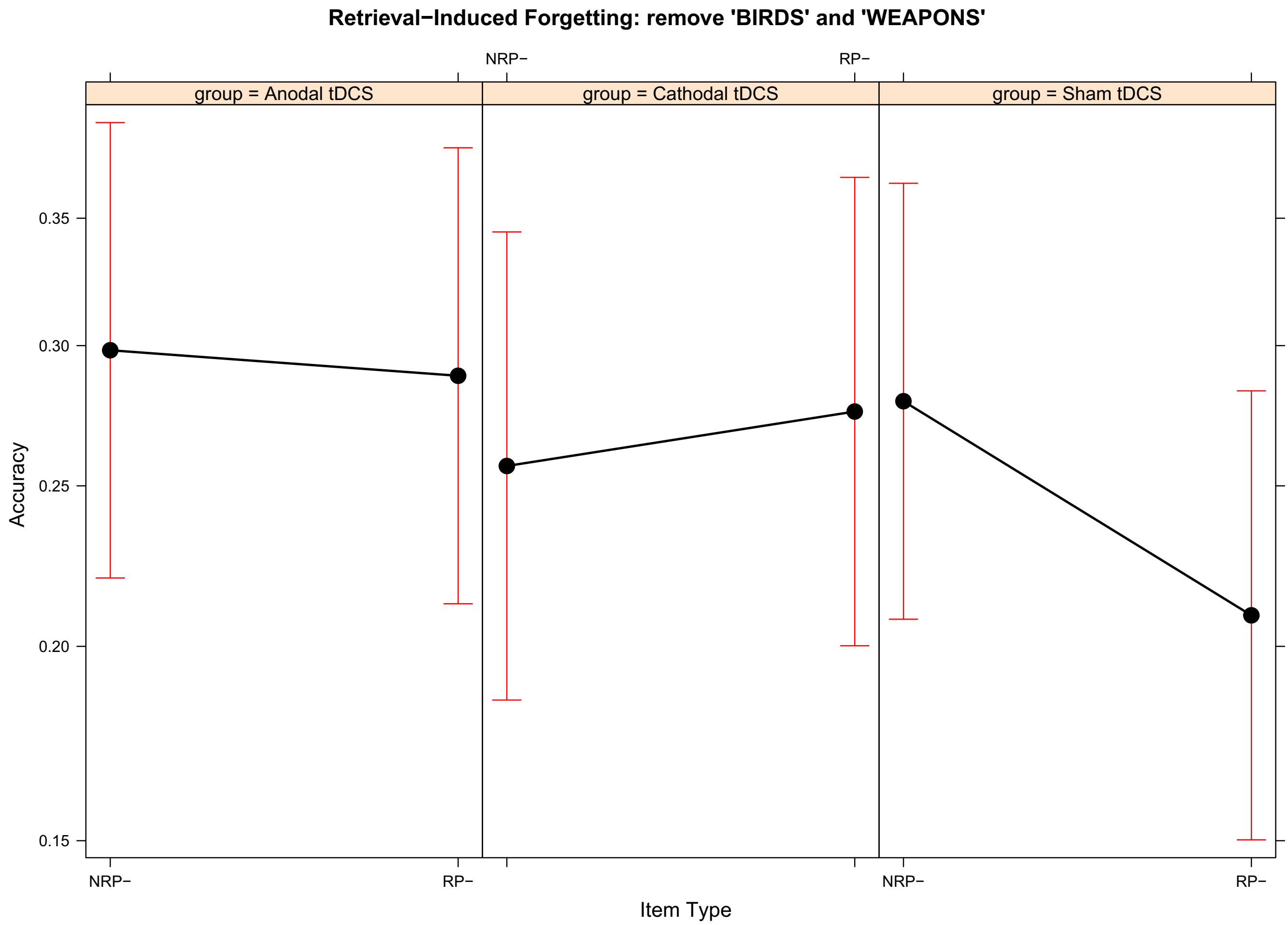

Fig. 6. Interaction plot showing recall accuracy in Experiment 1 as a function of item type in RIF (NRP– vs. RP–) for each stimulation group after removal of "BIRDS" and "WEAPONS" categories.

Inhibitory processing underlying RIF has been associated to a range of abilities closely tied to our wellbeing and cognitive efficiency, ranging from working memory to creative problem solving (Nørby, 2015; Storm, 2011). Therefore, it is important to note that it has been found to be impaired in a broad range of disorders traditionally characterized by impulsivity, worry, or rumination (e.g., in obsessive–compulsive disorder, Demeter, Keresztes, Harsányi, Csigó, & Racsmány, 2014; in clinical depression, Groome & Sterkaj, 2010; in schizophrenia, Soriano, Jiménez, Román, & Bajo, 2009; in ADHD, Storm & White, 2010; in substance-related disorders, Stramaccia, Penolazzi, Monego, et al., 2017; in Anorexia Nervosa, Stramaccia, Penolazzi, Libardi, et al., 2017), where alterations of PFC functioning have also been reported. For this reason, there is a great interest in identifying the neural underpinnings of RIF, as well as developing effective strategies to modulate their activity, and clarifying the relationship of the phenomenon with other expressions of cognitive control in different domains.

The tDCS procedure employed here targeted the rIFG, a key area in the brain network deputed to inhibitory control (e.g., Aron et al., 2014), whose activity during the inhibitory effort in the RPP has been associated with the amount of RIF in previous neuroimaging studies (Wimber et al., 2008, 2009, 2015). Across two experiments that followed a similar rationale, results indicated that cathodal tDCS had the highest, detrimental impact on memory control. On the one hand, our work provided causal evidence for the involvement of the rIFG in this ability, and confirmed the feasibility of tDCS modulation of RIF. On the other hand, future research efforts should aim at identifying stimulation parameters that improve cognitive control over interference, which would yield a relevant applied potential.

4.1. rIFG supports control over interference during memory retrieval

Numerous findings from past studies that investigated RIF with neuroimaging techniques revealed a strong association between activity in the PFC and the ability to overcome interference from competing memory traces (e.g., Wimber et al., 2008, 2009, 2011, 2015), as indexed by RIF through the RPP. In particular, the right DLPFC and IFG appear to be candidate brain regions for a primary role in supporting the cognitive mechanisms underlying RIF. This notion is also supported by neuroimaging and non-invasive brain stimulation studies that investigated putatively similar cognitive processes (e.g., Hanslmayr et al., 2012; Oldrati et al., 2016; Silas & Brandt, 2016). Whereas previous brain stimulation studies were focused on the role of the right DLPFC (Anderson et al., 2015; Penolazzi et al., 2014), the necessity of right IFG remained to be established. Across the two experiments presented here we demonstrated that perturbing the activity of the rIFG is sufficient to weaken memory control over competing memories. Specifically, in these experiments we delivered anodal, cathodal, or sham tDCS to healthy volunteers in a between-participants design, while they engaged in repeated selective retrieval of target items in the retrieval practice phase of the RPP. Overall, this manipulation selectively impaired RIF in one condition, whereas FAC was unaffected by tDCS. In particular, cathodal stimulation had the highest detrimental effects on memory control performance. Importantly, the disso-

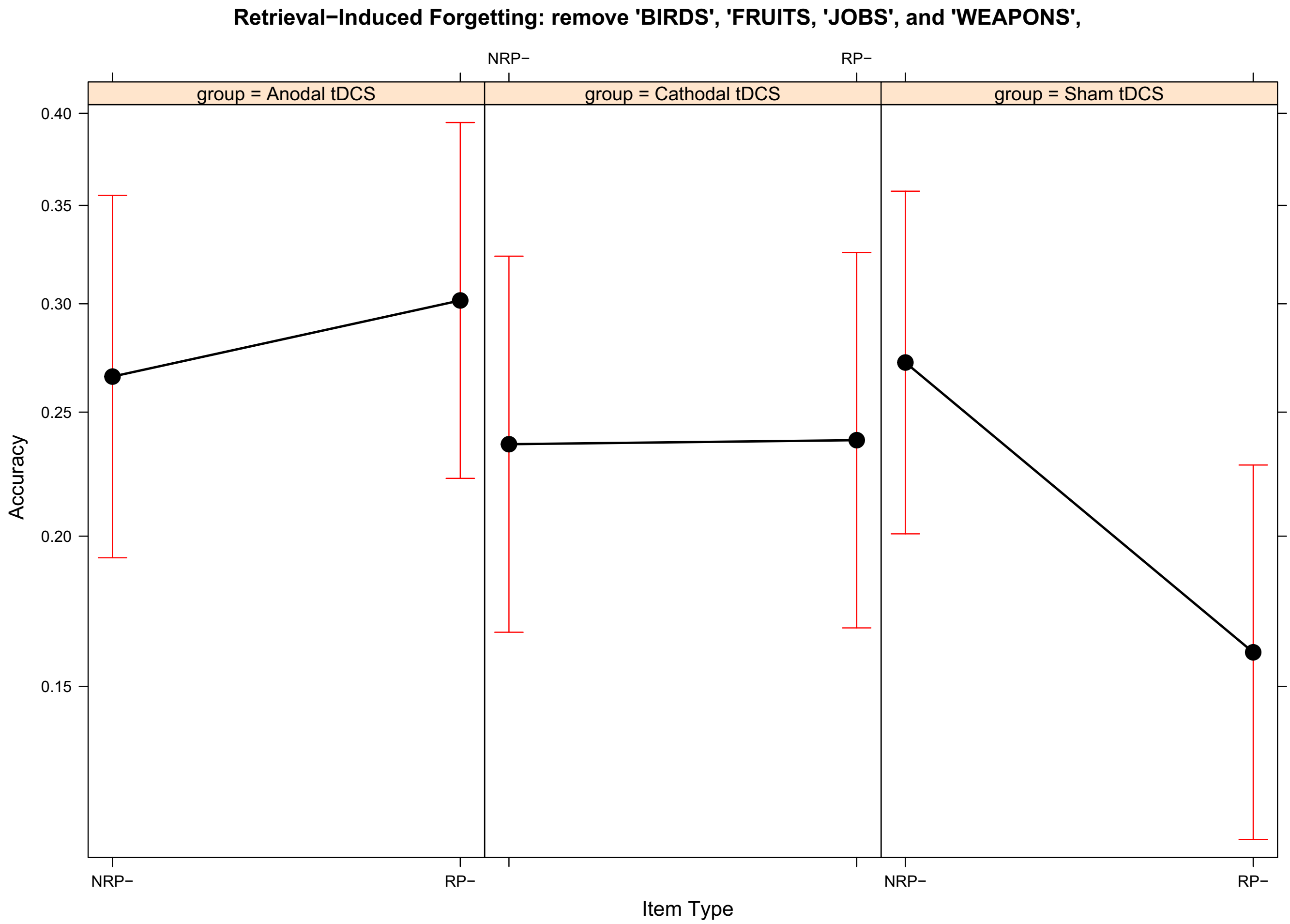

Fig. 7. Interaction plot showing recall accuracy in Experiment 1 as a function of item type in RIF (NRP− vs. RP−) for each stimulation group after removal of "BIRDS", "FRUITS", "JOBS", and "WEAPONS" categories.

ciation between tDCS effects on RIF and FAC suggests that the two measures may have different underlying cognitive mechanisms, thereby appearing mostly consistent with the inhibitory account of RIF (e.g., Anderson, 2003). These results are at odds with alternative theoretical models based on associative interference (e.g., Mensink & Raaijmakers, 1988), which posit the two phenomena to be directly proportional, and also computational modelling work on RIF (Norman, Newman, & Detre, 2007), which excluded a PFC contribution to the phenomenon. Future research could further clarify these results by employing a multi-method approach combining non-invasive brain stimulation with neuroimaging techniques (e.g., Venkatakrishnan & Sandrini, 2012), which would allow for a more refined characterization of tDCS effects elicited by anodal and cathodal stimulation on memory control. Importantly, future studies will also need to include different stimulation sites in order to test the specificity of the contribution of the right PFC in the genesis of RIF, and whether other areas outside the right PFC known for their involvement in memory control can also be modulated by tDCS.

4.2. RIF is variable across different semantic categories

Here we introduced an approach to analysis of RPP data that is rather different from the rationale typically employed in the literature (i.e. analysis of accuracy as percentage of correct answers). Specifically, after separating FAC- and RIF-relevant items, we fitted logistic mixed effects models using the glmer procedure in the lme4 package (Bates et al., 2015), with recall accuracy as our main dependent binary valuable. This particular approach is better suited at analysing accuracy data (and nowadays computationally feasible) in respect to repeated measures ANOVA (e.g., Jaeger, 2008), and allows to account for both participant- and item-related variability, the latter being particularly relevant when employing linguistic stimuli (e.g., Clark, 1973). The use of AIC weights (Wagenmakers & Farrell, 2004) to select the most informative models throughout the analysis has the additional advantage of enabling to explore and quantify the contribution of each individual semantic category to RIF in the control group, which we took advantage of when visual inspection of the data hinted at the possibility of category-specific patterns in RIF. As a matter of fact, we discovered a large variability in the amount of RIF associated to each semantic category in Experiment 1, where about half categories did not show any RIF at all, and a smaller but relevant variability in Experiment 2, with fewer categories displaying null or negative RIF in the control group. Because our experimental hypothesis concerned the presence of an interaction between stimulation with tDCS and item type, we gradually excluded categories from the analysis on the basis of their contribution to RIF in the control group, as looking at the impact on the interaction would have been recursive (i.e., we would have just discarded data that did not fit with our hypothesis). Crucially, removing these categories also substantially improved the interaction, as the increase in RIF in the control group was not mirrored by an increase of similar magnitude in the stimulated groups. In particular, the cathodal tDCS group consistently displayed the smallest amount of RIF.[1]

A number of considerations support the rationale of formulating hypotheses about category-specific effects in RPP data. For instance, it is possible that different categories display large variability in a number of psycholinguistic dimensions of their constituting exemplars (such as concreteness, imageability, memorability, and similarity, see Bäuml & Hartinger, 2002), that could interact with RIF. This, in turn, could also lead to varying degrees of semantic integration (Goodmon & Anderson, 2011), which is generally detrimental to RIF. Because our experiments, consistent with the vast majority of RIF studies, were designed to control for many other linguistic and semantic variables (see Method sections), we cannot fully rule out the possibility that all of these other psycholinguistic dimensions may have entered the experimental material and contributed in shaping the results. Nevertheless, future studies should take advantage of the category-wise analytical procedure presented here in order to better clarify how specific groupings of stimuli along defined features may moderate suppression of competing memories. It is worth noting that the semantic categories that showed the least amount of RIF in Experiment 1 were not fully overlapping with the problematic categories detected in Experiment 2, although one category in particular (i.e., "BIRDS") seemed to detrimentally affect RIF in the control group across the two experiments. This finding may imply that along with the linguistic features of the categories, certain characteristics pertaining to participants may also interact with the different semantic categories, and they should also be explored as possible moderators of RIF (e.g., pre-existing specific knowledge in a given category domain, which may promote integration).

Importantly, this approach to data analysis which takes into account category-specific effects could also benefit related studies aimed at uncovering memory biases for specific stimuli, i.e., stimuli relevant to a particular disorder (e.g., Kircanski, Johnson, Mateen, Björk, & Gotlib, 2016), and hence enrich the knowledge about memory functioning from both a theoretical and a methodological perspective. Findings from the present exploratory approach may therefore represent the focus of future studies, aiming at replicating and extending our results, before any firm conclusions can be drawn.

4.3. Memory control and motor stopping

The inclusion of a measure of motor stopping ability was a remarkable feature of Experiment 2, because, to the best of our knowledge, no other study so far has attempted to manipulate cognitive control in both action and memory with tES. Along with the two experiments reported here, past work hinted at the possibility to modulate control over interfering memories (Anderson et al., 2015; Penolazzi et al., 2014) or performance in putatively related task (Oldrati et al., 2016; Silas & Brandt, 2016), as well as motor stopping (e.g., Jacobson et al., 2011; Stramaccia et al., 2015), by delivering tDCS to the PFC. Indeed, neuroimaging and neuromodulation studies provided converging evidence for an involvement of similar brain areas in memory control and motor stopping, with regions within the PFC such as the DLPFC and the IFG putatively assuming a leading role in inhibitory control (e.g., for studies on memory control, Anderson, Bunce, & Barbas, 2015; Hanslmayr et al., 2012; Wimber et al., 2008, 2009, 2011; for motor stopping, Chevrier, Noseworthy, & Schachar, 2007; Jacobson et al., 2011; Li, Huang, Constable, & Sinha, 2006; see also Aron et al., 2014, for a review on evidence suggesting a primary role of the IFG in cognitive control over different cognitive domains). These relatively segregated lines of research support the notion that the two abilities may share similar neural underpinnings and cognitive mechanisms (e.g., Levy & Anderson, 2002). Indeed, according to some Authors, the memory control and motor stopping may constitute different but interrelated instances of inhibitory control (Levy & Anderson, 2002; Schilling et al., 2014). Within this perspective, we included the SST in Experiment 2, with two main objectives: (i) We sought to test the association between RIF and SSRTs, because of the mixed results provided so far by the literature concerning the positive relationship between memory control and motor stopping (Schilling et al., 2014; Storm & Bui, 2016); (ii) We expected to replicate the anodal rIFG-tDCS modulation on motor stopping, specifically showing a reduction in SSRTs that would have indicated a speeding-up of the underlying stopping process, as first shown by Jacobson et al. (2011) and then replicated in subsequent studies with different experimental conditions (e.g., Cunillera et al., 2014; Stramaccia et al., 2015).

Concerning the former objective, we did not find any significant correlation between RIF and SSRTs, consistent with the data recently reported by Storm and Bui (2016). Failures to find a positive association between different measures of cognitive inhibition is not new in the literature (e.g., Noreen & MacLeod, 2015), and calls for further studies employing behavioural paradigms that are maximally informative with respect to the theoretical debate between the inhibitory account of phenomena such as RIF and other explanatory proposals based on different mechanisms (e.g., by competition at test; see Raaijmakers & Jakab, 2013). To better illustrate this point, it is worth noting that recent work suggested that when recall performance in the final test of the RPP is probed by category-plus-one-letter-stem cued recall tests, interference may still contribute the amount of observed RIF (e.g., Rupprecht & Bäuml, 2016), whereas recognition tests may be better suited at detecting the amount of forgetting that could be genuinely ascribed to inhibitory mechanisms.

Regarding the latter objective of Experiment 2, no differences in SSRTs emerged as a function of group. While being at odds with the aforementioned studies (e.g., Jacobson et al., 2011), at least two accounts may reconcile our finding with the available evidence in the literature. On the one hand, one may hypothesize that anodal rIFG-tDCS may still have exerted an effect. For example, Cunillera, Brignani, Cucurell, Fuentemilla, and Miniussi (2016), observed prefrontal tDCS effects on electroencephalographic corre-

[1] As an alternative way of selecting null-RIF categories, we carried out additional analyses in which we selected semantic categories that displayed poor/null RIF across all participants, rather than in the Sham tDCS group only. Indeed, it could be argued that while the latter procedure has necessarily higher chances to improve RIF in this specific group, as compared to the Anodal tDCS and Cathodal tDCS groups (which could, in turn, increase the chances of observing higher evidence for an interaction), this however introduces a systematic bias in the data. Removing categories showing null evidence of RIF across the whole sample of participants, on the other hand, is a more bias-free approach but it is likely bound to remove most of the effects of our experimental manipulation from the Anodal tDCS and Cathodal tDCS groups, especially since we predicted a reduction of RIF (for the Cathodal tDCS group in particular) based on the results reported by Penolazzi et al. (2014). In the novel analytical approach, we estimated the full interactive model for both Experiment 1 and Experiment 2 after having removed null-RIF categories selected for their poor performance across the whole samples. In both cases, we observed a 50% overlap between null-RIF categories selected according to this alternative criterion and null-RIF categories reported in results sections (i.e., for Experiment 1 we removed "WEAPONS", "BIRDS", "CLOTHES", and "INSECTS", rather than "BIRDS", "WEAPONS", "JOBS", and "FRUITS" as reported in the results section, whereas for Experiment 2 we removed "FRUITS", "FISHES", "MUSICAL INSTRUMENTS", and "BIRDS", rather than "BIRDS" "FLOWERS", "FRUITS", and "SPORTS"). For Experiment 1, multiple contrasts revealed a pattern that closely resembled that reported by Penolazzi et al. (2014), with 0.084, 0.065, and −0.007 RIF magnitude for the Sham tDCS, Anodal tDCS, and Cathodal tDCS groups respectively, with $p = 0.09$ for RIF in the Sham tDCS group (all $ps < 0.05$ in the other groups). For Experiment 2, the same approach yielded a 0.129, 0.045, and 0.051 RIF magnitude for the Sham tDCS, Anodal tDCS, and Cathodal tDCS group respectively, with $p < 0.001$ for RIF in the Sham tDCS group (all $ps < 0.05$ in the other groups). Therefore, this novel approach suggested the presence of a RIF effect in the Sham tDCS group, and a reduced or null RIF in the Anodal tDCS and Cathodal tDCS groups respectively, across the two experiments, confirming the pattern reported in the results section.

lates of motor stopping, but failed to induce a behavioural modulation as concerns SSRTs. Because we did not collect concomitant measures of neural activity on our study, we cannot rule out that our manipulation induced differences that were not detected behaviourally. Similarly, a recent study from a different research group failed to observe any significant effect of anodal stimulation of the inferior frontal cortex over a different, but nonetheless widely used, task of behavioural inhibition, i.e., the go/no-go task (Dambacher et al., 2015). It is worth noting that both studies (Cunillera et al., 2016; Dambacher et al., 2015) employed a bilateral tDCS montage, as opposed to a fronto-polar montage such as the one used in Jacobson and colleagues' study (2011) to first modulate SST performance with tDCS, indicating that variables strictly related to stimulation parameters may play an important role in determining the behavioural effects. A second possibility to account for the present lack of behavioural effects, is that in the present study, unlike Jacobson et al. (2011) and Stramaccia et al. (2015), tDCS was administered online. Hence, we cannot rule out the possibility that we observed no effects because there might be variations in the time tDCS needs to produce effects detectable at the behavioural level (e.g., Penolazzi, Pastore, & Mondini, 2013).

To sum up, additional research integrating both neuroimaging and n euromodulatory techniques is needed to assess which one of the many tES protocols applied to modulation of motor stopping so far yields the highest consistency between behavioural and neural measures of the relevant outcomes, and also importantly why protocols targeting a similar area (i.e., rIFG) but employing different stimulation parameters (polarity, duration, intensity, etc.) produce different results (e.g., Sarkis, Kaur, & Camprodon, 2014).

5. Conclusions

The current study presented two experiments that overall provided evidence for a role of the rIFG in cognitive control over interfering memory traces as indexed by RIF. In particular, RIF was maximally reduced in the cathodal stimulation groups across the two experiments. However, the investigation of the relationship between RIF and cognitive control over prepotent motor responses, as well as the opportunity to jointly modulate the two abilities with tDCS, yielded inconclusive results. In this light, the main merits of the study are extending to the rIFG the ability of cathodal tDCS to affect RIF (as previously shown for cathodal rDLPFC stimulation by Penolazzi et al., 2014). This finding strengthens the notion that tDCS can be effectively used to modulate cognitive control, and raises new research questions worthy of future research efforts, especially concerning the development of stimulation protocols that may induce enhancement of memory control abilities, rather than disruption, which could in turn inform novel neurorehabilitative approaches to cognitive control impairments based on non-invasive electrical stimulation. Finally, the present study highlights the importance of adopting a data analysis approach taking into full account category-specific effects, which can heavily affect the results and allowing for a more fine-grained perspective on memory functioning.

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