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Cathodal Electrical Stimulation of Frontoparietal Cortex Disrupts Statistical Learning of Visual Configural Information

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Abstract

Attentional performance is facilitated by exploiting regularities and redundancies in the environment by way of incidental statistical learning. For example, during visual search, response times to a target are reduced by repeating distractor configurations – a phenomenon known as contextual cueing (Chun & Jiang, 1998). A range of neuroscientific methods have provided evidence that incidental statistical learning relies on subcortical neural structures associated with long-term memory, such as the hippocampus. Functional neuroimaging studies have also implicated the prefrontal cortex (PFC) and posterior parietal cortex (PPC) in contextual cueing. However, the extent to which these cortical regions are causally involved in statistical learning remains unclear. Here, we delivered anodal, cathodal, or sham transcranial direct current stimulation (tDCS) to the left PFC and left PPC online while participants performed a contextual cueing task. Cathodal stimulation of both PFC and PPC disrupted the early cueing effect, relative to sham and anodal stimulation. These findings causally implicate frontoparietal regions in incidental statistical learning that acts on visual configural information. We speculate that contextual cueing may rely on the availability of cognitive control resources in frontal and parietal regions.

Significance Statement

Recent non-invasive brain stimulation studies have provided causal evidence that the prefrontal cortex is involved in learning, decision-making, and the effects of training on performance (Filmer, Mattingley, & Dux, 2013a; Filmer, Mattingley, Marois, & Dux, 2013b; Filmer, Varghese, Hawkins, Mattingley, & Dux, 2016). This work relates to explicit forms of learning that involve goal directed behaviours or instructed training. Incidental statistical learning describes the process of adapting to regularities in the environment in an automatic manner, without instruction (Goujon, Didierjean, & Thorpe, 2015). The current study demonstrates that frontal and parietal brain regions are also causally involved in a form of incidental statistical learning that influences attentional performance.

Key Words

Contextual Cueing; Statistical Learning; Incidental Learning; tDCS

1.0 Introduction

Learning refers to a change in behaviour that occurs over time. There is converging evidence from neuroanatomical, neuroimaging, and lesion methodologies to show that the prefrontal cortex (PFC) is a critical neural substrate for many high-level functions that support advanced skill acquisition (e.g., when learning a language or musical instrument; Fuster, 2001). The PFC is also recruited for more basic forms of learning, such as when associating a visual stimulus with a particular button-press response (Fuster, 2001). Recent work using the non-invasive brain stimulation technique, transcranial direct current stimulation (tDCS), has begun to provide causal evidence regarding the prefrontal locus of learning and the effects of training on performance (Filmer et al., 2016; Filmer, Mattingley, & Dux, 2013a; Filmer, Mattingley, Marois, & Dux, 2013b). Yet it remains unclear whether other forms of learning that are believed to operate in a more automatic and incidental manner may also be modulated by brain stimulation.

During tDCS a subthreshold electrical current is passed from two electrodes – one anode and one cathode – through the scalp, and the resulting electric field is used to modulate neural activity. At the microscopic level, tDCS is believed to modulate cell membrane potentials. Anodal currents typically shift activity towards depolarization, whereas cathodal currents lead to hyperpolarization and a shift toward reduced overall activity (Bindman, Lippold, & Redfearn, 1964; Filmer, Dux, & Mattingley, 2014). While this polarity-dependent dichotomy appears to hold for stimulation targeting the motor cortex (Nitsche & Paulus, 2000; 2001; Rosenkranz, Nitsche, Tergau, & Paulus, 2000), tDCS induced changes to larger neural circuits are more complicated. In these cases tDCS effects depend on the stimulation parameters used (Bestmann, de Berker, & Bonaiuto, 2015); namely duration and intensity (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013) but also whether or not it is paired with a concurrent task. For this reason, attempts to predict the direction of behavioural changes can be challenging. Nevertheless, by exploiting the capacity of tDCS to exert a bi-directional influence on a neural system, one can perturb a target region and explore the resulting influence on measured behaviour.

Previous research has predominantly examined explicit or intentional forms of learning. These are cases where participants are aware that information must be retained for later use (e.g., specific items or response mappings). Under such conditions tDCS to functional regions has been shown to influence both the time course and outcomes of learning. For example, in language learning tasks, online anodal and bilateral tDCS to temporal regions increased the rate of acquisition and led to more successful outcomes (Boggio et al., 2009; Flöel, Rösser, Michka, Knecht, & Breitenstein, 2008). In a concealed-object detection task, anodal tDCS delivered to the right inferior frontal cortex or the right posterior parietal cortex (PPC) also increased the learning rate and improved overall performance, compared to sham and to a lower intensity control (Clark et al., 2012). Conversely, Filmer et al. (2013b) found that the typical performance gains produced by sensory-motor training were disrupted by offline tDCS to the left PFC. This occurred for both anodal and cathodal stimulation, compared to an active control region (right PFC) and to sham (Filmer et al., 2013b). Using computational modelling, these authors also demonstrated that stimulating the left PFC during training influenced the efficiency of information processing for decision-making (Filmer et al., 2016), or put differently, the rate of evidence accumulation as formally characterised using the Linear Ballistic Accumulator model (Brown & Heathcote, 2008). In the context of evidence accumulation models of choice behaviour, decision-making refers to the process of selecting an outcome from a given set of alternatives based on the available evidence (Gold & Shadlen, 2007). Unlike the mechanisms that support sensory input or motor output, which are largely immediate, decisions evolve over time (Forstmann, Ratcliff, & Wagenmakers, 2016) by repeatedly sampling evidence from a stimulus and accruing information towards a given outcome until an internal decision threshold is reached (Ratcliff & Rouder, 1998).

While this work is important for understanding brain regions that support intentional learning, much of knowledge and skill acquisition occurs in an incidental manner by way of adapting to statistical regularities in the environment (Goujon et al., 2015; Perruchet & Pacton, 2006). Indeed, this notion of prediction leading to the optimization of cognition is central to the Bayesian brain hypothesis and the free energy principle (Friston, 2010). When learning about the environment in this way, some work has proposed that cognitive control mechanisms, supported by the PFC, preference certain aspects of learning at the expense of others (Thompson-Schill, Ramscar, & Chrysikou, 2009). This has been demonstrated in the domains of language categorization (Lupyan, Mirman, Hamilton, & Thompson-Schill, 2012) and creativity (Chrysikou et al., 2013) where disrupting PFC function, via cathodal stimulation (but see discussion above regarding enhancement/inhibition in tDCS), benefited the incidental components of learning. Thus, contrary to the work of Filmer et al. (2013) on explicit sensory-motor learning, this line of work suggests that PFC involvement impairs learning (we return to this issue in the discussion). Nevertheless, collectively, the aforementioned work highlights the critical role of frontal and associated brain regions in an array of learning related operations. How these regions might contribute to uninstructed learning that affects other processes, such as visual attention and decision-making, remains an open question.

Statistical learning (Reber, 1967) and implicit learning (Saffran, Aslin, & Newport, 1996) both describe how exposure to regularities in the environment can produce sensitivity to the structured material as measured in behaviour, but without clear awareness or an ability to overtly express what has been learned (Conway & Christiansen, 2006; Perruchet & Pacton, 2006). Here, we use the term “incidental” to refer to the uninstructed property of the tasks, without making specific claims as to the “implicit” nature of the process or resulting knowledge. Incidental statistical learning is considered a domain-general learning mechanism (Perruchet & Pacton, 2006), and so it can exert effects at many stages of the processing hierarchy. For example, Visual Statistical Learning (Fiser & Aslin, 2001) refers to the facilitation of perceptual operations by passive exposure to object co-occurrences (see also Turk-Browne, Isola, Scholl, & Treat, 2008). Whereas, sequence learning affects motor processing, and is commonly assessed by the Serial Reaction Time (SRT) task (Nissen & Bullemer, 1987). In addition, functions such as attention and decision-making can also be influenced by incidental statistical learning. This is commonly demonstrated via contextual cueing in visual search paradigms (Chun & Jiang, 1998).

In visual search, typically, observers must locate a target item amongst an array of spatially dispersed distractors, and make a decision about a given target feature (e.g., left or right orientation). Contextual cueing (Chun & Jiang, 1998) refers to the facilitation of Response Times (RTs) as a result of learned associations between a target’s location and the visual context created by the distractor configurations. In spatial contextual cueing, several target-distractor configurations are repeated during the experiment, and RTs reduce for these repeat displays compared to those with novel distractor configurations. Critically, the target identity (which maps on to the motor response) is not predicted by the context. Only the target’s location in the search display is predicted. Thus, contextual cueing does not reflect motor learning (e.g., Nissen & Bullemer, 1987; Nitsche, Schauenburg, et al., 2003b).

The contextual cueing effect describes the RT difference between repeat and novel displays (typically 100 ms), and the timecourse of learning is measured by the change in the contextual cueing effect across blocks or epochs (Chun, 2000). This means that learning can be measured online, rather than in a subsequent test phase, which is the case for other statistical learning paradigms. Observers are typically not instructed as to the existence of the regularities, and so the learning is deemed incidental. Several cognitive mechanisms have been put forward to account for the benefit in RTs observed for repeated contexts. Taken en masse, associative mechanisms are believed to influence both attention (Chun & Jiang, 1998) and decision related processes (Chun & Jiang, 1998; Kunar, Flusberg, & Wolfe, 2008; Kunar, Flusberg, Horowitz, & Wolfe, 2007; Zhao et al., 2012). A recent computational modelling study directly tested these accounts and found that cuing largely influenced the components of decision related processing (Sewell, Colagiuri, & Livesey, 2017).

At a neural level, incidental statistical learning is believed to rely on medial temporal lobe (MTL) structures and, specifically, the hippocampus. This was based on studies of amnesic patients who had intact perceptual and skill learning but impaired contextual cueing (Giesbrecht, Sy, & Guerin, 2013). This early work has found further support in neuroimaging findings that show hippocampal BOLD activity is related to performance in contextual cueing tasks (Geyer, Baumgartner, Müller, & Pollmann, 2012; Greene, Gross, Elsinger, & Rao, 2007; Preston & Gabrieli, 2008). The subcortical involvement links learning in contextual cueing to the storage of representations in long-term memory. Yet the same fMRI studies consistently report activation in cortical areas. In one study, BOLD activity for the repeat-novel contrast in the left inferior parietal sulcus (IPS) correlated with the final magnitude of the contextual cueing effect (Manginelli, Baumgartner, & Pollmann, 2013a). Activity relating to learning, assessed via BOLD contrasts for the context by epoch interaction, has also been demonstrated in the dorsolateral PFC (Manginelli et al., 2013a) and bilateral PPC (Giesbrecht et al., 2013). Given the correlational nature of these imaging results, it is possible that the frontal and parietal activation seen in these studies reflect concurrent processes that occur during contextual cueing, or act on the material as a consequences of cuing, without being directly related to the statistical learning per se.

Frontoparietal involvement is consistent with other forms of statistical learning (Janacsek & Nemeth, 2013; Rieckmann, Fischer, & Bäckman, 2010). Together, these brain regions may operate as part of a larger cortical-hippocampal network responsible for integrating sensory information into memory (Sestieri, Shulman, & Corbetta, 2017; Staresina, Cooper, & Henson, 2013). Indeed recently, Wang and colleagues (2014) delivered an excitatory transcranial magnetic stimulation (TMS) protocol to lateral parietal cortex during an overt associative learning memory task and found that stimulation improved memory performance and increased functional connectivity between parietal cortex and the hippocampus.

To date, no study has investigated the causal involvement of cortical regions in incidental statistical learning assessed via contextual cueing. Based on fMRI reports of increased PFC and PPC activity associated with learned repeat displays, here, we used tDCS to investigate the extent to which perturbing these brain regions may directly influence contextual cueing. Thus, the present work seeks to establish whether activity in PFC and PPC is causally involved in incidental statistical learning for visual configural information that comes to affect decision-making. Given the purported role of the DLPFC and PPC in various intentional learning and decision-making processes, tDCS to one or both regions may modulate learning. Alternatively, there may be a dissociation between tDCS effects for the frontal and parietal regions, based on their involvement in potentially interacting learning systems (i.e., Thompson-Schill et al., 2009).

2.0. Method

2.1. Participants

One hundred and twenty individuals participated in the study; 60 in the frontal region condition (mean age = 21 years, SD = 1.93 years, 17 male), and a different 60 individuals in the parietal region condition (mean age = 21 years, SD = 3.65 years, 16 male). For each brain region, participants were pseudo-randomly allocated to receive either anodal, cathodal or sham stimulation, with 20 participants in each group. The sample size was determined a priori based on an effect size ($\eta^2_p = 0.175$) taken from a previous single session tDCS study conducted by our group (Filmer, Mattingley, Marois, & Dux, 2013b). A power analysis using G-Power (Faul, Erdfelder, Lang, & Buchner, 2007) indicated that 18 participants per group would be required to achieve 80% power with an alpha level of .05. An additional two participants from the frontal condition and seven participants from the parietal condition were excluded for the following reasons: six for not responding on more than 5% of trials; two for failing to follow instructions; and one for performance below the minimum average accuracy cut off of 85% (determined pre–study).

Participants were screened for history of any neurological conditions or trauma; family history of epilepsy; metal in the body; and the current use of neuroactive medication. All participants met the tDCS safety criteria (Nitsche, Liebetanz, et al., 2003a), and had normal or corrected-to-normal vision. According to the Edinburgh Handedness Inventory (Oldfield, 1971) there were 49 right-handed, five left-handed, and six ambidextrous participants in the frontal condition. There were 57 right-handed, zero left-handed and three ambidextrous participants in the parietal condition. Participants gave informed written consent prior to the experiment, and received $10 compensation for their involvement. The study was approved by The University of Queensland Human Research Ethics Committee.

2.2. Transcranial Direct Current Stimulation

Stimulation was delivered via a Neuro-Conn stimulator attached to two 5 × 5 cm electrodes. The electrodes were secured to the scalp using Ten20 electrode paste. In the frontal condition, the target electrode was placed over the left PFC, which corresponded to 1 cm posterior to the F3 site (see Figure 1b) according to the 10-20 Electroencephalography (EEG) system (Jasper, 1958). Previous work has shown F3 corresponds to the left DLPFC (Coffman, Clark, & Parasuraman, 2014; Herwig, Satrapi, & Schönfeldt-Lecuona, 2003; Utz, Dimova, Oppenländer, & Kerkhoff, 2010). In the parietal condition, the target electrode was placed over the left parietal cortex corresponding with the P3 site (see Figure 1a). This site has commonly been used to target the posterior parietal cortex (Sparing et al., 2009; Stone & Tesche, 2009), with proximity to the inferior parietal sulcus (IPS; Herwig et al., 2003). For both region conditions, the reference electrode was located over the contralateral (right) mastoid. This sought to minimise any confounding activation differences caused by the reference electrode. Current flow modelling was conducted a priori using HD-Explore software (Soterix Medical). As shown in Figure 2, the montages resulted in current flow localized to the target regions, being the left dorsolateral frontal lobe and left lateral parietal lobe.

During active stimulation constant currents (anodal and cathodal) were applied at an intensity of 0.7mA for 15 minutes (including a 30 second ramp up/ramp down). This protocol had been used in previous studies by our group investigating the modulation of learning with tDCS (e.g., Filmer et al., 2013a, 2013b, 2016). For sham stimulation, the electrodes were left in place for the full 15 minutes, however stimulation was turned off after 90 seconds (30 seconds constant current with a 30 second ramp up/ramp down). This procedure has been shown to reliably blind participants to the stimulation manipulation (Gandiga, Hummel, & Cohen, 2006).

Current densities for all sessions were kept below the safety limit of 0.04 mA/cm^2 (Kessler, Turkeltaub, Benson, & Hamilton, 2012; Nitsche et al., 2008). In order to ensure adequate contact of the electrodes with the scalp, impedances were kept below 20 Ω prior to commencing stimulation.

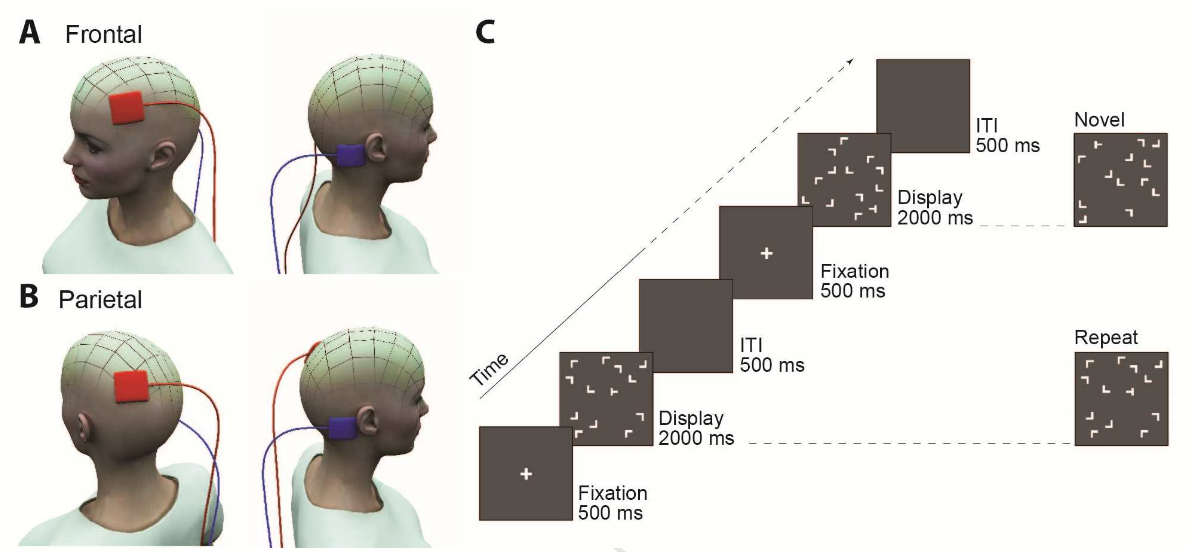

Figure 1.

Experimental design. Electrode placement for the target electrodes (red) and reference electrode (blue) for the (A) frontal and (B) parietal regions. Each region was stimulated with anodal, cathodal and sham current types in a between-subjects design. (C) Stimuli and trial outline for the contextual cueing task. For repeat displays, the location and orientation of distractors, as well as the target location, was held constant across blocks, with only the target orientation changing randomly from trial to trial. For novel displays, all items in the display varied randomly. Note that displays were not response terminated.

2.3. Behavioural Task

2.3.1. Stimuli and Apparatus. The contextual cueing task was adapted from Chun and Jiang (1998), and was programmed in Matlab 2015b using the Psychophysics toolbox extension (Brainard, 1997; Kleiner, Brainard, Pelli, Ingling, & Murray, 2007). The computer was connected to a 19” CRT monitor which had a resolution of 1024 × 768, and a refresh rate of 100

Hz. Participants were seated unrestrained approximately 63 cm from the monitor. Items were coloured white against a grey background (RGB: 80, 80, 80), and could appear within an invisible 15 × 15 grid that extended 10° × 10° visual angle. Displays consisted of one target stimulus, a T-shaped item, among a set of 12 distractor stimuli, L-shaped items. The orientation of distractors was determined randomly for each element and could be either 0°, 90°, 180° or 270° clockwise relative to vertical. Targets could be either 90° (‘right oriented’) or 270° (‘left oriented'). For each participant, a unique set of 12 configurations was generated in which the target location (but not its orientation), and the distractor locations and orientations were to remain constant across blocks – these we refer to as ‘repeat’ displays. For ‘novel’ displays, the target and distractor locations varied randomly across blocks.

2.3.2. Contextual Cueing Task. On each trial, participants reported the orientation of the target T using the ‘m’ key for right oriented (90°) targets and the ‘z’ key for left oriented 270° targets. Responses were made via an Apple Macintosh keyboard, and participants were instructed to use their index fingers on both hands to respond. Each trial began with a white fixation cross (2.5° visual angle) presented for 500 ms, followed by the visual search display for 2000 ms, followed by a blank grey screen for 500 ms. The display time was held constant to ensure all participants viewed the configurations for the same duration, regardless of individual RTs. If no response was made during the display window it was recorded as a missed response and the program moved on to the next trial. Correct/incorrect feedback was provided during a practice block that comprised 12 trials of novel displays. The main task consisted of 10 blocks of 24 trials, with each block containing 12 repeat displays and 12 novel displays. Display type (repeat or novel), configuration (1 to 12) and target orientation (left or right) was pseudorandomised for each block. After each block the program paused and participants were required to press a key to continue. There was no feedback during the main task.

2.3.3. Awareness Questions. In keeping with previous contextual cueing paradigms, we probed for awareness any repetition in the task using computer administered questions immediately after the contextual cueing task. The questions followed the recommended procedure (Smyth & Shanks, 2008). Question one asked, "During the experiment, did you think any of the particular configurations of Ls were repeated?" Participants who responded 'yes' received two follow-up questions. Question two: "Approximately, when did you begin to notice this repetition?" Participants indicated a block number (being from 1 to 10) using the number keys on the keyboard. Question three: "After you realized particular configurations of Ls were being repeated, did you try to memorize these displays?" This required a yes/no response.

2.3.4. Recognition Test. Following the awareness questions, all participants were informed about the repetition of a portion of displays in the task, and that the next section would probe their ability to detect these regularities. The recognition test consisted of 4 blocks of 24 trials with each block containing the 12 repeated displays from the contextual cueing task, and 12 completely novel displays. The instructions were to respond as to whether a display was one that had previously been repeated (press 'R') or one that was new (press 'N'). Participants were told that speed was not important, and to try to be as accurate as possible.

2.4. General Procedure

After completing the tDCS safety screening and filling out the pre-tDCS adverse effects questionnaire, participants' heads were measured and the stimulation pads were secured. Following the practice trials, stimulation was switched on and allowed to ramp up for 30 seconds before participants began the main contextual cueing task. Participants completed the task in 12 min on average, meaning that the stimulation was active for the entire task duration. Once the stimulation had ended, the pads were removed and the program proceeded to the awareness questions followed by the recognition test. Participants were monitored for 45 minutes following the end of stimulation as recommended by safety guidelines.

2.5. Data Analysis

Individual mean RTs were calculated for correct responses only. Outliers greater or less than 3 SDs from an individual’s mean RT were excluded for each display type condition separately. The mean number of discarded trials per participant was 1% in the frontal condition, and 0.9% in the parietal condition. The overall error rates for these groups were low, at 3.47% and 3.74%, respectively. In order to investigate how stimulation may have been influencing learning in contextual cueing, we investigated the contextual cueing effect at two stages of the task. Previous research has indicated that the contextual cueing effect emerges early, typically within the first three blocks (Chun & Jiang, 1998; Jiang & Chun, 2001; Jiang & Wagner, 2004), after which time the learning benefit stabilizes. We therefore defined two stages of learning: an early stage being blocks 1 to 3, and a late stage being blocks 4 to 10.

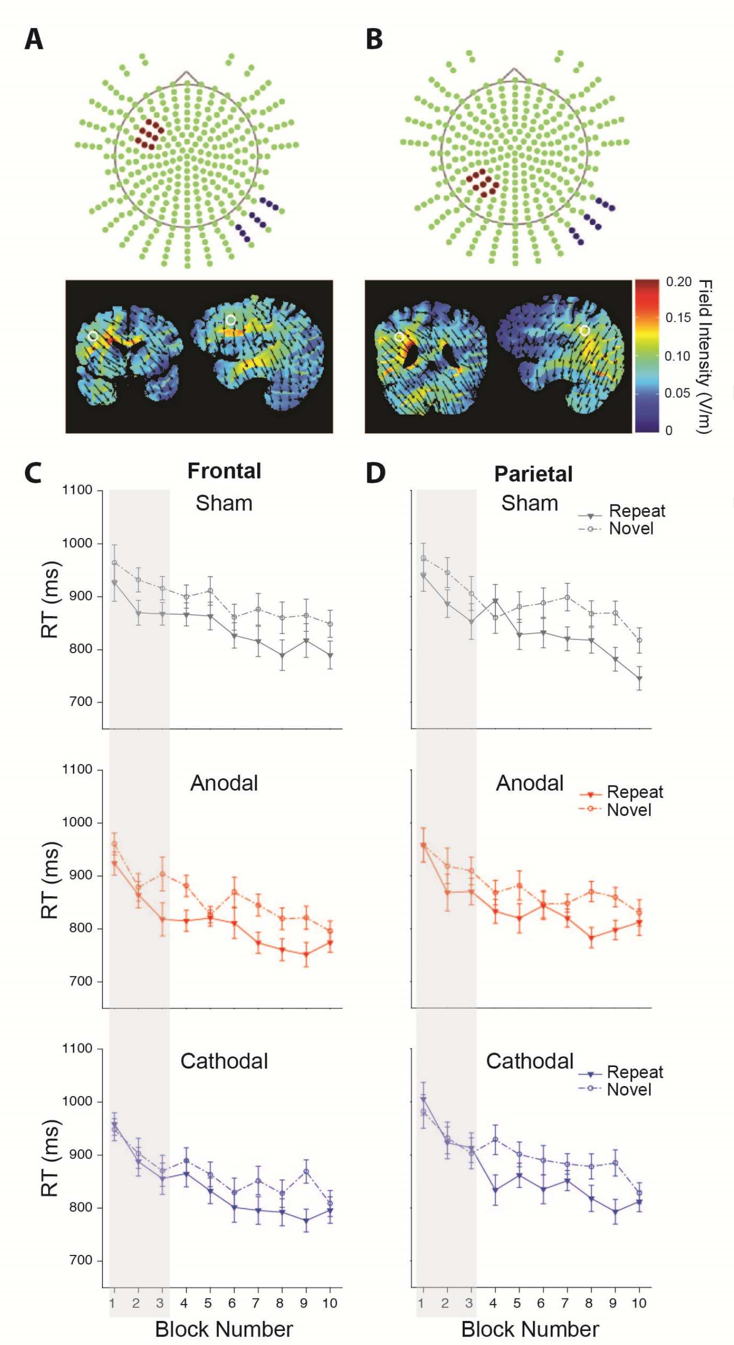

Figure 2.

Current flow modelling and main behavioural results. A) tDCS montage targeting the frontal region with the target electrode (red) 1 cm posterior to F3. Modelling shows the strongest field intensity localized to the anterior prefrontal region in the left hemisphere. B) tDCS montage targeting the parietal region with the target electrode over P3 (red). The strongest field intensity was localized to the lateral parietal region in the left hemisphere. RT data for the contextual cueing task as a function of display type, block, and stimulation type (Sham, Anodal and Cathodal), with data shown separately panels for the (C) frontal and (D) parietal regions. Error bars reflect within-subjects confidence intervals (Loftus & Masson, 1994).

3.0. Results

3.1. Response Time Analysis

As can be seen in Figure 2, RTs decreased over time and were faster for repeat displays compared to novel displays. In order to quantify the effects of tDCS on contextual cueing, we conducted a 4-way ANOVA with factors Display Type (repeat vs novel; within-subjects), Epoch (early vs late; within-subjects), Stimulation Type (sham, anodal and cathodal; between-subjects), and Stimulation Region (frontal vs parietal; between-subjects) on the RT data (see Table 1). There were significant main effects of Display Type ($F_{1,114} = 43.05$, $p < .001$) and Epoch ($F_{1,114} = 200.94$, $p < .001$); along with a significant Display Type × Epoch interaction ($F_{1,114} = 7.64$, $p = .007$). This indicated that RTs became increasingly faster for repeat displays compared to novel displays, thus demonstrating robust contextual cueing. Importantly, the 3-way interaction – Display Type × Epoch × Stimulation Type – was significant ($F_{2,114} = 4.135$, $p = .018$), indicating that the contextual cueing effect was modulated by stimulation type; however, this did not interact with Stimulation Region ($F_{2,114} = .37$, $p = .693$). All other *p*s > .168. We therefore collapsed across Region for the following analyses.

Our comparisons of interest regarding tDCS effects were the two active stimulation conditions (anodal and cathodal), compared to our sham control, and compared to each other. To follow up the 3-way interaction, we conducted separate 3-way ANOVAs with factors Display Type, Epoch and Stimulation Type to assess the following comparisons: cathodal vs. sham, anodal vs. sham, and anodal vs. cathodal. The critical interaction – Display Type × Epoch × Stimulation Type – was significant for cathodal compared to sham ($F_{1,78} = 7.85$, $p = .012$) and cathodal compared to anodal stimulation ($F_{1,78} = 4.93$, $p = .039$), but not for anodal stimulation compared to sham ($F_{1,78} = 0.16$, $p = .678$). This indicated that cathodal stimulation to frontoparietal regions interfered with contextual cueing in the early stages of learning compared to anodal and sham stimulation.

Table 1.

Group response times (ms) by epoch for the contextual cueing task.

		Early Epoch		Late Epoch	
		Repeat	Novel	Repeat	Novel
Frontal					
	Anodal	868.83 (142.09)	914.35 (159.74)	786.86 (124.72)	837.03 (132.66)
	Sham	888.13 (155.68)	937.52 (140.01)	824.47 (158.38)	874.84 (143.12)
	Cathodal	900.67 (141.67)	907.25 (133.35)	808.65 (132.07)	848.56 (131.37)
Parietal					
	Anodal	899.06 (150.68)	928.59 (152.44)	815.76 (124.58)	857.82 (121.54)
	Sham	892.80 (145.50)	941.31 (143.73)	817.02 (120.80)	868.74 (125.27)
	Cathodal	947.41 (171.98)	938.95 (123.95)	829.26 (110.57)	884.71 (120.04)

Note: Values represent Means (SDs).

3.2. Error Rates. Errors were low across all conditions (Table 2). There was a significant effect of Display Type ($F_{1,114} = 11.89$, $p = .001$) and Epoch ($F_{1,114} = 9.62$, $p = .002$), such that participants made fewer errors overall for repeated displays (3.31%) compared to novel displays (4.18%), and made more errors in the early epoch (4.15%) compared to the late epoch (3.33%). Repeated displays were therefore associated with both faster and more accurate responses over time. Collectively this indicates there were no speed/accuracy tradeoffs for learning related to contextual cueing. In terms of stimulation effects on errors, there was a significant interaction between Epoch, Stimulation Type and Stimulation Region ($F_{2,114} = 5.17$, $p = .007$). Importantly, there were no main effects of Stimulation Type or Region, suggesting tDCS did not alter the ability to perform accurately. Lastly, there were no interactions between Stimulation Type or Region with Display Type ($F_{2,114} = .87$, $p = .421$), indicating stimulation did not modulate errors related to our learning measure of interest, being the contextual cueing effect. (All other *ps* > .067.)

Table 2.

Group percentage errors by epoch for the contextual cueing task.

		Early Epoch		Late Epoch	
		Repeat	Novel	Repeat	Novel
Frontal					
	Anodal	5.00% (7.48)	5.69% (9.35)	2.14% (4.23)	3.39% (5.59)
	Sham	3.06% (4.49)	4.44% (5.72)	2.98% (5.28)	3.99% (6.12)
	Cathodal	2.08% (4.35)	3.75% (6.00)	3.27% (5.48)	3.69% (5.75)
Parietal					
	Anodal	3.75% (4.91)	4.44% (5.62)	3.15% (5.34)	3.51% (5.19)
	Sham	3.75% (5.39)	3.33% (6.45)	2.80% (4.78)	4.05% (6.08)
	Cathodal	4.72% (6.09)	5.83% (5.75)	3.04% (5.25)	3.99% (6.86)

Note: Values represent Means (SDs)

3.3. Awareness Questions. Around half the participants reported being aware of some form of repetition (Figure 3). Pearson's chi-squared test indicated there were no significant differences in the frequency of reported awareness between the stimulation types as assessed for each stimulation region separately (Frontal: $\chi^2 = 2.83$, $p = .243$; Parietal: $\chi^2 = .53$, $p = .63$), nor were there differences between overall ($\chi^2 = .53$, $p = .47$).

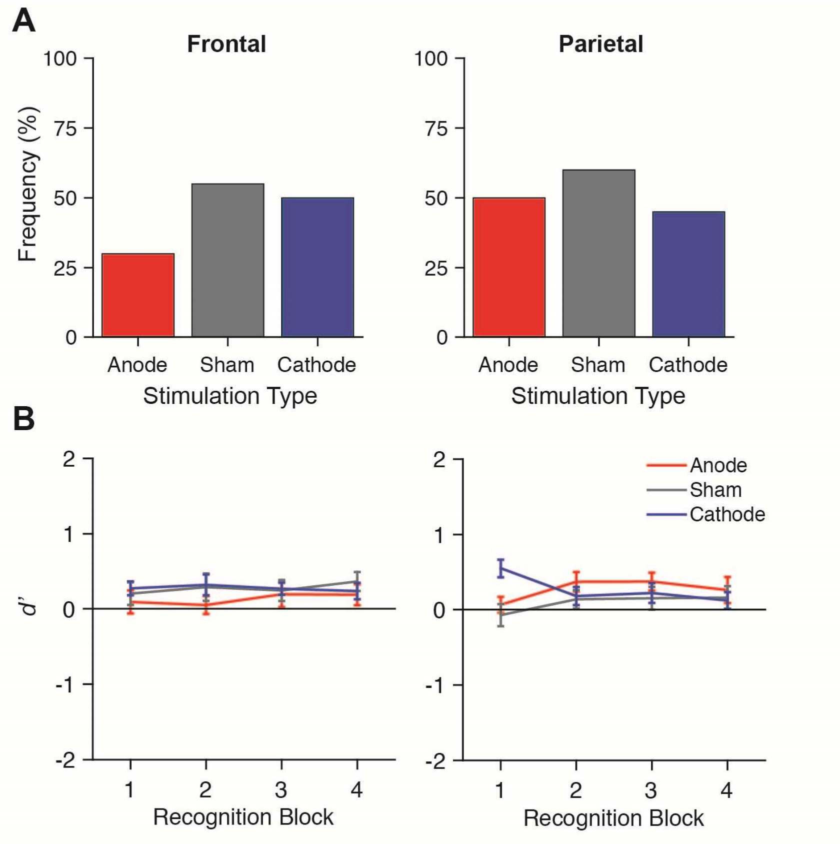

Figure 3.

Reported awareness and recognition test results. A) Percentage of participants who subjectively reported being aware of repetition following the contextual cueing task. This was approximately 50% of participants across all groups. B) Behavioural results from recognition test. Data represents mean *d'* for each recognition block, and error bars represent SEM.

3.4. Recognition Test. Accuracy in the recognition test was around chance, ranging between 48% and 59% across groups. To assess participants' sensitivity when distinguishing repeated displays from novel displays, *d'* (d-prime) was computed for each of the four blocks in the recognition test (shown in Figure 3B). A 3-way ANOVA with factors Recognition Block (1 to 4; within-subjects), Stimulation Type (anodal, sham, cathodal; between-subjects), Stimulation Region (frontal vs parietal; between-subjects) was conducted on the *d'* data. There were no significant effects of Recognition Block ($F_{3,342}$ = .226, p = .878), Stimulation Type ($F_{3,114}$ = .744, p = .477), or Stimulation Region ($F_{1,114}$ = .069, p = .794), and no significant interactions (all other ps > .115). While this indicates that recognition was not affected by stimulation, it may be worth noting that *d'* overall was reliably different from zero. A one-sample *t*-test on *d'* collapsed across the four Recognition blocks was significant, (t_{119} = 6.924, p < .001, *Mean d'* = 0.203). This is perhaps not surprising as it may reflect the ability of participants to learn the repetitions over the course of the four blocks once they have been made aware of the regularities. There was no difference in overall *d'* between those who reported being aware (n = 58) and those who were classified as unaware (n = 62), based on the probe awareness question after the contextual cueing task. An independent samples *t*-test on *d'* scores revealed no reliable difference in recognition performance between the groups (t_{118} = 1.519, p = .131).

4.0. Discussion

We sought to determine whether frontal and parietal brain regions are causally involved in statistical learning that occurs in spatial contextual cueing. We applied anodal, cathodal or sham tDCS online, either to the left PFC or left PPC. The contextual cueing effect, which is characterized by faster RTs for repeated relative to novel search displays, was disrupted in the early epoch by cathodal stimulation, relative to sham and anodal stimulation, for both the frontal and parietal conditions.

The current results extend previous neuroimaging findings regarding the cortical locus of learning during contextual cueing. Early investigations into the neural structures responsible for incidental statistical learning highlighted the importance of subcortical brain regions such as the hippocampus (Chun & Phelps, 1999) and striatum (Rieckmann, Fischer, & Bäckman, 2010). Since then, fMRI studies of contextual cueing corroborated the involvement of the hippocampus and its relation to learning performance (i.e., the typical interaction observed between display type and epoch/block). In addition, these studies consistently reported activity in cortical areas such as the dorsolateral PFC and regions within Posterior Parietal Cortex (PPC) that was associated with the repeat-novel contrast (Giesbrecht et al., 2013; Manginelli et al., 2013a; Pollmann, 2012). These correlational findings did not allow inferences about whether such cortical activity was necessary for learning to occur, or was a by-product of other cognitive process operating on the learned repeated displays.

The present results provide the first causal evidence that both frontal and parietal regions are directly involved in the evolution of the contextual cueing effect, as evidenced by modulation of early learning observed here. Based on the functional and structural interconnectivity of these targeted regions with the hippocampus (Wang et al. 2014), one may question the contribution of hippocampal activity to the effects seen here. To comment on such dynamics would be speculative and is outside the scope of this study. Our tDCS modelling suggests that our stimulation protocol produced concentrated areas of current flow surrounding the left DLPFC and the left IPL. We therefore adopt the most parsimonious conclusion that frontal and parietal areas are critical for learning during contextual cueing.

Our results do not appear to be due to baseline differences in RTs. The variation in RTs for the first block was not reliable across stimulation region, stimulation type, or display type (all *p*s > .129). These differences are most likely attributable to inter-participant noise, rather than systematic differences between conditions. Looking at the two sham groups, there appeared to be a visual difference in the size of the contextual cueing effect between the frontal and parietal groups. Once again, these differences were not reliable (all *p*s > .526). It also seems unlikely that the effect of cathodal stimulation can be explained by modulation of general performance or response speed. If this were the case, why would stimulation selectively affect performance for repeat displays? Here, the novel trials constituted a control task in the form of standard visual search. If we take mean RTs for the novel displays to indicate baseline task performance, and hence arousal, we see no effects of Stimulation Type or Region (all *p*s > 0.359). Put differently, stimulation only affected performance when we included the repeat versus novel contrast – i.e. the contextual cueing/learning effect. This deems it unlikely that general changes in attention or responding could account for the pattern of results observed here.

Furthermore, while we argue that tDCS interrupted processes specifically related to the incidental learning of repeated configurations, one alternative explanation may be that tDCS affected generalized motor processes, rather than processes specific to statistical learning. We believe this is unlikely as any changes in motor processing should influence responses for repeat and novel displays to the same degree, as both display types required identical response mappings for the orientation judgment. Therefore, a purely motor account cannot readily explain the increasingly faster RTs seen for repeated contexts compared to novel contexts and the interaction with cathodal stimulation.

Given the apparent criticisms regarding the spatial specificity of tDCS, it is reasonable to question whether cathodal stimulation of any brain region might explain the modulation of contextual cueing seen here. We rebut this point based on the fact that we evaluated and selected our electrode configurations a priori using tDCS current-flow modelling software. The patterns of current flow were distinct for the two stimulation montages, and the areas of peak current density were located in the respective target regions. However, given the well known structural and functional connectivity between the frontal lobe and parietal lobe as part of the frontoparietal network (Sestieri et al., 2017), it remains possible that targeting one region may have modulated activity in the other region, and these changing network dynamics may have contributed to the effects seen here rather than changes in a local brain region. Indeed, a study using resting-state fMRI found that anodal tDCS targeting the left prefrontal cortex increased coactivations between frontal and parietal regions (Keeser et al., 2011). Future studies should investigate how interactions between frontal and parietal regions may influence behaviours relating to incidental learning, and how these may be modulated by brain stimulation. For now, it seems plausible that frontoparietal regions may support statistical learning via activation of necessary cognitive control resources supplemented by these regions.

Contextual Cuing typically emerges quickly, with evidence of learning after only three repetitions (Chun & Jiang, 1998; Jiang & Chun, 2001; Jiang & Wagner, 2004; Zellin, Mühlenen, Müller, & Conci, 2014). The key finding in our study was that cathodal tDCS disrupted this early learning. At first, it may seem surprising that stimulation at a constant intensity caused behavioural changes in a limited time window of the task. Yet this makes sense when considering the non-linear dynamics of tDCS (e.g., Batsikadze et al., 2013), and the complexity of associated behavioural outcomes (Bestmann et al., 2015; de Berker, Bikson, & Bestmann, 2013). We conceptualize our result as reflecting an impairment, or a delay in learning, rather than complete disruption of this process. Cathodal stimulation appears to make learning the repeating target-context associations more difficult to begin with, but does not render learning impossible, given sufficient exposure to the regularities. In behavioural studies of contextual cueing, there is evidence of delayed learning when concurrent WM tasks are administered during the early learning phase (Annac et al., 2013; Manginelli, Langer, Klose, & Pollmann, 2013b) and when displays are associated with certain types of feedback (Tseng & Lleras, 2012). At the neural level, reports of tDCS affecting a network without preventing it from operating are also consistent with our findings. Using computational modelling, a recent study showed that tDCS to left DLPFC altered network dynamics, which affected behaviour, yet did not prevent transmission of task-related neural activity (Bonaiuto, de Berker, & Bestmann, 2016). In our study, the temporal specificity of cathodal effects may have been due to the recruitment of other networks to compensate for the lost functioning. It is also possible that processing in the targeted regions was transient rather than sustained, and thus minimally affected. Alternatively, homeostatic mechanisms may have compensated for the effects of tDCS by returning network activity to its baseline levels after a sustained increase in excitability (Iyer, Schleper, & Wassermann, 2003; Turrigiano, Leslie, Desai, Rutherford, & Nelson, 1998; Wright & Krekelberg, 2014).

It should also be noted, that our finding of PFC involvement in contextual cueing is consistent with stimulation studies of other statistical learning processes. Repetitive TMS (rTMS) delivered to contralateral DLPFC was found to disrupt sequence learning in the SRT task compared to ipsilateral DLPFC and SMA controls (Pascual-Leone, Wassermann, Grafman, & Hallett, 1996). A later study replicated this finding showing that rTMS to DLPFC abolished learning compared to a parietal target, and further stipulated that this was specific to learning of spatial information, compared to a colour or a combined version of the SRT task (Robertson, Tormos, Maeda, & Pascual-Leone, 2001). Using a probabilistic category learning task, anodal tDCS to left PFC improved incidental learning compared to cathodal and sham stimulation (Kincses, Antal, Nitsche, Bártfai, & Paulus, 2004). While the processing demands of these tasks may be quite different from those that underlie contextual cueing, it appears PFC involvement is common across forms of statistical learning.

The present results must also be considered in relation to the proposed benefits of reduced frontal involvement for incidental learning. As described in the introduction, according to this work, reduced cognitive control, mediated by PFC disengagement, is advantageous for tasks that involve processing bottom-up stimulus-response information (Thompson-Schill et al., 2009). This account might predict that disrupting the left PFC with tDCS (either from anodal, cathodal, or both) would improve contextual cueing, whereas we found that cathodal stimulation disrupted learning by reducing the early cuing contextual cueing effect. The first point to make here, and as noted earlier, is that we cannot be sure that cathodal stimulation actually reduced activity in the target region (Batsikadze et al., 2013). Even if it did, there is fMRI work showing that reduced activity does not always indicate reduced involvement of a region (see Garner & Dux, 2015; Kok, Jehee, & de Lange, 2012), as it can also reflect sharper neural coding in a brain area and enhanced representations. Another point of difference concerns the type of tasks used. The work on hypofrontality has employed high-level conceptual or language-based tasks. These have involved generating verbal responses (Chrysikou et al., 2013) or categorizing stimuli based on abstract concepts (Lupyan et al., 2012), and were predominantly accuracy based. These tasks, no doubt, exert quite distinct processing demands from those recruited during visual search with speeded responses. Finally, this literature emphasizes a dissociation between the brain regions that support performance in line with current goals (e.g., distinguishing targets from non-targets) and those that underpin learning about the environment (e.g., forming target-context associations). Thus, this hypothesis might predict different response strategies for target and distractor processing when PFC function is disrupted. We see this as an avenue for future research into the potential ways that incidental learning for target-context regularities may be acted upon by the system.

In summary, we found that the evolution of statistical learning for configural visual information relies on activity in frontoparietal brain regions. These findings show for the first time that cortical areas are directly involved in the early emergence of the contextual cueing effect, and perhaps incidental learning generally. This result provides a common link between the frontal networks involved in explicit forms of learning, such as goal-directed training and intentional skill learning, and those tapped during incidental statistical learning that acts on higher-level information processing. Understanding the causal brain-behaviour relationships that support incidental statistical learning is important for developing more comprehensive models of how the brain computes associations between stimuli and uses this information to inform decisions in an automatic manner.

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