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Task and Regions Specific Top-Down Modulation of Alpha Rhythms in Parietal Cortex

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Abstract

Alpha (8–12 Hz) power desynchronization is strongly associated to visual perception but has been observed in a large variety of tasks, indicating a general role in task anticipation. We previously reported in human observers that interference by repetitive transcranial magnetic stimulation (rTMS) of core regions of the dorsal attention network (DAN) disrupts both anticipatory alpha desynchronization and performance during a visuospatial attention (VSA) task. Here, we test the hypothesis that alpha desynchronization is task specific, and can be selectively modulated by interfering with activity in different higher-order parietal regions. We contrast the effects of rTMS on alpha rhythms and behavior on 2 different tasks: a VSA and a semantic decision task, by targeting the posterior intraparietal sulcus (pIPS), a core region of the DAN, or the angular gyrus (AG), a core region of the default mode network (DMN). We found that both performance and anticipatory alpha desynchronization were affected by stimulation of IPS only during VSA, and of AG only during semantic decisions. These findings indicate the existence of multiple dedicated parietal channels for the modulation of anticipatory alpha rhythms, which in turn reflect task-specific modulation of excitability in human parieto-occipital cortex.

Key words: anticipatory alpha, parietal cortex, rTMS, semantic decision, visuospatial attention

Introduction

The ability to anticipate predictable events is of great ecological importance. For example, human observers can use cues for orienting attention to relevant aspects of a forthcoming task (Posner 1980), or for processing more rapidly semantic information (e.g. priming; Noguera et al. 2007). One robust electrophysiological correlate of anticipation is the modulation of posterior scalp electroencephalographic (EEG) alpha oscillations (8–12 Hz) (Klimesch 2012). Specifically, the pre-stimulus alpha power reduction (i.e. desynchronization), particularly in the upper alpha sub-band (10–12 Hz) (Klimesch et al. 1998), is thought to reflect an attentional (top-down) modulation of cortical excitability that relates to enhancement (suppression) of

task relevant (irrelevant) information (Jensen and Mazaheri 2010; Foxe and Snyder 2011).

Even though pre-stimulus alpha desynchronization has been reported for tasks in a variety of cognitive domains (Klimesch 1996; Filipovic et al. 2001; Babiloni et al. 2004; Min et al. 2008), its modulation has been more strongly associated with visual perception. Alpha rhythms are most consistently localized in parieto-occipital cortex (Vanni et al. 1997), and its generators have been identified in the thalamus and visual cortex (Pfurtscheller and Lopes da Silva 1999) (Bollimunta et al. 2011). The role attributed to alpha rhythms in top-down (feed-back) modulation of visual information is thought to

complement the role of gamma (40–90 Hz) activity in bottom-up (feedforward) processing (reviewed in Jensen et al. 2015).

However, several important issues concerning the relationship between alpha rhythms and expectation remain unknown. Firstly, it is unclear whether alpha desynchronization reflects a general or task-specific preparation signal. Secondly, most studies on alpha rhythms and expectations have been correlative, and as a consequence little is known on the cortical or subcortical mechanisms controlling alpha desynchronization. Finally, it is unknown whether putative control mechanisms are task general or task specific. In a series of studies that combined EEG recordings with transcranial magnetic stimulation (TMS) we have demonstrated that, as observers expect a stimulus at a location in the visual field, inhibitory magnetic stimulation of left/right intraparietal sulcus (IPS) and frontal eye field (FEF), core regions of the so-called dorsal attention network (DAN) (Corbetta and Shulman 2002), affects both pre-stimulus alpha desynchronization in parieto-occipital cortex and performance (Capotosto et al. 2009, 2012, 2015). These findings therefore suggest that prefrontal and parietal regions of the DAN modulate alpha rhythms during visuospatial attention (VSA) in agreement with anatomofunctional models in which DAN regions top-down modulate visual occipital areas (Kastner and Ungerleider 2000; Corbetta and Shulman 2002).

Here we extend our investigation of the cortical mechanisms of task anticipation and alpha power modulation to other cognitive domains by asking 2 first-order questions. First, do parietal regions of the DAN modulate anticipatory alpha desynchronization only during orienting of VSA or do they have a more general influence on task preparation, sensory encoding or arousal? Second, do other higher-order parietal regions modulate anticipatory alpha activity in other contexts? Answers to these questions represent ground knowledge to clarify whether anticipatory alpha rhythms, and putative control cortical mechanisms, are general or task specific.

We contrasted the effects of TMS interference over left posterior IPS versus left angular gyrus (AG) on both preparatory alpha rhythms and behavioral performance during the execution of both a VSA and a semantic decision task. This choice was motivated by recent neuroimaging work showing that while posterior IPS is involved in VSA, the left AG, one of the main nodes of the default mode network (DMN) (Shulman et al. 1997; Raichle et al. 2001), is recruited during the selection of relevant information in semantic (Wirth et al. 2011) and episodic (Sestieri et al. 2010) memory. Since 1) a large meta-analysis of imaging studies indicates that the left AG is at the top of the semantic processing hierarchy (reviewed in Binder and Desai 2011); 2) anticipatory processes have been also recognized in the context of memory retrieval tasks, in terms of the adoption of a retrieval mode/orientation that facilitates subsequent memory discriminations (reviewed in Rugg and Wilding 2000); and 3) modulations of alpha power have been associated with semantic memory (SM) (Klimesch 1996), we therefore hypothesized that left IPS and left AG may provide task-specific top-down modulation of pre-stimulus alpha power desynchronization during VSA and SM, respectively.

Materials and Methods

Subjects and Stimuli

A total of 19 right-handed (Oldfield 1971) volunteers (mean age \pm SE = 28.5 \pm 4.9 years old; 11 females), with no previous

psychiatric or neurological history, participated in the experiment. One participant was excluded due to the presence of artifacts in the EEG recordings (see Electroencephalography recordings section). Participants gave written consent according to the Code of Ethics of the World Medical Association, and the Institutional Review Board and Ethics Committee of the University of Chieti. The experiment was conducted at the Institute of Technology and Advanced Bioimaging (ITAB). The participants were seated on a comfortable reclining armchair and kept their hands on the response box (Cedrus RB-830). Stimuli were presented on a LCD screen placed at a distance of about 80 cm.

The study included 2 tasks: 1) SM; and 2) VSA. Both tasks included 3 TMS conditions (see below), each with a different randomized list of stimuli. The order of tasks and TMS conditions was counterbalanced across subjects. Participants were allowed to take a break in the middle of each condition, each lasting approximately 6 min. The 2 tasks used the same stimuli and timing, and were carried out in a single experimental session. Stimuli were generated using E-Prime software v2.0 (Psychological Software Tools, Pittsburgh, PA), and included 150 four-letters Italian nouns, matched for frequency (mean frequency : 13.4), and were drawn from a linguistic database (Corpus e Lessico di Frequenza dell'Italiano Scritto (CoLFIS), Bertinetto and colleagues, 2005). Words were written in upper case. In both tasks, subjects were instructed to maintain fixation on a central black cross (subtending 0.2° of visual angle), displayed on a white background at the center of the screen.

During the SM task, every 4 \pm 0.5 s a cue stimulus (a red small cross) was presented for 200 ms. After 2 s, a target word was presented for 500 ms at the center of the screen and represented a living (50%) or a non-living entity (50%). Therefore, the cue was temporally, but not spatially, informative. Participants were instructed to make a living/non-living judgment by pressing a corresponding button of the response box with their left/right index finger (Fig. 1A). Of note, living/non-living subcategories included plants (e.g. vegetables, fruits, and flowers), animals (e.g. birds, mammals, and insects), and body-parts for the living category, and buildings, vehicles, apparel, music instruments, and tools for the non-living category. Each TMS condition contained 50 trials, so that a single target was presented only once during the 3 SM conditions (3 conditions \times 50 trials = 150 trials).

During the VSA task, every 4 \pm 0.5 s a cue stimulus (a black arrow subtending about 0.2° visual angle and overlapping with the horizontal segment of the fixation cross) was presented for 200 ms duration, randomly cueing either a left (50%) or a right (50%) visual field location. After 2 s from cue onset, the target stimulus (word) was presented for 500 ms at either the cued (valid) or the uncued (invalid) location along the horizontal meridian at 0.7° of visual angle from fixation. The ratio of valid/invalid target was 80/20 (Posner 1980). The subject's task was to maintain central fixation throughout the trial, covertly pay attention to the location indicated by the cue and report whether the letter "A" was present or not in the target word by pressing the corresponding button of the response box with their left/right index finger (Fig. 1B). Of note, the spatial cue only indicated the likely position of the target, but did not provide any information about the actual response. The same set of 150 nouns used in the SM task were presented in the VSA task, although we ran more trials (3 conditions \times 80 trials = 240 trials) to have a sufficient number of invalid trials ($N = 16$) and calculate a validity effect. Accordingly, some words were presented more than once.

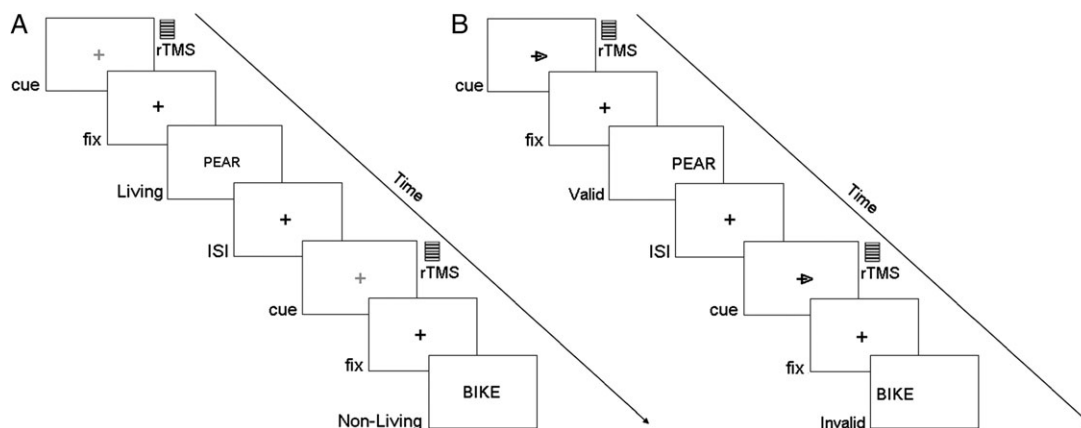


Figure 1. (A) Example of the display sequence in the SM task. Of note, in figure the red cross (cue) is displayed in gray. (B) Example of the display sequence in the visual attention task (VSA).

In both tasks, subjects were instructed to respond as quick and as accurate as possible. Reaction times (RTs) and response accuracy were recorded for behavioral analyses.

rTMS Procedures and Identification of Target Scalp Regions

TMS stimulation was delivered through a focal, figure-eight coil, connected with a standard Mag-Stim Rapid 2 stimulator (maximum output 2.2 T). Individual resting excitability threshold for right motor cortex stimulation was preliminarily determined following standardized procedure (Rossini et al. 1994). The rTMS train was delivered simultaneously with the cue onset using the following parameters: 150 ms duration, 20-Hz frequency, and intensity set at 100% of the individual motor threshold. These parameters are consistent with published safety guidelines for TMS stimulation (Rossi et al. 2009). Of note, previous work from our lab has demonstrated the inhibitory nature of the present stimulation protocol (Capotosto et al. 2009, 2012, 2013; Sestieri et al. 2013). This is in line with the idea that this high-frequency stimulation introduces neural noise leading to a delayed /impaired performance (Miniussi and Ruzzoli 2013).

In both tasks, participants performed 2 active rTMS (AG, IPS) and one inactive TMS (i.e. Sham) conditions, applied in different blocks. In the “Sham” condition, a pseudo rTMS was delivered at scalp vertex; stimulation was ineffective due to the reversed position of the coil with respect to the scalp surface (i.e. the magnetic flux was dispersed to air). Notably, this Sham stimulation produces a similar tactile sensation and alerting (sound, somesthetic stimulation, etc.) to the active rTMS. The location of left AG and left IPS was automatically identified on the subject’s scalp using the SofTaxis navigator system (E.M.S. Italy, www.emsmedical.net), which uses a set of digitized skull landmarks (nasion, inion, and 2 pre-auricular points), about 40 scalp points entered with a Fastrak Polhemus digitizer system (Polhemus), and an averaged stereotaxic MRI atlas brain in Talairach space (Talairach and Tournoux 1988). The average Talairach coordinates in the SofTaxis navigator system were transformed through a linear transformation to each individual subject’s scalp. Such method has an error of about 5 mm over a method in which each subject’s own MRI is used for localization (Carducci and Brusco 2012). This strategy has been successful in previous rTMS studies (Capotosto et al. 2009, 2012, 2014; Sestieri et al. 2013; Passeri et al. 2015). A mechanical arm

maintained the handle of the coil angled at about 45° away from the midline and the center of the coil wings was positioned on the scalp, to deliver the maximum rTMS intensity over each site (individual peak of activation). The coordinates of the 2 cortical regions were based on previous fMRI studies assessing task-evoked activity during spatial attention (He et al. 2007) and SM (Wirth et al. 2011) tasks and were as follows: left AG: $-48, -67, 19$ (x, y, z in millimeters); left IPS: $-25, -63, 47$ (x, y, z in millimeters) (Fig. 2A). Of note, we only stimulated left hemisphere regions since the literature indicates a general left-ward asymmetry of semantic retrieval effects (Binder and Desai 2011). Moreover, the stimulation of both left and right hemisphere regions would have exceeded the total number of pulses allowed by the current stimulation guidelines (Rossi et al. 2009).

Electroencephalography Recordings

To assess the physiological impact of rTMS on anticipatory neural activity we simultaneously recorded EEG activity from the scalp. Specifically, we measured the effect of magnetic stimulation delivered over different cortical sites on the mean amplitude as well as on the peak latency and amplitude of EEG alpha desynchronization in parieto-occipital cortex.

EEG data were recorded (BrainAmp; bandpass, 0.05–100 Hz, sampling rate, 256 Hz; AC couple mode recording) from 32 EEG electrodes placed according to an augmented 10–20 system, and mounted on an elastic cap resistant to magnetic pulses. Electrode impedance was set below 5 K Ohm. The artifact of rTMS on the EEG activity lasted about 10 ms and did not alter the EEG power spectrum. Two electro-oculographic channels were used to monitor eye movements and blinking. The acquisition time lasted from -1 s before to $+3.5$ after cue onset. EEG trials contaminated by eye movements, blinking, or other involuntary movements (e.g. mouth, head, trunk, or arm) were off-line rejected. To remove the effects of the electric reference, EEG single trials were re-referenced by the common average reference, which includes the averaging of amplitude values at all electrodes and the subtraction of the mean value from the amplitude values at each single electrode. Following artifact removal, an average number of $40 (\pm 2)$ and $64 (\pm 1)$ trials per TMS condition for the SM and the VSA task, respectively, was available for the EEG analysis. One subject was excluded from the analysis since the corresponding profile of EEG power density spectra was clearly abnormal/artifactual in both tasks and

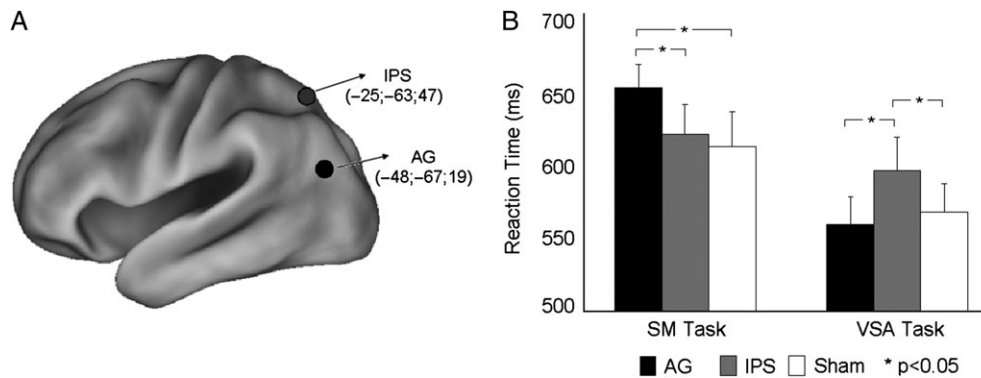


Figure 2. (A) Inflated view of left hemisphere atlas brain with regions of DAN and DMN as in meta-analysis of He et al. (2007) and Wirth et al. (2011). Regions with coordinates (millimeters) are stimulated with rTMS in this experiment. (B) Group means (\pm standard error, SE) of the RT (ms) for the 3 rTMS Conditions (AG, IPS, and Sham) as a function of Tasks (SM and VSA). Duncan post hoc tests: * $P < 0.05$.

all TMS conditions. Therefore, the reported behavioral and EEG results were obtained in the remaining 18 subjects.

Electroencephalography Analysis

To compare the desynchronization/synchronization (ERD/ERS) mean amplitude between the 3 TMS conditions in both tasks we carried out a stationary analysis, in which the frequency bands of interest were low and high alpha. These frequencies were determined in according to a standard procedure based on the peak of individual alpha frequency (IAF; Klimesch et al. 1998b). With respect to the IAF, these frequency bands were defined as follows: 1) low alpha, IAF - 2 Hz to IAF; and 2) high alpha, IAF to IAF + 2 Hz. This power spectrum analysis was based on an FFT approach using the Welch technique and the Hanning windowing function. The length of the EEG periods used as an input for FFT was of 1 s. The event-related desynchronization/synchronization (ERD/ERS) of alpha EEG oscillations was obtained using:

$$\text{ERD \%} = (E - R) / R \times 100$$

where E indicates the power density at the “event” (lasting 1 s) and R the power density at the “rest” (lasting 1 s). The ERD/ERS was computed for the IAF-based low- and high-alpha sub-bands. The “rest” of ERD/ERS computation was defined as a period from -1 to 0 s before the cue onset. The “event” of ERD/ERS computation was defined as a period from -1 s to 0 s before target onset. Notably, the results of the present study do not reflect an effect of the IAF since no significant statistical difference was observed in the measure of IAF across conditions and TMS task (SM: AG = 10.3 ± 0.2 , IPS = 10.4 ± 0.2 , Sham = 10.3 ± 0.2 ; VSA: AG = 10.4 ± 0.2 , IPS = 10.3 ± 0.2 , Sham = 10.4 ± 0.1).

Statistical Analyses

Statistical analyses were conducted using within-subject ANOVAs for repeated measures. Mauchley’s test was used to evaluate sphericity assumption, Greenhouse-Geisser procedure for correcting the degrees of freedom, and Duncan tests for post hoc comparisons ($P < 0.05$).

For the behavioral analyses we used RTs or percentage of correct responses (Hits) as dependent variables, and TMS Condition (AG, IPS, Sham) and Task (SM, VSA) as the within-subject factors. For the main analysis including both tasks the

averaged RTs of valid and invalid trials of the VSA task was used. In addition, a restricted preliminary analysis on the VSA task directly compared performance for valid versus invalid trials in order to test whether subjects effectively allocated attention to a specific portion of the visual field.

To test the influence of rTMS on EEG alpha rhythms during the anticipatory period, separate low- and high-alpha ERD/ERS mean amplitude were used as the dependent variables, and TMS Condition (AG, IPS, Sham) and Task (SM, VSA) as the within-subject factors. All statistical analyses were performed on the regional average of 4 parieto-occipital electrodes (i.e. P7, P8, O1, O2). Electrodes of interest were located in a more postero-ventral position with respect to the TMS sites (i.e. P3, CP3) to avoid any possible TMS residual artifact due to the charge/discharge of the coil. Importantly, alpha rhythms are dominant in the whole parieto-occipital region including P7/P8/O1/O2. To test for significant relationships between electrophysiological measures and visual performance, a correlation analysis (Pearson test, $P < 0.05$) was computed between alpha ERD/ERS mean amplitude and RTs to target stimuli in both tasks, separately for each TMS conditions and alpha sub-band.

Finally, a control analysis with low- and high-alpha power as the dependent variables and TMS condition as the within-subjects factor were conducted during the fixation-rest period of each task to ensure that rTMS delivered at different cortical sites did not affect the baseline power of each band of interest.

Results

Behavior

In the VSA task there was an overall significant main effect of target validity (RTs: valid, 551 ± 19 ms; invalid, 597 ± 19 ms; $F(1,17) = 18.3$, $P = 0.0005$; statistical power = 0.98) indicating that subjects effectively allocated attention to a specific location of the visual field.

The main analysis tested the behavioral effect produced by rTMS stimulation over different parietal sites during the execution of the VSA and SM tasks. Figure 2B presents the behavioral results during the 3 TMS conditions (i.e. AG, IPS, and Sham) in both tasks. A clear double dissociation was observed with AG stimulation affecting the SM task, and IPS stimulation affecting the VSA task. This impression was supported by a significant interaction of TMS Condition (AG, IPS, Sham) by Task (SM, VSA)

($F_{2,34} = 7.42$, $P = 0.002$, statistical power = 0.91), and relevant Duncan post hoc tests ($P < 0.05$). In particular, the speed of target discrimination during the SM task was significantly impaired following stimulation of AG (651 ms \pm 16) as compared to IPS (620 ms \pm 20; $P = 0.02$) or Sham (612 ms \pm 24; $P = 0.005$). In contrast, the speed of target discrimination during the VSA task was significantly delayed following rTMS over IPS (596 ms \pm 23) as compared to AG (559 ms \pm 19; $P = 0.01$) or Sham (567 ms \pm 19; $P = 0.035$). Importantly, there was no difference between Sham and IPS in the SM task ($P = 0.5$), and between Sham and AG in the VSA task ($P = 0.5$). The ANOVA on accuracy scores (Supplementary Table 1) did not reveal any significant effect indicating a selective interference with the speed of target discrimination.

Overall, these results confirm that IPS stimulation interferes with performance on a VSA task (as in Capotosto et al. 2012); in addition, we show a specific causal role of AG interference on a semantic decision task (see also Price et al. 2016).

ERD/ERS Mean Amplitude

Since the rTMS train lasted for 150ms, and was delivered simultaneously to the onset of the cue, we first verified that the EEG signals chosen for the analysis of alpha rhythms (-1 s to $+0$ s before target stimulus onset) were free of rTMS artifacts, and that an alpha frequency peak was clearly recognizable at all electrodes of interest (see Supplementary Fig. 1). Next, we examined whether rTMS interference delivered over distinct nodes of parietal cortex (AG or IPS) had a specific effect on the pre-target EEG alpha rhythms over parieto-occipital regions during SM and VSA tasks.

The mean amplitude of anticipatory low-frequency (~ 8 – 10 Hz) alpha ERD/ERS in parieto-occipital electrodes during the SM task was disrupted by AG, but not IPS, stimulation with a significant decrease of the desynchronization observed in Sham. In contrast, during the VSA task stimulation of IPS, but not of AG, disrupted the characteristic desynchronization observed in Sham. These observations were confirmed by a significant TMS Condition (AG, IPS, SHAM) by Task (SM, VSA) interaction ($F_{(2,34)} = 8.34$, $P = 0.001$, statistical power = 0.95). Duncan post hoc test indicated that magnetic stimulation of AG disrupted the ERD during the SM task compared to both IPS ($P = 0.03$) and Sham ($P = 0.02$) conditions, and that rTMS over IPS affected the ERD during the VSA task compared to both AG ($P = 0.005$) and Sham ($P = 0.0005$) conditions (Fig. 3A).

An even more robust double dissociation was observed in the analysis of the anticipatory high-frequency (~ 10 – 12 Hz) alpha desynchronization. There was a significant TMS Condition (AG, IPS, SHAM) by Task (SM, VSA) interaction ($F_{(2,34)} = 11.6$, $P = 0.0001$, statistical power = 0.99). Duncan post hoc tested indicated that magnetic stimulation of AG disrupted the ERD during the SM task compared to both IPS ($P = 0.007$) and Sham ($P = 0.006$) conditions, and that rTMS over IPS affected the ERD during the VSA task compared to both AG ($P = 0.001$) and Sham ($P = 0.0008$) conditions (Fig. 3B). As observed for the behavioral results, no significant difference was observed between Sham and IPS in the SM task ($P = 0.8$ for both low and high alpha), and between Sham and AG in the VSA task ($P = 0.3$ for low alpha and $P = 0.9$ for high alpha), corroborating the specificity of the stimulated site in both tasks. Interestingly, for both low- and high-alpha sub-bands, TMS over AG and IPS induced a paradoxical alpha synchronization (ERS) during the SM and VSA task, respectively.

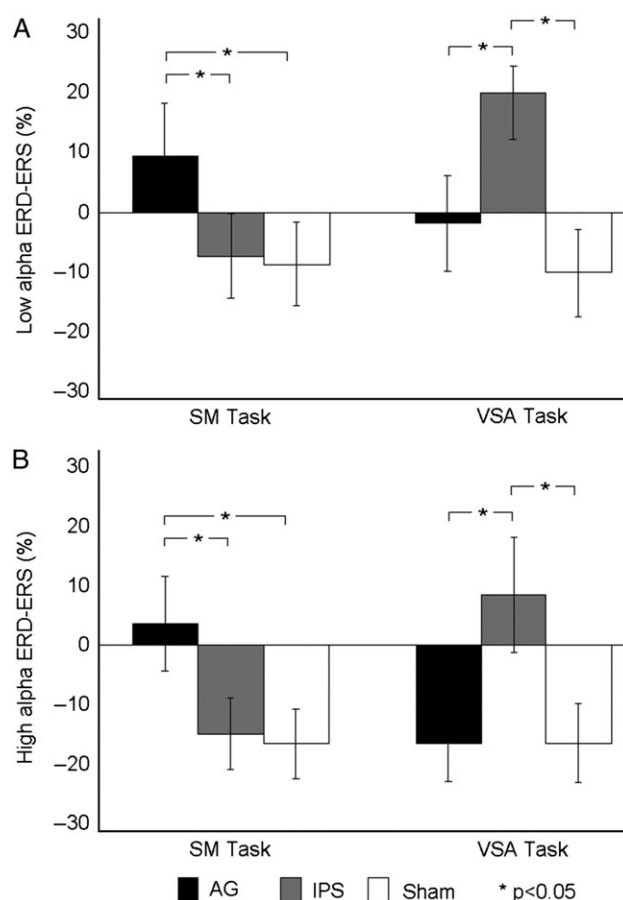


Figure 3. (A) Group means (\pm SE) of the low-alpha anticipatory ERD/ERS for the 3 rTMS Conditions (AG, IPS, and Sham) as a function of Tasks (SM and VSA). Duncan post hoc tests: $*P < 0.05$; (B) Group means (\pm SE) of the high-alpha anticipatory ERD/ERS for the 3 rTMS Conditions (AG, IPS, and Sham) as a function of Tasks (SM and VSA). Duncan post hoc tests: $*P < 0.05$.

Furthermore, we observed a stronger ERD in the high- compared to low-alpha band, regardless the TMS condition, in line with the stronger anticipatory effects on the high-alpha sub-band (10–12 Hz) observed in previous studies (Klimesch et al. 1998a; Capotosto et al. 2009, 2012). This was confirmed by the presence of a main effect of Band ($F_{(1,17)} = 16.3$, $P = 0.0001$, statistical power = 0.97) in an additional 3-way ANOVA with TMS Condition (AG, IPS, Sham), Task (SM, VSA) and Band (high and low alpha) as factors. Moreover, only for the high alpha we observed a significant positive correlation with the speed of semantic decisions across subjects during SHAM ($r = 0.47$, $P = 0.049$) and IPS ($r = 0.50$, $P = 0.037$) conditions, such that faster subjects had stronger parieto-occipital ERD. Interestingly, this brain-behavior correlation was lost during the AG condition (Supplementary Fig. 2). No significant correlation with behavior was observed in the VSA task.

Finally, a control analysis conducted separately for the 2 tasks and alpha sub-bands ruled out the possibility that the significant site-related differences of the EEG power during the cue-target period reflected corresponding differences of power modulation in the baseline period ($P > 0.2$ for each frequency band, see statistical analyses section).

Overall, these results support a double dissociation between the effect of AG and IPS magnetic stimulation over parieto-occipital alpha ERD during a semantic decision and VSA task, respectively.

Discussion

By combining EEG recordings with rTMS, the present study examined whether pre-stimulus alpha desynchronization in parieto-occipital cortex is specifically affected by suppression of 2 higher-order regions in human posterior parietal cortex: posterior IPS part of the DAN, and AG part of the DMN. The results indicate a clear double dissociation of task by cortical location. In particular, stimulation of IPS, but not AG, impaired both the typical anticipatory alpha desynchronization and the speed of target discrimination on a VSA task. Conversely, stimulation of AG, but not IPS, impaired both anticipatory alpha desynchronization and the speed of semantic judgments during a semantic decision task. These findings suggest the existence of multiple dedicated parietal channels for the modulation of anticipatory alpha rhythms, and support the notion that alpha rhythms reflect task-specific modulation of excitability in occipito-parietal cortex.

A Specific Role for Posterior IPS in Controlling Alpha Rhythms During Perceptual Attention

Alpha (8–12 Hz) power desynchronization is strongly associated to visual perception (Jensen et al. 2015) but has also been observed in a large variety of tasks, indicating a general role in task anticipation (Klimesch 2012). In previous work, we showed that suppression of preparatory activity in prefrontal (FEF) and dorsal parietal (posterior IPS) nodes of the DAN interferes with anticipatory alpha power in parieto-occipital electrodes (Capotosto et al. 2009, 2012) and the ability to discriminate visual targets. This effect was interpreted according to current models of attention in which regions of the DAN provide a top-down modulatory effect on visual areas in occipital cortex (Kastner and Ungerleider 2000; Corbetta and Shulman 2002). However, the task specificity of this modulation was not tested. It is possible for example that IPS plays a more general role in task preparation including maintenance of attention during the delay (temporal or sustained) or sensory encoding of the target irrespective of task demands.

The first novel result of the present study was to show that IPS stimulation plays an interference effect on parieto-occipital alpha desynchronization and behavior only in the VSA task, not in the SM task, in which attention was maintained during the delay. This result indicates that IPS contributes to the anticipation for the target specifically in the context of a visuo-spatial task. The region/s that we presumably interfere with lies along the IPS (horizontal and vertical segment) straddling toward the superior parietal lobule, and contains several retinotopic regions (IPSO–IPS5) (Silver and Kastner 2009) that have been implicated not only in covert VSA but also in eye movements and motion processing. This system contributes to different aspects of VSA. For instance while lateral areas within the IPS are specialized in maintaining attention, more medial areas in precuneus are involved in shifting attention from one location to another (Shulman et al. 2009; Spadone et al. 2015). Accordingly, in recent work we have been able to double dissociate with rTMS the causal role of these regions for different operations of visual attention (shifting vs. maintenance) (Capotosto et al. 2015).

Another important physiological feature of IPS modulation is the bilateral effect on visual target discrimination. In this study we stimulated only left IPS, and found bilateral slowing of RTs to left and right visual field stimuli and bilateral suppression of alpha desynchronization. This result is consistent

with previous studies from our group (Capotosto et al. 2009, 2012) in which we showed that separate left and right IPS stimulation have similar bilateral effect on alpha rhythms and visual performance. These bilateral modulatory effects can be understood by the observation that 1) focal TMS has widespread effects on the activity of large-scale neural networks (Eldaief et al. 2011; Andoh et al. 2015; Cocchi et al. 2015); 2) left and right regions of the DAN are strongly synchronized at rest and during tasks (Fox et al. 2005); and 3) lesions on one side of the brain have bilateral effects on brain network synchrony (e.g. Baldassarre et al. 2014, for effects of focal lesions on DAN synchrony bilaterally). From this point of view, stimulation of left IPS will affect contralateral regions of the DAN (i.e. right IPS and FEF) resulting in a bilateral effect in occipital cortex.

Finally, the present results fit with the idea that the modulation of IPS on alpha rhythms is stronger in the high-alpha sub-band (Capotosto et al. 2009, 2012; Spadone et al. 2015), consistent with a model in which distinct frequencies of alpha rhythms reflect different functional modes of thalamo-cortical and cortico-cortical loops that facilitate/inhibit the transmission and retrieval of sensorimotor and cognitive information (Pfurtscheller and Lopes da Silva 1999). Specifically, low-frequency alpha rhythms would diffusely regulate global brain arousal and alertness, whereas high-frequency alpha rhythms would reflect task-related oscillations of selective neural systems involved in the elaboration of task-specific information (Klimesch et al. 1998a).

Task and Regional Specificity of Anticipatory Alpha Rhythms

The second question addressed in the present study is the possibility that different higher-order parietal regions play a similar modulatory role on anticipatory alpha activity in different task context. This question is critical for the more general issue of whether anticipatory alpha rhythms are task general or task specific. In fact pre-stimulus alpha desynchronization has been observed during the anticipation of a variety of cognitive domains, including VSA (Jensen and Mazaheri 2010; Foxe and Snyder 2011), visual perception (Min et al. 2008), somatosensory (Babiloni et al. 2004), visuomotor (Filipovic et al. 2001), and SM tasks (Klimesch 1996).

To contrast IPS stimulation, we selected left AG, a region of the semantic network (Binder and Desai 2011) and one of the core parietal nodes of the DMN (Shulman et al. 1997). The DMN is recruited during semantic judgments, memory retrieval, and other internally directed processes. Moreover, there was prior evidence for a competitive relationship between DAN and DMN activity not only at rest but also during task processing (Sestieri et al. 2010, 2011). Finally, we had prior evidence that transient suppression of AG, but not IPS, in the resting state, characterized by spontaneous mind wandering and retrieval, modulates alpha power in parieto-occipital cortex (Capotosto et al. 2014).

The results clearly show a double dissociation both in terms of behavior and alpha power modulation of IPS versus AG stimulation. AG stimulation has no detectable effect on the VSA task, but causes delays in semantic judgments and disrupts the normal alpha desynchronization in parieto-occipital electrodes. Moreover, AG stimulation disrupts the significant correlation between ERD and speed of discrimination during the SM task observed during Sham and IPS stimulation. These findings strongly support the idea that AG has a modulatory effect on anticipatory alpha rhythms in occipital lobe, which is in turn consistent with previously described modulations of

alpha activity during the execution of SM tasks (Klimesch 1996; Klimesch 1999), and with behavioral TMS/transcranial direct current stimulation (tDCS) works showing that AG suppressive stimulation disrupts episodic memory retrieval (Sestieri et al. 2013) and semantic decisions (Price et al. 2016).

We can speculate about the preparatory processes in AG affected by rTMS. Anticipatory processes are important for memory retrieval tasks, since subjects can adopt a retrieval mode/orientation that facilitates subsequent memory discriminations (reviewed in Rugg and Wilding 2000). Since the left AG is thought to lie at the top of the hierarchy of the cortical regions involved in semantic decisions (reviewed in Binder and Desai 2011), it might be involved in the control of the preparatory activity through the modulation of alpha rhythms. In contrast to the spatial cue, here the cue did not provide task-specific information but mainly a temporal warning signal. However, the cue could have allowed a precise temporal alignment of a preparatory set for semantic decision that clearly involved a distributed network including sensory regions in the occipital lobe. It is known that cues can reset the phase of ongoing oscillations in task relevant regions, which aligns the phase of the oscillation with the onset of the expected target leading to more sensitive target processing (Fries 2005) (Fiebelkorn et al. 2011).

More generally, the results of IPS vis-à-vis AG magnetic stimulation extend recent models of “alpha gating”. Specifically, anticipatory alpha desynchronization is thought to index regional excitability for processing of task relevant information, complementing the role of neuronal synchronization in the gamma band in feedforward processing (Jensen and Mazaheri 2010; Jensen et al. 2015). Despite the apparent ubiquitous nature of alpha rhythms across multiple tasks (vision, attention, sensory-motor, memory, semantic, etc.), the “control” of alpha rhythms appears to be highly task and regional specific as shown here. Therefore local processes in parieto-occipital cortex indexed by alpha rhythms can be precisely controlled by different top-down mechanisms from higher-order cortices. While recent work in animals have shown the richness of these top-down influences in visual (Bosman et al. 2012) our work shows task-specific influences on alpha and behavior during semantic processing.

Conclusions

The present study shows that modulation of anticipatory alpha rhythms is both task and regional specific. While confirming the causal role of regions of the DAN in the control of spatial attention through modulation of anticipatory alpha rhythms, the present study demonstrates that magnetic stimulation of a regions of the DMN associated to a quite different cognitive domain (SM) also affects oscillatory alpha activity and behavioral performance in a task-specific manner. These findings demonstrate the presence of multiple dedicated parietal channels for the modulation of anticipatory alpha rhythms indicating that this oscillatory activity can be used by different brain networks as a mechanism to modulate cortical excitability depending on functional context.

Supplementary Material

Supplementary material can be found at: <http://www.cercor.oxfordjournals.org/>.

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Notes

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