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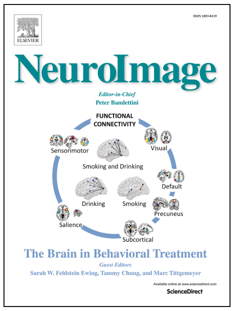

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Theta and Alpha oscillations as signatures of internal and external attention to delayed intentions: A magnetoencephalography (MEG) study

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Abstract

Background: Remembering to execute delayed intentions (i.e., prospective memory, PM) entails the allocation of internal and external attention. These processes are crucial for rehearsing PM intentions in memory and for monitoring the presence of the PM cue in the environment, respectively.

Aim: The study took advantage of the excellent spatial and temporal resolution of magnetoencephalography (MEG) to delineate the neural mechanisms of such memory and monitoring processes underlying PM.

Method: The spatio-temporal dynamic of theta and alpha oscillations were explored in 21 participants in two PM tasks and compared respect to a baseline condition (i.e., a lexical decision task with no PM instruction). The PM tasks varied for the load of internally-directed attention (Retrospective-load task) vs externally-directed attention (Monitoring-load task).

Results: Increase in theta activity was observed in the Retrospective-load task, and was particularly expressed in the regions of the Default Mode Network, such as in medial temporal regions, precuneus, posterior cingulate cortex and medial prefrontal cortex. By contrast, alpha decrease was the most relevant feature of the Monitoring-load task, and it was expressed over bilateral occipital, occipito-parietal and fronto-temporal regions, as well as over left dorsal fronto-parietal regions.

Conclusions: Theta and alpha oscillations are strictly associated with the direction of attention during the PM tasks. In particular, the theta increase is linked to internal attention necessary for maintaining the intention active in working memory, whereas the alpha decrease supports the external attention for detecting the PM cue in the environment.

Keywords: prospective memory, MEG, theta, alpha, attention, internal attention, delayed intention

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1. Introduction

"Life can only be understood backwards; but it must be lived forwards" is the famous quote by Søren Kierkegaard cited in the incipit of Cohen & Hicks's book (2017) on prospective memory (PM). Indeed, PM can be considered one of the cognitive functions that best exemplifies this concept. PM has been defined as the ability to remember to carry out future intentions at the appropriate moment (time-based PM) or when the appropriate event -the PM cue- occurs in the environment (event-based PM) (McDaniel & Einstein, 2007). Everyday PM intentions include, for example, remembering to take prescription pills after lunch or remembering to stop for gas as soon as an open station is seen. Most of literature has focused on event-based PM tasks and has revealed that the execution of PM tasks can be supported by multiple processes, typically clustered under the name of strategic monitoring and spontaneous retrieval (Einstein et al., 2005; Guynn, 2003). The extent to which these processes are involved strictly depends on the features of the PM task, such as the salience, predictability, emotional valence and focality of the PM cue (Cona et al., 2014, 2015a,2015b; McDaniel & Einstein, 2000; Einstein et al., 2005). In particular, the PM cue focality – which refers to the degree to which processing of the ongoing stimuli overlaps and stimulates processing of the PM cues – modulates the neurocognitive processes underlying the execution of PM tasks (e.g., Cona et al., 2014; 2016; Ihle et al., 2013; McDaniel & Einstein, 2000; McDaniel et al., 2013).

It has been proposed that the detection of the PM cue and the retrieval of PM intentions are mediated by bottom-up/spontaneous and top-down/strategic processes (Shelton et al., 2019). For example, in tasks with single, salient and/or focal PM cues, the intentions are triggered bottom-up by the PM cue and "pop up" into mind without strategic monitoring (Moscovitch, 1994; McDaniel & Einstein, 2007). Conversely, during tasks with nonfocal, less distinctive PM cues or multiple intentions, strategic monitoring is required (Einstein et al., 2005). Strategic monitoring entails two main processes: attentional, monitoring processes necessary for detecting the presence of the PM cue in the environment, and memory processes involved in maintaining and rehearsing the intention in mind (Guynn, 2003).

A recent neurocognitive model -the Attention to Delayed Intention (AtoDI) model- has defined strategic monitoring as a set of top-down attentional processes allocated to external and internal stimuli and has mapped such processes in the brain (Cona, Scarpazza, Sartori, Moscovitch, & Bisiacchi, 2015c). More specifically, PM tasks may imply the allocation of top-down attention, which is directed both externally -towards the external/environmental stimuli- and internally -

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towards the representation of intention (Cona et al., 2015c; 2016). These processes rely on the activation of dorsal frontoparietal network (Cona et al., 2015c, see also Cona & Rothen, 2019 for a recent review). On the other hand, when the PM cue occurs in the environment, the ventral frontoparietal network is activated to support bottom-up attention, which would be captured by the external stimulus (the PM cue) and internally, by the associated intention to fulfil (Cona et al., 2015c).

The dissociation between dorsal and ventral frontoparietal networks has been also highlighted by another model, the Dual Pathways model, which proposed the existence of two pathways to fulfil PM intentions (McDaniel et al., 2015). The first pathway comprises dorsal frontal regions, such as the frontal eye fields and dorsolateral prefrontal cortex (DLPFC), insular cortices and anterior cingulate cortex (ACC), as well as parietal regions as the precuneus. Similar to the AtoDI model, the Dual Pathways model posits that this pathway underpins top-down attentional and memory processes involved in strategic monitoring. According to both the AtoDI and the Dual Pathways model, the extent to which this pathway is recruited depends on the features of the PM task. The second pathway involves the ventral frontoparietal network and medial temporal regions, supports bottom-up spontaneous retrieval processes, and is mainly activated when focal and/or salient PM cues occur in the environment (McDaniel et al., 2013; 2015).

Aside from frontoparietal networks, anterior prefrontal cortex (aPFC) has been shown to play a central role in PM. In particular, a consistent pattern of lateral aPFC activation coupled by medial aPFC deactivation has been found across the studies (Burgess et al., 2011; Barban et al., 2013; Cona et al., 2015c; Gilbert, 2011). This pattern has been interpreted within the ‘gateway hypothesis’ framework (Burgess et al., 2007; Gilbert et al., 2005; Henseler et al., 2011), according to which lateral and medial aPFC regions are deputed to stimulus-independent and stimulus-oriented processes, respectively. Lateral and medial aPFC regions would thus act to bias the attention between the internally representation of PM intention and the external stimuli (Barban et al., 2013, 2014; Henseler et al., 2011).

All these findings have been obtained, however, by using fMRI: a neuroimaging technique characterized by good spatial resolution but poor temporal resolution. Also, fMRI relies on hemodynamic data, not on the actual electromagnetic neuronal activity.

In the present study we explored for the first time the neural underpinnings of strategic monitoring processes implied in event-based PM tasks with magnetoencephalography (MEG). This technique owns good spatial resolution and excellent temporal resolution. More importantly, this technique allows the direct and non-invasive measure of neuronal magnetic activity, rather than relying on indirect hemodynamic and metabolic estimations. So far, only one old study explored the neural

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mechanisms of event-based PM using MEG (Martin et al., 2007). Martin and collaborators focused on the processes engaged when the PM cue occurs and did not explore strategic monitoring processes. The study focused on theta and alpha bands and showed that PM cues elicited an earlier activation in parietal regions – likely associated with PM detection – followed by hippocampal activation, likely related to the search of the intention in the memory (Martin et al., 2007). Importantly, its conclusions should be considered with caution, as five participants only were tested.

Besides this study, Cruz and co-authors have applied EEG time-frequency analysis to a time-based PM task (Cruz et al., 2017). They focused on brain activity located at the anterior cingulate cortex and showed reduced theta power and stronger alpha suppression evoked by the ongoing stimuli while participants were maintaining time-based intentions respect to the ongoing task-only condition (Cruz et al., 2017).

Our study is thus aimed at characterizing the dynamics and location of theta and alpha activity during an event-based PM task, disentangling the neural mechanisms of the two main processes composing strategic monitoring: attentional monitoring and PM intention maintaining/rehearsing. As postulated in the AtoDI model, these processes imply attention to be directed towards external stimuli and internal representation of intention, respectively (Cona et al., 2015c).

We specifically recorded brain activity during two different PM tasks: a 'Monitoring-load' PM task and a 'Retrospective-load' PM task. These tasks have been already validated in a previous study as they are effective in emphasizing externally and internally directed attention, respectively (Cona et al., 2017). The PM cue is nonsalient and nonfocal in the Monitoring-load PM task, thus requiring top-down attention to be detected. By contrast, the PM cue is highly salient and focal in the Retrospective-load PM task, but multiple intentions are to remember. As such, the successfully rehearse and retrieve of PM intentions require a greater amount of resources.

In this previous transcranial magnetic stimulation (TMS) study, we have shown that the superior parietal cortex causally contributes to bias and balance the allocation of top-down attention between the external stimuli and the internal representation of PM intention. As the TMS was focally delivered over the superior parietal cortex, no information about other brain regions can be inferred from this study. In this regard, the MEG exploration is powerful in providing a characterization of whole-brain dynamics.

We opted to focus on theta (4-7 Hz) and alpha (8-13 Hz) activity in line with the study by Martin et al. (2007) and on the basis of previous evidence on the functional significance of these brain oscillations. The alpha rhythm is the dominant oscillatory rhythm of the human brain (Niedermeyer & Lopes da Silva, 2005). The reduction of alpha activity has been classically shown associated with

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increasing attentional load of the task. The most general and consistent observation is indeed that brain regions that are activated during a cognitive task exhibit a decrease in alpha activity (alpha desynchronization), whereas brain regions that are "at rest" or that are involved in irrelevant/interfering processes show alpha increase (alpha synchronization) (Pfurtscheller, Stancak, & Neuper, 1996; see Klimesch et al., 2012 *for a recent review*). Alpha band oscillations have been proposed to act as a sensory gating mechanism, associated with the enhancement of relevant sensory information processing coupled by suppression of irrelevant information processing (Foxe and Snyder, 2011; Jensen & Mazaheri, 2010). Alpha activity plays a crucial role for attention by regulating processes within and outside the focus of attention (Klimesch, 2012). Notably, some studies have explored posterior alpha as a possible index of internal and external attention, showing that external attention has been linked to alpha decreases, whereas internally directed attention has been primarily associated with alpha increases (Benedek et al., 2014; Pfurtscheller et al., 1996; O'Connell et al., 2009).

A great emphasis has been given to theta band oscillations in memory processes in both animal (Huxter et al., 2003; O'Keefe and Recce, 1993) and human research (Caplan et al., 2003; Ekstrom et al., 2005; Guderian and Duzel, 2005; Osipova et al., 2006; Raghavachari et al., 2001; see for a recent review Duzel et al., 2010). There is now consistent evidence that cortical theta activity plays a central role in memory-related processes, such as episodic, autobiographical and working memory (Fuentemilla et al., 2014; Raghavachari et al., 2001). In particular, recent studies found that theta oscillations mediate a dynamic orchestration between medial temporal lobe and neocortical regions (especially precuneus and medial prefrontal cortex), and they proposed that this interplay supports memory integration and reinstatement during recollection (Backus et al., 2016; Fuentemilla et al., 2014).

According to such body of evidence, we hypothesized that alpha decrease would be the elective candidate for indexing attentional monitoring processes and for driving external-directed attention. If so, we expected that alpha decrease was more prominent in the Monitoring-load PM tasks, especially over attention-related regions. Theta activity would instead index internally directed attention, which would be allocated towards the representation of intention stored in memory and thus would contribute to PM cue-intention mapping integration and refresh. Based on this view, theta activity should be more pronounced in the Retrospective-Load PM tasks, especially over memory-related regions.

2. Methods

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2.1 Participants

A sample of 21 healthy participants took part voluntarily in the study. The mean age of participants was 24.67 years (SD = 2.24, range = 21-29), and their mean education was 16.86 years (SD = 1.1, range = 15-20).

All participants were right-handed. The study was approved by the local ethics committee (ASL Veneto Regional Committee) and it was conducted following the guidelines of the Helsinki declaration. All subjects signed a written informed consent prior to their participation.

2.2 Recording Procedure

MEG data acquisition and analysis have been carefully described in our previous work (e.g., Pellegrino et al., 2019). MEG scans were performed at the MEG-lab (IRCCS S. Camillo Hospital, Venice) using a whole head, 275-channel system (CTF-MEG). This system is in a magnetically shielded room. Before entering the magnetically shielded room, participants underwent the initial preparation, which consisted of the placement of three head coils on three anatomical landmarks (nasion, left and right preauricular points) to monitor head position with respect to the MEG sensors during the recording. Six external electrodes were also placed to record VEOG, HEOG, ECG (bipolar montage). Head shape and coil position were digitized using a Polhemus Fastrak system. Data were sampled continuously during the tasks. The sample rate was set at 1200 Hz, with a hardware anti-aliasing low pass filter at 300 Hz. The total duration of the experiment was approximately 45 minutes. In a separate session, all participants underwent an MRI scanning session (Philips Achieva, 1.5 T) to obtain a T1-3d scan, which was then used for estimating an individual head model for source imaging.

2.3 Task procedure

The tasks were similar to those used in the study by Cona et al. (2017), to which the reader is referred for further details. Briefly, the experiment was programmed with the free software Psychopy (version 1.85.2; Peirce, 2007). Visual stimuli (letters and words) were presented with a video-projector located outside the shielded room. The images were projected over a MEG-compatible screen, subtended about 4° of visual angle on the horizontal plane. Stimuli were presented in black color, Lucida Console, font on a gray background screen. Salient words (PM words) were underlined. An MEG compatible response box (Lumitouch) comprising five different keys was used. Participants were instructed that they would be required to perform a lexical decision task (i.e., the ongoing task) and no mention was made about the focus on prospective memory. They were required to respond to the stimuli as fast and accurate as possible, always with

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the right hand. In the first block (*Baseline Block*), the participants were asked to perform a simple lexical decision task, i.e., the *Ongoing Task.* This block consisted of 120 trials, each of which was organized as follow: a fixation symbol (+) with a pseudorandom duration (1250, 1500, or 1750 ms) was presented, followed by a string of letters. Participants were asked to respond whether the string of letters was an existing word or not by pressing two keys (key 1 and key 2) with the index finger and the middle finger, respectively. The mapping between keys and responses was counterbalanced across participants.

After the *Baseline Block*, participants were asked to perform two PM blocks – the *Retrospective-load Block* and the *Monitoring-load Block*, administered in counterbalanced order across participants. In both the blocks, together with the ongoing task, i.e. the lexical decision task, the participants were asked to perform an additional - Prospective Memory (PM) - task.

In the *Retrospective-load Block*, participants were instructed to remember to execute three distinct intentions associated with three different PM words. More specifically, they had to remember to press the key 3 with the middle finger when the word 'GRIGIO' (grey in English) occurred, the key 4 with the ring finger when the word 'AZZURRO' (cyan) occurred, and the key 5 with the little finger when the word 'ROSSO (red) occurred. Importantly, these PM words were always underlined. As such, they were highly salient. Also, participants were informed that only PM words would have been underlined, thus the monitoring load was minimized.

In the *Monitoring-load Block*, participants were asked to remember to execute only one intention, that is pressing the key 3 with the middle finger when the syllable ('PRA') occurred within the string of letters. The PM cue was never underlined so it was not salient. A large body of studies demonstrated that this task was able to emphasize monitoring processes (e.g., Einstein et al., 2005; Scullin et al., 2010). Each PM block comprised 120 ongoing trials and 10 PM trials. The PM cues were presented in the sequence of the ongoing trials in a pseudo-random fashion. Importantly, in each PM block, at least 10 ongoing trials occurred before the first PM cue and at least 8 were presented between two consecutive PM cues. At the beginning of the experiment, a practice block involving only the ongoing task (five words/nonwords trials) was administered.

2.4 MEG Preprocessing

MEG data pre-processing was performed with MATLAB and Brainstorm (Tadel, Baillet, Mosher, Pantazis, & Leahy, 2011) (March 2018 version), which is documented and freely available for download under the GNU general public license (http://neuroimage.usc.edu/brainstorm). Continuous raw data were initially downsampled at 600 Hz. Signal-Space Projection algorithm was used to identify and remove cardiac, eye movement, and dental artifacts from the recordings.

To improve accuracy of trigger timing, digital triggers were adjusted off-line according to the actual stimulus presentation assessed with a photodiode. Data were cut in segmented epochs starting from -1.5 seconds from the beginning of the stimulus (word or nonword) to 1.5 seconds after the stimulus. The length of the epochs was chosen to avoid border effects in the time-frequency analysis. The trials were then visually inspected and those containing artifacts were excluded. After trial rejection each participant had an average of 107.61 trials (SD = 6.21) for each block.

2.5 Source estimation

For the source analysis, Individual T1 MRI scans were segmented by means of the *recon-all* routine of Freesurfer image analysis suite, which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/). The technical details of this segmentation procedure are described in prior publications (Dale, Fischl, & Sereno, 1999). MRI and MEG data were aligned using the digitized position of head coils and head shape. The MEG forward model was calculated from the segmented MRI data, with overlapping spheres method (Pellegrino et al., 2018). The inverse problem was resolved by applying the weighted Minimum Norm Estimate algorithm with Brainstorm default settings [depth weighting (Order[0,1]) = 0.5, Maximal amount = 10; Noise covariance regularization = 0.1; 1/λ = 3)]. The solution was restricted to the cortical surface and the dipole direction was constrained to be orthogonal to the surface meshes (constrained sources). The noise covariance was calculated from 3 minutes of empty room recording, performed immediately after each participant's recording session.

2.6. Time Frequency analysis

Time-frequency (TF) analysis was performed taking into account the *Ongoing* trials of each block (words and nonwords). Only ongoing trials with correct responses were included in the analysis. The PM trials were excluded for two reasons: 1) from a theoretical standpoint, because the processes related to monitoring and intention rehearsal are typically studied analyzing the ongoing trials; 2) from a practical standpoint, because there were too few PM cues to enable a reliable analysis.

To extract Time-Frequency activity in each frequency band (Theta (4-7 Hz) and Alpha (8-13 Hz)), we used the Hilbert transform, which consists of filtering the data in the frequency of interest, and then calculating the envelope of the filtered signal. We extracted the Magnitude value for each source vertex, and for each timepoints, and we then averaged the values within each block. We finally calculated the Event-Related Synchronization/Desynchronization (ERS/ERD), using the -500 ms -200 ms time window prior to the target presentation as baseline, by applying the following

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formula: [(Epoch_Signal - Baseline_mean)/(Baseline_mean)]*100. The final result of this procedure was an ERS/ERD cortical map for each timepoint.

2.7. Statistical analysis

Behavioural data were analysed using a repeated measure ANOVA with *Block* as a within factor (three levels: *Baseline, Retrospective-Load, Monitoring-Load*). Two separate ANOVAs were run, using mean Reaction Times (RTs) and proportion of accuracy as dependent variables. The significance level of the post-hoc comparisons was adjusted with the False Discovery Rate (FDR) correction for multiple comparisons whenever appropriate (Benjamini & Hochberg, 1995).

Differences in MEG oscillations among the three blocks were tested with a cluster-based permutation analysis (Groppe et al., 2011; Maris & Oostenveld, 2007). In the initial step of this analysis, significant t-values that were found spatially or temporally adjacent from univariate analysis were grouped in clusters (in this phase, negative and positive clusters were treated separately and t-values whose p-value was inferior to .025 were considered to be significant). The statistics for each cluster (i.e. cluster mass) were computed as the sum of the all t-values associated with that cluster. A large number of permutations across conditions (typically one thousand) were then performed to build a null distribution of the cluster mass. For each cluster, the cluster mass of the observed clusters was compared to this null distribution to derive a single p-value. This procedure provides a good balance between type 1 error and power to detect significant effects, taking into account the spatiotemporal correlation of EEG or MEG data. For all these reasons, it is one of the most commonly used approaches for MEG analysis. It should be noted that this procedure accounts for multiple comparisons. We run six cluster-based permutation analyses with 1000 permutations, one for each paired comparison (Baseline Block vs Retrospective-Load Block, Baseline Block vs Monitoring-Load Block, Retrospective-Load Block vs Monitoring-Load Block), and separately for theta and alpha. For each contrast, a single cluster-based permutation was performed in the 0-800 ms time window, and the Time-Frequency maps were downsampled at 150 Hz to reduce the computational burden. For each cluster-based permutation, we report the cluster mass (that is the sum of all t-values), and the cluster size, which is the total number of vertices (also along adjacent timepoints) with the corresponding t-values.

2.8 Data and code availability

The main results of the analyses can be found online in the Open Science Framework, at this link: https://osf.io/7wfbv/, in the form of a Brainstorm protocol. The same link includes the videos

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illustrating the time course of the MEG effects for both the theta and alpha activity and for each comparison investigated. The raw data and codes are available only for the researchers afferent to IRCCS San Camillo Hospital, in line with the national rules for research institutes of the Ministry of Health.

3. Results

3.1 Behavioral Results

Ongoing task. The ANOVA on the mean reaction times (RTs) in the Ongoing task showed the significant effect of Block [F(2,40)= 54.53; p < 0.0001; ges= 0.26]. Post-hoc comparisons showed that RTs were longer in the Monitoring-load Block [Mean = 915 msec; Standard Deviation (SD) = 129], intermediate in the Retrospective-load Block [Mean = 815 msec; SD = 132], and shorter in the Baseline Block [Mean = 737 msec; SD = 116] (p < 0.0001, consistently).

The ANOVA on the proportion of accuracy revealed the significant effect of Block [F(2, 40) = 3.42; p < 0.04; ges = 0.07]. Post-hoc FDR comparisons showed that performance accuracy was slightly higher in Retrospective-load Block [Mean = 0.98; SD = 0.14] than in Monitoring-load Block (Mean = 0.96; SD = 0.18), showing a marginally significant difference (p = 0.05). Conversely, no significant differences were observed comparing the two blocks with the Baseline Block (Mean = 0.97; SD = 0.16).

PM task. Participants took longer to execute intentions in the Retrospective-load PM task (Mean = 1206 msec; SD = 299) than in the Monitoring-load PM task (Mean = 907; SD = 145), [F(1,20) = 34.62, p < 0.0001, ges = 0.30]. The ANOVA on the PM accuracy indicated that the level of performance did not significantly differ between the Monitoring-load PM task (Mean = 0.83; SD = 0.13) and the Retrospective-load PM task (Mean = .87; SD = 0.14) [F(1,20)= 1.11; p = 0.30; ges= 0.19].

3.2 MEG Results

In the following paragraphs, the differences in theta and alpha band activity between the three experimental blocks of interest have been presented.

Additional materials can be found online in the Open Science Framework, at this link: https://osf.io/7wfbv/. The online material includes the main results of the analyses, in the form

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of a Brainstorm protocol, and the videos illustrating the time course of the MEG effects for both the theta and alpha activity and for each comparison shown below.

Retrospective-load Block vs. Baseline Block

Theta. Time-frequency analysis was run to compare theta band activity evoked in the ongoing trials in Retrospective-load Block versus Baseline Block (Figure 1). The analysis showed that Retrospective-load Block was characterized by an increase in theta band activity [Cluster 1: left hemisphere, p = 0.004, cluster mass = 472538, cluster size = 170118; Cluster 2: right hemisphere, p = 0.002, cluster mass =536589, cluster size=195420;]. The effect was stronger around 250-350 ms over bilateral occipital regions and over a set of right anterior regions (insular and inferior frontal regions and ventral premotor cortex and frontal eye fields). Such theta activity become more pronounced around 500 ms and lasted for several hundred milliseconds, involving both lateral and medial regions of both the hemispheres. Laterally, the theta band was widespread over bilateral posterior regions, inferior temporal regions and anterior temporal poles, and inferior frontal/insular regions coupled by dorsal frontal activity (Figure 1a). Medially, theta activity was long-lasting and expressed over medial temporal regions, over medial PFC (mPFC), precuneus, and supplementary motor cortex as well as over both the anterior the posterior cingulate cortices (Figure 1b). The greatest difference in theta activity between Retrospective-load Block and the Baseline block was shown in the late windows, around 600 and 800 ms, when theta band was widely expressed over the scalp.

Alpha. No significant difference was observed in the alpha band activity between the Retrospective-load Block versus the Baseline Block.

Monitoring-load Block vs. Baseline Block

Theta. The analysis of theta activity between the Monitoring-load Block and the Baseline Block showed two opposite patterns of distribution (Figure 2a) [Cluster 1: left hemisphere, p = 0.008, cluster mass =354445, cluster size=129925; Cluster 2: left hemisphere: p = 0.04, cluster mass= -231078, cluster size=80612; right hemisphere, p = 0.047, cluster mass = -219999, cluster size = 80188]. In the Monitoring-load Block, an initial reduction of theta activity was shown starting at the onset of the ongoing stimulus and distributed first over the right regions of the ventral pathway (occipital and temporal), and then (at 150 ms) spreading over more anterior regions located mainly over right fronto-temporal regions. A long-lasting reduction of the theta band was also observed over fronto-central regions in the left hemisphere. Such pattern of theta reduction was coupled by an increase in theta activity starting later (at ~ 300 ms) and occurring selectively in the left hemisphere: first in the occipital and in the inferior temporal regions, subsequently (at ~ 500 ms) over inferior frontal and prefrontal regions and finally over left medial regions that included medial temporal lobe, posterior cingulate cortex, anterior cingulate cortex and mPFC (at ~ 600 ms), and dorsal fronto-parietal regions (at ~ 750 ms).

Alpha. The analysis indicated a general reduction of alpha activity in the Monitoring-load Block respect to the Baseline Block (Figure 2b) [Cluster 1: left hemisphere, p = 0.01, cluster mass =-650151, cluster size = 236917; Cluster 2: right hemisphere, p = 0.02, cluster mass =-523187, cluster size =186891]. Such reduction was observed early, at the onset of the stimulus, and was expressed over bilateral posterior regions, internally over cuneus and precuneus, and over left insular/inferior frontal regions. Subsequently (at ~ 350 ms) the alpha activity reduction was also expressed over left dorsal frontal regions, extending over left central regions and medially towards left supplementary motor regions and anterior cingulate cortex. Later, at ~ 700 ms, such reduction involved bilateral dorsal parietal regions and precuneus, and right angular gyrus. Over the occipital regions, a bilateral sustained alpha desynchronization was present over the entire time-window.

Retrospective-load Block vs. Monitoring-load Block.

Theta. As compared with the Monitoring-load Block, the Retrospective-load Block was characterized by the increased sustained theta activity selectively over the right hemisphere (Figure 3a) [Cluster 1: right hemisphere, p = 0.02; cluster mass =414888, cluster size =155721). This theta activity was observed starting around 100 ms over right insular and right superior parietal regions, and then (~ 300-400 ms) spreading and being pronounced over inferior parietal regions (e.g., angular gyrus and supra-marginal gyrus), fronto-temporal regions and central regions (which include pre-central and post-central gyri). In later time windows (~ 600-800 ms), theta activity was more confined over right central and parietal regions, and medially, over precuneus and posterior cingulate cortex.

Alpha. As compared with the Monitoring-load Block, the Retrospective-load Block showed an increased alpha activity [Cluster 1: left hemisphere, p = 0.01, cluster mass = 727172, cluster size =258427; Cluster 2: right hemisphere, p = 0.02, cluster mass = 532616, cluster size =184664], which was first observed over the inferior-temporal and temporo-occipital regions of the left hemisphere (~ 100) and over bilateral medial posterior temporal regions (Figure 3b). At around 250 ms, the increased alpha activity in the Retrospective-load Block was shown over bilateral parieto-occipital regions, and right precuneus. In later time windows (~ 650-800 ms), the difference in alpha activity between the two blocks became more pronounced and widespread, with Retrospective-load Block being characterized by higher alpha activity over posterior regions,

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ventral prefrontal and temporal regions. Interestingly, in these time windows, alpha activity was increased in the Retrospective-load Block than in the Monitoring-load Block in medial regions of that included precuneus, posterior cingulate and anterior cingulate cortices, medial temporal regions and mPFC.

4. Discussion

This study investigated theta and alpha dynamics accompanying strategic monitoring and memory processes that are involved when individuals are required to remember future intentions. Within the AtoDI model (Cona et al., 2015c), these PM processes are conceptualized as top-down externally and internally directed attention, respectively. In many circumstances, for a successful fulfilment of PM tasks, attention needs to be allocated both toward environmental stimuli and the representation of prospective intentions.

The MEG dynamics during 'Retrospective-load' PM task showed that internally directed attention, involved in maintaining and rehearsing multiple intentions in working memory, is associated with an increase in theta oscillations, especially in late time windows (when individuals were likely to be no longer engaged in responding to ongoing stimuli). The increase in theta oscillations was observed over both lateral and medial regions. Over lateral regions, the increase in theta oscillations was first evoked in parieto-occipital regions, and then became widely distributed bilaterally, over temporal and frontal regions. Interestingly, the theta activity was prominently expressed in medial regions of temporal lobe (hippocampal formation), in precuneus and posterior cingulate cortex, as well as over mPFC.

These brain regions constitute the default mode network (DMN), as previously identified with fMRI and PET (Damoiseaux et al., 2006; Fox et al., 2005; Raichle et al., 2001; Shulman et al., 1997). In particular, several studies showed that the increase in frontal midline theta activity is associated with decreased BOLD signal in DMN regions, and is linked to increasing working memory demands (Michels et al., 2010; Scheeringa et al., 2009). A recent MEG study showed that hippocampal-mPFC theta oscillations facilitate memory processes by supporting memory integration (Backus et al., 2016). Theta oscillations would enable communication between the hippocampus and mPFC by orchestrating the integration of memories. Functional interaction between these two structures is indeed supported by strong anatomical inter-connections (Jay and Witter, 1991; Xu and Südhof, 2013). This interpretation fits nicely with our pattern of findings as multiple PM cue-intention associations needed to be maintained in 'Retrospective-load' PM task,

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and has been also adopted by Landsiedel and Gilbert (2015) to describe the reduction of deactivation in task-negative brain regions when the memory load was increased.

Moreover, in line with the pattern of findings documented by Landsiedel and Gilbert (2015), we found a theta increase selectively over mPFC, whereas no MEG modulations were observed over lateral PFC. The authors proposed that, while mPFC plays a role in representing the content of delayed intentions, lateral PFC has instead a content-free role in PM tasks (Gilbert, 2011), likely mediating a general predisposition to act.

The absence of theta (or alpha) modulation over lateral PFC might appear in contrast with previous findings from PET and fMRI studies on PM. This discrepancy could however be easily explained by the analysis approach used in the present study. We indeed extracted the event-related activity evoked in the ongoing trials by subtracting the activity in the pre-stimulus baseline. This kind of analysis is more suitable to capture transient processes, closely related to stimulus occurrence, rather than to detect sustained, stimulus-independent processes, which characterize the PFC involvement in PM tasks.

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As compared with the Monitoring-load Block, the Retrospective-load Block was characterized by an increased theta activity selectively over the right hemisphere, expressed over insular, fronto-temporal, central and parietal regions. It is difficult to ascertain whether such lateralization is mainly due to the difference between strategic monitoring versus memory processes (or in other words, between external versus internal attention) or is due to intrinsic features of the PM cue to look for (color word versus syllable). Nevertheless, the involvement of the right parietal regions selectively in the Retrospective-load PM task is consistent with our previous TMS study (Cona et al., 2017). We indeed demonstrated that, while TMS of the left parietal site produced a facilitation of the PM performance in both Monitoring- and Retrospective- tasks, only the Retrospective-load condition was coupled by a concurrent slowing down of responses to the ongoing task when TMS was applied not only to the left but also to the right parietal site.

The Monitoring-load PM task was characterized by an early reduction of theta activity over lateral regions including parietal regions and insular, fronto-temporal regions, followed by a late increase in theta activity, expressed especially in medial regions such as precuneus and posterior cingulate cortex. The pattern of theta activity might indicate a balance between external and internal attention. The reduction of theta oscillations might indeed reflect the process of directing attention towards the external stimuli, in order to monitor for the presence of the PM cue, which is less distinctive in the Monitoring-load PM task then in the Retrospective-load PM task. By contrast, the medial theta activity might act to maintain and retrieve the intention in memory, which is a process that – although with a less extent respect to the Retrospective-load PM task – is involved in the Monitoring-load PM task as well.

Importantly, the Monitoring-load PM task is characterized by a marked and sustained reduction of alpha activity, which occurred early over posterior regions (occipital, parietal regions), and over frontal regions mostly of the left hemisphere. According to previous literature, alpha decrease is thought as an index of attention, and acts as a sensory gating mechanism, enhancing processing of relevant stimuli while inhibiting irrelevant information processing (Foxe & Snyder, 2011; Jensen & Mazaheri, 2010; Klimesch, 2012). Such bias of attention plays indeed a key role in strategic monitoring, thus it is plausible that is mainly involved in the Monitoring-load PM task, which entails the top-down allocation of selective attention to detect the PM cue (i.e. a specific syllable) embedded within PM-irrelevant information (i.e., the ongoing stimuli) (Barban et al., 2015; Cona et al., 2015c; McDaniel et al., 2015). Importantly, new insights about the temporal dynamics of the alpha decrease associated with strategic monitoring can be inferred. Very early, at the onset of the stimulus, the alpha reduction is observed over bilateral posterior regions and over left insular/inferior frontal regions and might reflect the "readiness mode" (Cona et al., 2012). The readiness mode indeed entails the recruitment of attentional resources in order to be in a state of readiness and preparedness to respond to the PM cues. An early, event-related potential, modulation over the same regions - posterior and frontal sites - has been indeed found in a study exploring strategic monitoring processes and has been linked to readiness mode (Cona et al., 2012). Subsequently (at around 350 ms), such alpha reduction was spread over left dorsal frontal regions, left supplementary motor regions (and frontal eye field) and anterior cingulate cortex. At around 700 ms, it was extended also over bilateral dorsal parietal regions and precuneus, and right angular gyrus. Dorsal fronto-parietal regions form the so-called dorsal attention network (Corbetta et al., 2008; Power et al., 2011) and would contribute to the allocation of top-down attention toward the external stimuli needed to detect the presence of the PM cue in the envirorment according to both the AtoDI model and the Dual Pathway model (Cona et al., 2015c; McDaniel et al., 2015). The comparison of the alpha power between the Monitoring-load task and the Retrospective-load task corroborates this view, showing an increased alpha activity in the Retrospective-load task or, in other words, a long-lasting reduction of alpha activity in the Monitoring-load task in occipital and parieto-occipital and posterior temporal regions. In later windows (650-800 ms), such decreased alpha power in the Monitoring-load task became more widespread, involving also ventral prefrontal and temporal regions. Interestingly, in these time windows, the alpha activity was higher in the Retrospective-load Block than in the Monitoring-load Block, especially in medial regions that include precuneus, posterior cingulate and anterior cingulate cortices, medial temporal regions and

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mPFC. Most of these regions are part of the Default Mode network, classically linked to memory and ‘more internal’, stimulus-independent, processes, such as mind-wandering and introspection (Buckner et al., 2008).

Yet, when comparing the Retrospective-load Block with the Baseline Block, we did not find any modulation in the alpha power and, more specifically, any increase in the alpha power as instead expected based on previous literature. Indeed, alpha decrease and alpha increase were suggested to be associated with externally-directed and internally-directed attention, respectively (Benedek et al., 2014; Bonnefond & Jensen, 2012; Pfurtscheller et al., 1996; O'Connell et al., 2009). For example, according to Mo et al. (2013), increased occipital alpha oscillations elicited by internal attention tasks would serve to suppress visual activity in order to protect internal processes from being perturbed by external sensory information. By contrast, decreased alpha over occipital regions triggered by external attention tasks would enhance the excitability of visual cortex in order to improve processing of external sensory inputs.

Our study confirmed the function of alpha decrease in signal enhancement, which would serve in PM tasks to monitor for the presence of the PM cues in the environment, but did not provide a clear evidence for a contribution of alpha increase in suppressing the processing of external information in order to direct internally the attention toward the representation of intention. As such, our findings are more in line with the most recent views (e.g., Foster & Awh, 2018, *for a review*), according to which the alpha activity plays a pivotal role in signal enhancement but has not a crucial involvement in inhibiting irrelevant information.

Concerning the operations related to activating (or inhibiting) the intended action, we observed an intriguing finding related to theta increase/decrease over pre-motor, motor and sensorimotor areas. We indeed found a long-lasting reduction of the theta band over fronto-central regions in the left hemisphere in the Monitoring-load task. Since in this PM task session the intended action was only one and must be performed using the right hand, a possible interpretation is that the theta reduction over left motor and premotor areas during the ongoing trials (thus when the PM response was not needed) may reflect the inhibition of an inappropriate action. Notably, in the Retrospective-load task as compared with the Monitoring-load task, we observed the opposite pattern, namely an increase in motor and sensorimotor theta activity over the right hemisphere. In the Retrospective-load task, the prospective actions have to be performed using the right hand, which was always placed over a keyboard, and multiple PM cue-action mappings needed to be retained and refreshed. We hypothesized that participants might refresh the mapping with their free hand, the left one, thus they were engaged in the motor simulation of the PM cue-action mappings. This hypothesis has been also driven by the subjective reports of the participants, who referred us to use sometimes the

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left hand to simulate and refresh the mapping of response. Although speculative, this suggestion is also coherent with same studies showing that theta activity acts as a key mechanism for sensorimotor integration (Cruikshank et al., 2012) and might stimulate new researches to further explore this phenomenon. Also, the current study has some limitations that could be addressed in future work. First, the Baseline Block was always administered first. This is a common approach in PM experiments to avoid possible carry-over effects of having previously formed and no longer relevant PM intentions on a subsequent ongoing-only block. Nevertheless, it might add a possible temporal confound (e.g., practice and/or fatigue effects). Second, the addition of a PM condition characterized by low load in both monitoring and retrospective component would help to better isolating brain oscillations specifically associated with these strategic processes. Third, future studies could explore other frequency bands (e.g., delta, beta, gamma) and adopt alternative analysis strategies to tap other neurocognitive mechanisms of strategic monitoring, such as the sustained processes mediated by PFC regions.

5. Conclusion

This study shows that theta and alpha oscillations play a pivotal role in modulating the direction of attention toward the external stimuli - to search for the PM cue - or toward the internal representation of the intention. In particular, theta increase is linked to internal attention and to memory processes necessary for maintaining the intention active in working memory. Such increase, indeed, has been particularly observed in the Retrospective-load task, and was expressed not only over lateral regions, but also over medial regions of the Default Mode network, such as medial temporal regions, precuneus, posterior cingulate cortex and mPFC, crucially involved in memory and internal processes. By contrast, the Monitoring-load task was mainly characterized by an alpha decrease, first expressed over occipital, occipito-parietal and fronto-temporal regions, and then spreading over dorsal fronto-parietal regions. This pattern of alpha decrease was suggested to support the external attention, which is necessary for detecting the PM cue in the environment.

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Figures

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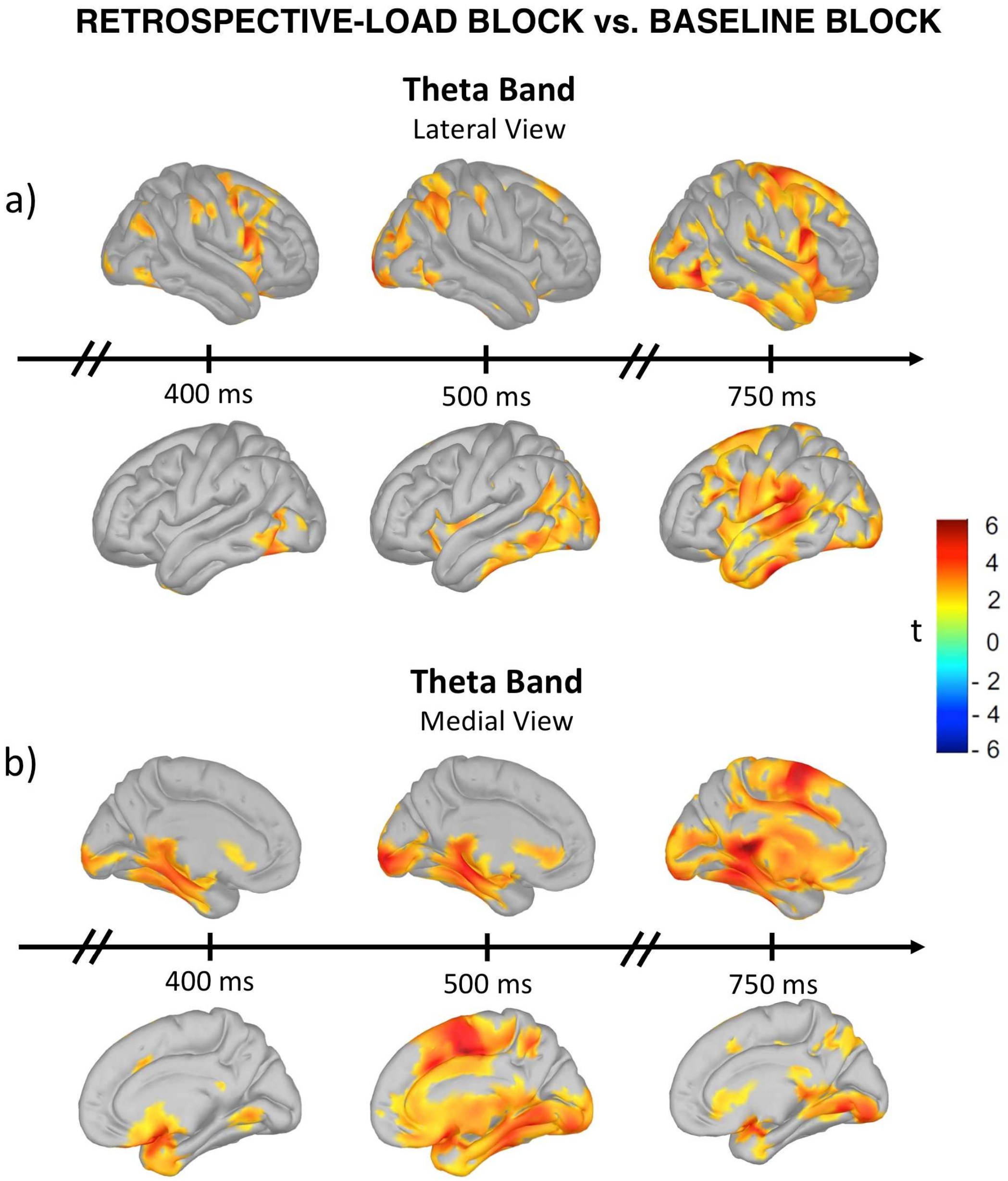

Figure 1. Theta activity in Retrospective-load Block vs Baseline Block.
Panel a). Laterally, the theta band increase in the Retrospective-load Block starts around 350 ms over bilateral occipital regions and over a set of right frontal regions. It becomes more pronounced in the later time windows (500-800 ms) and involves bilateral posterior regions, inferior temporal regions and inferior frontal/insular regions coupled by dorsal frontal activity of both the hemispheres.
Panel b). Medially, the theta activity increase in the Retrospective-load Block is long-lasting and expressed over temporal regions, over medial PFC (mPFC), precuneus, and supplementary motor cortex as well as over both the anterior the posterior cingulate cortices, especially in the late windows, around 600 and 800 ms.

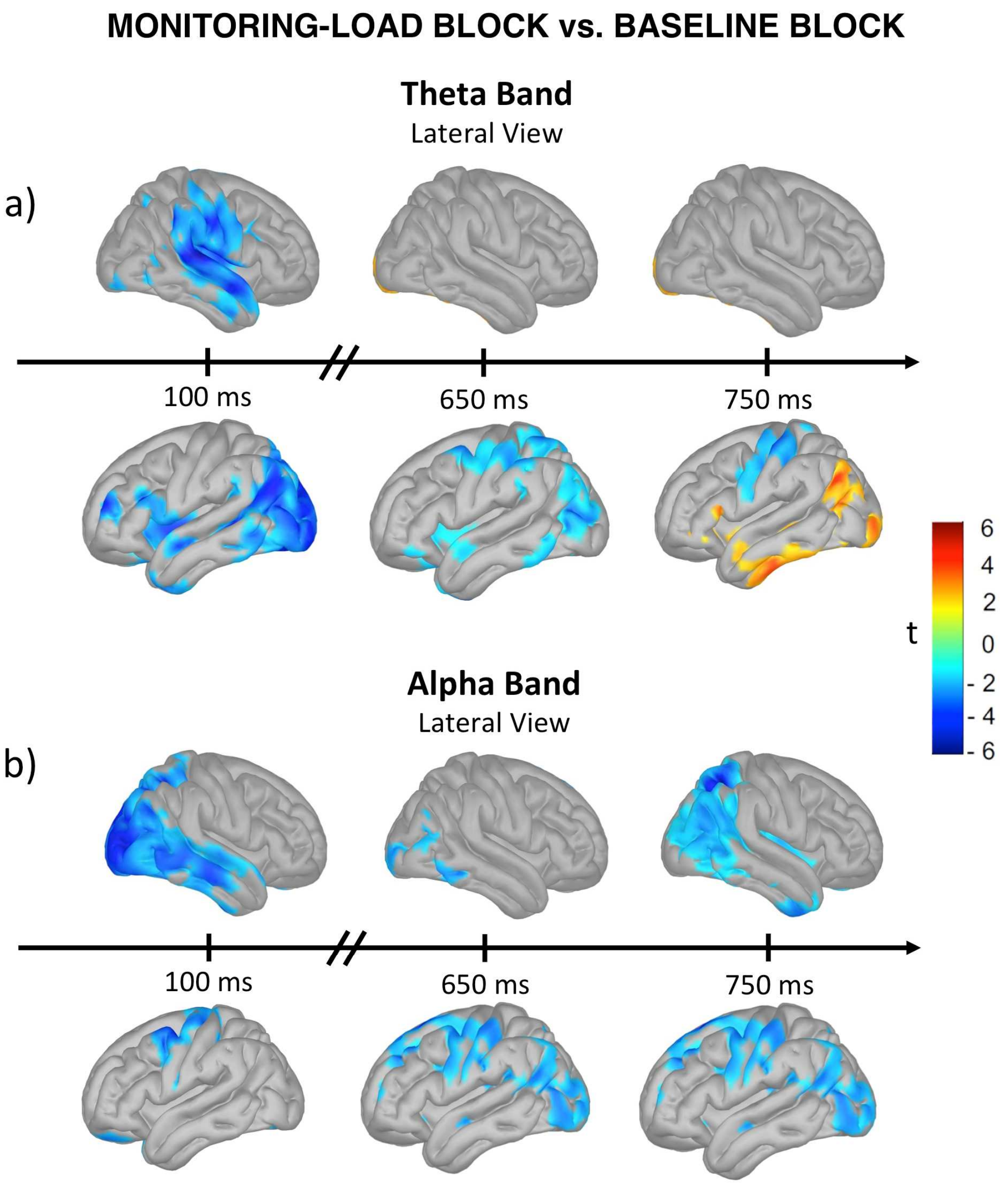

Figure 2. Theta (a) and Alpha (b) activity in Monitoring-load Block vs Baseline Block. *Panel a).* Respect to the Baseline Block, the Monitoring-load Block shows: an initial reduction of theta activity, distributed over the right regions of the ventral pathway (occipital and temporal) and over right fronto-temporal regions; a long-lasting reduction of the theta band over fronto-central regions in the left hemisphere; a late increase in theta activity selectively in the left hemisphere over occipital, parieto-temporal and inferior temporal regions.
Panel b) The Monitoring-load Block shows an early and sustained reduction of alpha activity as compared to the Baseline Block, mostly over bilateral posterior regions, and in the left central and frontal regions.

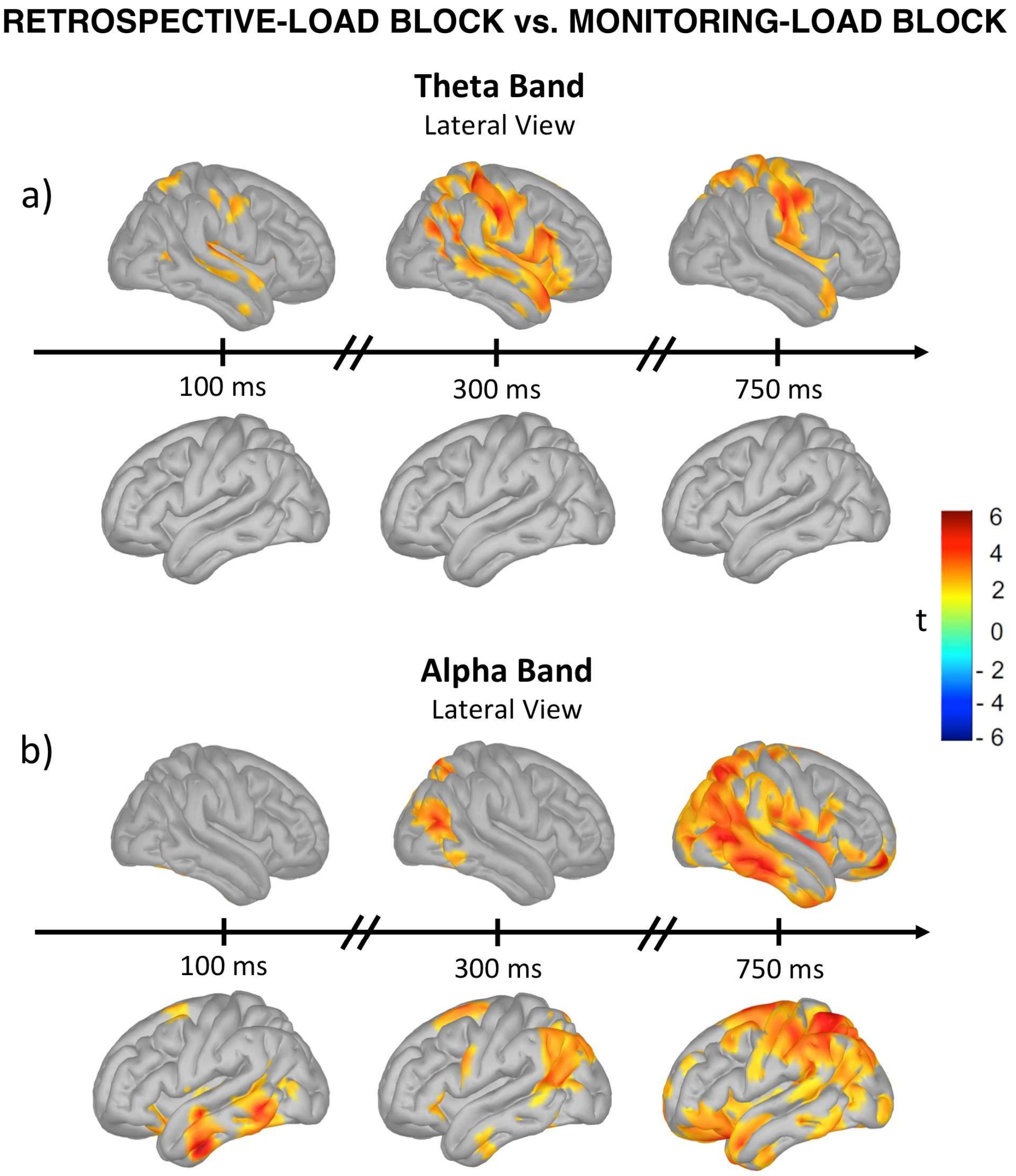

Figure 3. Theta (a) and Alpha (b) activity in in Retrospective-load Block vs. Monitoring-load Block.
Panel a) As compared with the Monitoring-load Block, the Retrospective-load Block shows an increased sustained theta activity selectively over the right hemisphere, especially over insular/frontal and superior parietal and central regions.
Panel b) As compared with the Monitoring-load Block, the Retrospective-load Block is characterized by an increase in the alpha activity over inferior-temporal and temporo-occipital regions. In later time windows (~ 650-800 ms), the increase in alpha activity becomes widespread, occurring over posterior regions, ventral prefrontal and temporal regions.