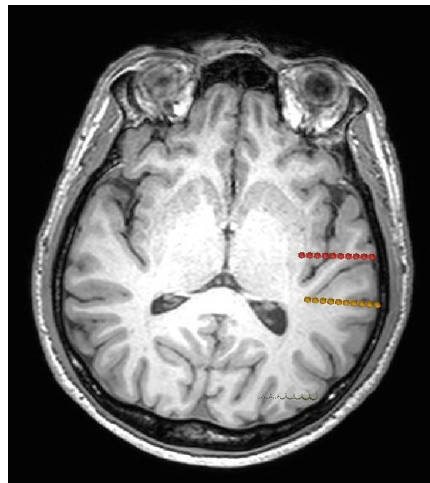**Université Claude Bernard Lyon 1**
Master Physiologie et Neurosciences

MEMOIRE DE RECHERCHE
Présenté en vue de l'obtention du

Master Recherche (M2-R) en NEUROSCIENCES
2013-2014

PREPARATORY ATTENTION MECHANISMS IN THE AUDITORY CORTEX

Par :
Clara FONTENEAU

Laboratoire d'accueil :
Centre de Recherche en Neurosciences de Lyon (CRNL)
INSERM 1028 – CNRS 5292

Equipe d'accueil :
Equipe "Dynamic and Cognition" (DYCOG) - Olivier Bertrand

Responsable du stage :
Aurélie BIDET-CAULET

RESUME

L'attention est une fonction cérébrale qui permet de faciliter le traitement de certaines informations tout en ignorant les autres. L'attention volontaire permet de sélectionner les informations pertinentes pour réaliser efficacement la tâche en cours. Celle-ci peut agir par différents mécanismes tels que des mécanismes facilitateurs ou inhibiteurs ainsi que des mécanismes de préparation attentionnelle. Ces derniers ont été étudiés majoritairement dans la modalité visuelle et sont reflétés, dans le cortex visuel avant l'arrivée du stimulus attendu, d'une part par une onde soutenue et d'autre part par une désynchronisation dans la bande de fréquence alpha (8-14Hz). Dans la modalité auditive, peu d'études ont pu mettre en évidence ces processus généré dans le cortex auditif, du fait de sa faible surface corticale. De plus, les méthodes utilisées étant non-invasives, la fiabilité de la mesure et le rôle fonctionnel de ce rythme alpha auditif sont constamment remis en question.

Cette étude se focalise donc sur les mécanismes de la préparation attentionnelle dans le cortex auditif. Pour cela, nous avons adapté le paradigme d'indication de Posner en utilisant des indices visuels centraux (informatifs ou non-informatifs) et des cibles auditives monaurales. Nous avons enregistré l'électroencéphalogramme intracrânien (iEEG) grâce à l'implantation d'électrodes dans les deux hémisphères cérébraux chez 10 patients souffrant d'épilepsie partielle résistante aux traitements pharmacologiques. Par ces enregistrements, nous avons exploré les mécanismes neurophysiologiques liés à la préparation attentionnelle pendant le délai entre l'indice visuel et la cible auditive, uniquement sur les électrodes localisées dans le cortex auditif (primaire et/ou associatif). Nous avons calculé, en réponse à l'indice visuel, les potentiels évoqués (onde soutenue) et les temps-fréquences (oscillations alpha) pour chaque patient individuellement. Au niveau comportemental, une augmentation du temps de réaction est observée en condition non-informative. Au niveau électrophysiologique, d'une part, les patients ont présenté une onde soutenue générée dans le cortex auditif (800-1200ms après le début de l'indice), se propageant progressivement du cortex auditif primaire vers la partie postéro-latérale du cortex auditif gauche. Cette onde présente aussi une plus grande amplitude lors d'une orientation de l'attention (condition informative), et plus particulièrement lorsque la cible est orientée du côté controlatéral de l'hémisphère enregistré. D'autre part, une modulation des oscillations alpha (400-1000ms après le début de l'indice) est majoritairement observée dans les aires associatives postéro-latérales du cortex auditif gauche. De plus, l'amplitude de ces oscillations est modulée par l'attention. Plus particulièrement, la puissance de l'alpha est majoritairement augmentée lorsque la cible est orientée du côté controlatéral à l'hémisphère enregistré.

Ces résultats suggèrent qu'il existe bien des mécanismes de préparation attentionnelle générés au niveau du cortex auditif, reflétés par une onde soutenue et des oscillations alpha.

Mots Clés : préparation attentionnelle, cortex auditif, EEG intracrânien, oscillations alpha, réponse évoquée

INTRODUCTION

Attention is the cognitive function by which we, voluntarily or not, optimize the processing of specific information in our environment while other information is disregarded. This is due to the fact that there are limited capacities for processing simultaneous information. Two types of attention processes have been identified: voluntary attention (endogenous), i.e., top-down (TD) attention, and involuntary (exogenous), i.e., bottom-up (BU) attention (James, 1890). Top-down attention enables a good behavioral performance by voluntarily selecting the relevant information in the environment. It has been characterized by facilitatory (increased cortical responses to task-relevant stimuli) and inhibitory (reduced responses to task-irrelevant stimuli) mechanisms (Bidet-Caulet et al., 2007, 2010, 2014b), as well as anticipatory/preparatory mechanisms (e.g. Brunia & Van Boxtel, 2001; Jensen & Mazaheri, 2010; Foxe & Snyder, 2011; Bidet-Caulet *et al.*, 2012).

Preparatory attention is the ability to allocate attention to a stimulus prior to its occurrence and is a crucial component of attentional control. It has been studied mostly with variants of the cueing Posner paradigm. In behavioral studies, a valid indication of an upcoming target enables faster responses compared to invalid cues, reflecting a deployment of anticipatory attention process. Both scalp electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) studies, using paradigms recruiting auditory and/or visual systems, show that preparatory attention increases the processing of expected stimuli, reflected by increased amplitude of early sensory responses (Hillyard *et al.*, 1998), and in facilitated stimulus detection (Posner, 1980). These attentional effects support the deployment of preparatory processes, i.e., attentional preparation, during stimulus expectancy.

Neuroimaging studies have demonstrated the activation of prefrontal and posterior parietal cortices during expectation of an object at a particular location or during preparation of a specific response (Corbetta *et al.*, 2008). This dorsal fronto-parietal network has been shown to serve preparatory attention by influencing sensory-specific regions in order to select the relevant information. For example, preparatory attention in the visual cortex is reflected before the target appearance, by a baseline shift, reflecting preactivation of visual areas (e.g. Kastner *et al.*, 1999; Giesbrecht *et al.*, 2006; Silver *et al.*, 2007; Sylvester *et al.*, 2007). These attentional modulations were also observed in the auditory modality (Voisin *et al.*, 2006; Wu *et al.*, 2007; for a meta-analysis of fMRI studies see Alho *et al.*, 2014). More specifically, sound anticipation was found to be indexed by preactivation of auditory associative areas whereas activation related to sound processing was observed both in the primary auditory cortex and its associative auditory areas (Voisin *et al.*, 2006). Although these neuroimaging experiments have shown preactivation of sensory areas during anticipation, electroencephalographic experiments have been informative in regards to the timing of these activations.

EEG studies seem to indicate the deployment of sustained responses between a warning stimulus and a target stimulus onset, both in frontal and sensory areas, reflecting preparatory processes. Brunia & Van Boxtel (2001) described a sustained frontal negative wave, called the contingent negative variation (CNV), slowly increasing from 550ms after the presentation of a warning stimulus until a target stimulus onset. In addition, studies comparing informative and uninformative trials, observed an enhanced CNV when the attention was correctly

oriented, reflecting an enhanced preparatory attention (Bidet-Caulet et al., 2014a). This slow wave is also associated with a motor preparation component, called the readiness potential. These slow potentials have been shown to be generated in the frontal cortex, as well as in subcortical structures. In addition, the readiness potential has been described as, at least partially, generated from the motor cortex (Brunia and Van Boxtel, 2001). It can be assumed that an activation of sensory cortices is also present during preparatory attention, comparable to that of the motor cortex during motor preparation. This has been suggested by Lamarche et al., (1995) who observed, using an auditory forewarned reaction time task, intracranial 'CNV-like' potentials in two cortical zones: motor areas and auditory cortex. Moreover, some crossmodal cueing studies have suggested that a late directing attention positivity (LDAP) or a biasing-related negativity (BRN) is generated, at least partially, in modality specific areas prior to the target onset and leads to spatially specific excitation in sensory areas involved in processing of the upcoming target. This response is present contralateral to the attended side, from 500ms post-cue and up until the target onset. Thus, this sustained process seems to reflect preparatory activity in sensory areas that would be activated by the upcoming target stimulus (LDAP: Harter et al., 1989; Hopf & Mangun, 2000; Green & McDonald, 2006; Jongen et al., 2006; Kelly et al., 2009; BRN: Grent-'t-Jong & Woldorff, 2007) . These studies seem to indicate the deployment of sustained responses during target expectancy both in frontal and sensory areas, reflecting preparatory attention.

This preparatory mechanism during the 'pre-target' period is also reflected by oscillatory activity in the alpha band (~8-14Hz). Ongoing alpha rhythms were first discovered by Berger (1929) when the subject was awake, but with eyes closed. This observation lead scientists to believe for a long period that alpha activity reflected 'cortical idling'. It seemed as though alpha activity increased when subjects were awake but not engaged in any task (Pfurtscheller et al., 1996). Recently, strong evidence has accumulated against this hypothesis and it has become clear that alpha activity has an important functional role.

Indeed, these oscillations have been well documented in the visual domain either with tasks that vary stimulus modality or stimulus side. In spatial cueing studies, preparatory biasing is observed as a decrease in alpha activity in visual areas contralateral to the attended stimulus (Worden et al., 2000; Sauseng et al., 2005; Rihs et al., 2007; Kelly et al., 2009), and as an alpha increase in ipsilateral visual areas (Worden et al., 2000; Rihs et al., 2007). Therefore, alpha activity seems to reflect active inhibition of brain areas not involved in the current brain operation. A decrease in alpha power would reflect a release of inhibition whereas an enhanced excitability of cortical areas would be involved in processing the expected visual stimuli (Foxe et al., 1998; Jensen and Mazaheri, 2010; Klimesch, 2012). The functional relevance of these oscillations has been assessed in few studies showing, on a trial-by-trial basis, that reaction time to a predicted stimulus decreases as a function of the pre-target alpha decrease (Thut et al., 2006; Kelly et al., 2009). These observations in the visual modality suggest a functional role of alpha activity in preparatory attention.

Concerning the auditory modality, only few studies have investigated alpha oscillations due to the relatively small spatial extent of auditory cortical areas. Indeed, the small size of the auditory cortex leads to less obvious activity that may be masked by non-auditory alpha generators when recording non-invasively (magnetoencephalography (MEG) or EEG) (Weisz et al., 2011). Moreover, alpha oscillations generated in

auditory cortices may not propagate well to the scalp surface given the orientation of the underlying generators, which are buried along the supratemporal plane. Studies using non-invasive technics seem to support the existence of an auditory alpha-band activity with functional relevance. Lehtelä *et al.* (1997) have reported a reactive auditory cortical rhythm in the human temporal cortex. More recently, other studies showed a decrease in alpha activity in the auditory cortex during target expectancy (Weisz *et al.*, 2013) and that this modulation is selective to the anticipation of an auditory target and not of a visual target (Frey *et al.*, 2014). Nevertheless, doubts remain on the functional relevance and measurability of an auditory alpha activity. In order to investigate more precisely the existence of an auditory alpha rhythm, the use of intracranial electrodes implanted directly in the auditory cortex would allow for a more sensitive measure of the auditory alpha rhythm thanks to good spatial and precise time resolutions.

The purpose of this work is to characterize preparatory mechanisms of auditory attention within the primary auditory cortex and its associative auditory areas. Here, we adapted the Posner cueing task using central visual cues and monaural auditory targets. To assess top-down anticipation, visual cues could be either informative (arrow indicating the side of the upcoming target, Left or Right) or uninformative (double arrow pointing to both sides). We recorded intracranial EEG from 10 patients suffering from pharmacologically resistant partial epilepsy and implanted with depth electrodes. We investigated on the electrodes located within auditory cortices (primary and/or associative areas), brain responses elicited by the visual cues, prior to target onset, reflecting the deployment of preparatory attention during expectancy of an auditory target. Both event-related-potentials and time-frequency analyses were performed to explore sustained evoked response and alpha-band oscillations, respectively. We hypothesized that prior to target onset, 1) the slow sustained component would be larger with contralateral informative cues (in regards to the recorded hemisphere) than with ipsilateral and uninformative cues, and 2) Alpha power would decrease after cue-onset, indexing enhanced excitability in auditory areas, with a larger decrease for contralateral cued location.

MATERIALS and METHODS

Subjects

10 patients (3 females and 7 males, age ranging from 19 to 42 years) suffering from pharmacologically resistant partial epilepsy and candidate for surgery participated in this study. Because the location of the epileptic focus could not be identified using noninvasive methods, they were stereotaxically implanted with multicontacts depth probes. Electrophysiological recording is part of the brain functional evaluation that is performed routinely before surgery in these patients. Electrode coverage was entirely based on clinical criteria, with no reference to the present experiment. All patients gave their written informed consent to participate in the experiment. The signals described here were recorded away from the seizure focus. Several days before recordings, antiepileptic drugs administered to the patients had been either discontinued or drastically reduced. No patient was administered with benzodiazepines. None of the patients reported any auditory complaint.

Stimuli

A visual cue was presented to the patient followed by an auditory target. The visual cue of 200ms duration was presented centrally. This cue came in two forms, either as an informative cue (a one sided arrow pointing either left or right) or as an uninformative cue (a two sided arrow). The target sound was a monaural harmonic sound of 50ms duration. The delay between cue and target onset was randomized between 968-1098ms (mean 1042ms). In 25% of the trials, an auditory distractor could be played between the cue and the target. 30 different distracting sounds of 300ms duration were presented binaurally (bell ring, phone ring...). The distractor could be played at any time between 350 and 945ms before target onset. Three categories of distractors were considered based on the latency before target onset, from 750 to 945ms (DIS1), from 550 to 745ms (DIS2), and from 350 to 545ms (DIS3).

Concerning the cue, the trials were equally divided: Informative Left 33.33% / Informative Right 33.33% / Uninformative 33.33%. As for the target sound, when the cue is informative, its side corresponded in 100% of the trials to the side indicated by the cue. With an uninformative cue, the target sound was presented half of the time in the left and the other half in the right ear. The detailed percentages of each type of trials are presented in Table 1. Stimuli were presented using the Presentation software (Neurobehavioral Systems, Albany, CA, USA).

Cue	Distractor	Target	Percentage of trials (%)	
INFORMATIVE Left	no	Left	25.00	66.66
	yes	Left	8.33	
INFORMATIVE Right	no	Right	25.00	
	yes	Right	8.33	
UNINFORMATIVE	no	Left	12.50	33.33
	yes	Left	4.17	
	no	Right	12.50	
	yes	Right	4.17	

Table 1 - Proportion of each type of trials (%). Relationship between cue, distractor and target events are presented in this table.

Task

Subjects were asked to keep their eyes fixated on a cross in the center of the monitor screen. They were asked to orient their attention, in the presence of an informative cue, towards the indicated side, whereas this orientation was not possible with uninformative cues. In each condition, the subjects were asked to press the left button on the mouse as soon as they heard the target sound. The subjects were informed that in some trials a distracting sound could be played between the cue and the target sound. In that case, they had to try to ignore it.
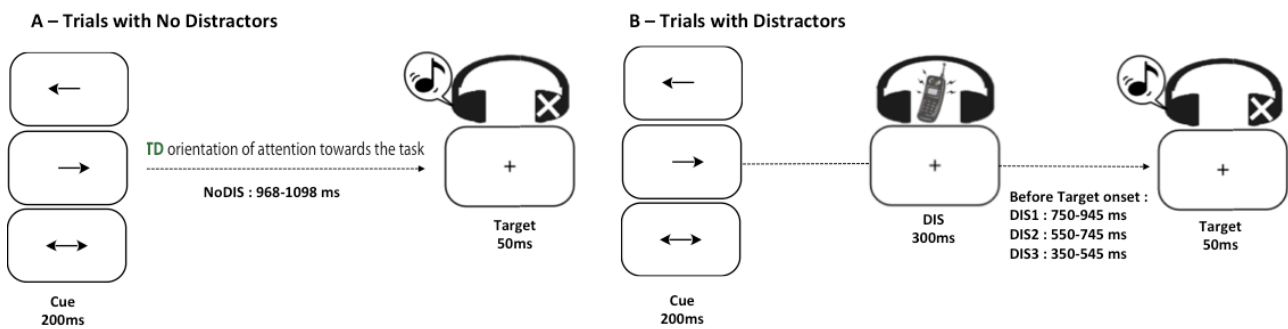
Figure 1 - Schematic representation of the protocol used in the experiment. The paradigm consisted in the presentation of central visual cues and monaural auditory targets to which subjects were instructed to react as fast as possible. The TD modulation (Fig 2-A) was triggered with the use of informative (Left or Right) or uninformative cues. Binaural distracting sounds were played between the cue and the target (Fig 2-B), in 25% of the trials. Three categories of distractors (DIS1, DIS2, DIS3) were used with different latencies relative to the target onset.

Procedure

Subjects sat in their hospital bed in a sound attenuated and electrically shielded room at 80cm from the screen. The subjects were equipped with headphones positioned over their bandages. Before each recording, we measured the hearing threshold in each ear using the Bekesy tracking method with the target sound. In the experiment, the target and distractor sounds were then presented 15dB and 60dB, respectively, above the hearing threshold in each ear. Moreover, we ran a practice block to test the comprehension of the attention task in itself and so that subjects could familiarize themselves with the sounds.

During the experiment, 6 to 10 blocks were presented to each patient. Each block lasted approximately 5 minutes making it a maximum of 90 minutes per recording (breaks included). All blocks contained, in a random order, the different previously exposed trials. Hits, False Alarms (FA) and Reaction Times (RT) were collected using Presentation software (Neurobehavioral Systems, Albany, CA, USA).

Intracranial EEG recordings and Signal Analysis

Intracranial EEG recordings were performed at the Functional Neurology and Epilepsy Department (Lyon Neurological Hospital, Lyon, France). Intracranial EEG recordings were made from a mean of 128 intracranial electrode contacts referenced to an intracranial contact away from the superior temporal cortex and free of epileptic activity. The ground electrode was an intracranial contact. Signals were amplified, filtered (0.1-200Hz bandwidth) and sampled at 512Hz (Brain Quick System Plus; Micromed, Treviso, Italy) for all patients. All processing and analysis were done using ELAN software (Aguera et al., 2011), http:// elan.lyon.inserm.fr/), a

software bundle for electrophysiology data analysis developed in the Brain Dynamics & Cognition team of the Lyon Neuroscience Research Center.

The analysis was restricted to electrodes located in or near auditory cortical regions. Electrode contacts with excessive noise and trials showing epileptic activity were excluded. Thus, the final number of electrode contacts kept was 187 across all patients. To clean the data from residual artifacts, an automatic then manual rejection was done trial by trial. Only blocks with correct performances, i.e. showing the 'Posner effect' of a shorter reaction time with informative compared to uninformative cues, were considered for further analysis. In addition, trials with anticipation, false alarms, or incorrect responses were rejected from further analysis. After rejection, the mean number (±SEM) of remaining non-artifacted trials was 74±6.35, 77.8±6.09 and 80.5±6.8 for the Informative Left, Informative Right, Uninformative conditions, respectively.

Event-related-potentials (ERPs) were separately averaged for each event of the trial. Cue-ERPs were averaged between -250 and 1800ms locked on the cue-onset and corrected with a -100 to 0ms baseline before all trial onsets. ERPs were computed both from monopolar montages (all contacts referred to the same reference site) and from bipolar montages (every contact referred to its immediately adjacent neighbor). Whereas monopolar montages facilitate comparison of the response polarity with those of scalp-recorded ERPs, bipolar montages emphasize the contribution of local generators. Only bipolar results are shown here.

The alpha frequency band (6-16Hz) was analyzed by means of a wavelet decomposition, which provides a good compromise between time and frequency resolutions. Each single-trial signal was transformed in the time-frequency (TF) domain by convolution with complex Gaussian Morlet's wavelets with a ratio f/σ_f of 7 with f being the central frequency of the wavelet and σ_f its standard deviation (for details, see Tallon-Baudry and Bertrand, 1999). For example, at 10Hz, the wavelet duration is 223 ms and the spectral bandwidth 2.86 Hz. Thus the time resolution of this method increases with frequency, whereas the frequency resolution decreases. These resulting time-frequency powers were then averaged across trials. This method led to a power estimate of both evoked (phase-locked to stimulus onset) and induced (jittering in latency) activities in the time-frequency domain. To assess the deployment of oscillatory activities after cue onset, we analyzed the oscillation power on a large time-window (-1000; 1600ms) around cue onset. We then applied a baseline correction by subtracting, in each frequency band, the pre-stimulus power between -800 and -400ms before cue onset. From this time-frequency analysis, time profiles of the power at 8 and 10Hz could be computed.

Statistical Analysis

Because the electrode implantation was different for each patient, data from each patient were tested independently, using single trials as statistical units.

Behavioral Data

Reaction times (ms) and accuracies (%) were averaged for each condition individually (Uninformative, Informative Left and Informative Right). To compare mean accuracies and mean reaction times of informative left, informative right, and uninformative trials, a non-parametric Friedman test was performed. Significance was set at $p<0.05$. If an effect was observed, *post-hoc* tests after Friedman test were realized to assess differences. The significance was determined if the observed difference was superior to the critical difference. These tests were conducted on the software R. To give an idea of the variability within the population, we computed the standard error of the mean (SEM). All results are reported as mean ± SEM.

To investigate preparatory attention, we focused our analysis on trials without distractors and compared trials according to the type of cue (Informative Left, Informative Right or Uninformative) and by taking into account the recorded hemisphere: cued location being contralateral or ipsilateral to the recorded hemisphere. The three cue conditions were ipsilateral, contralateral and uninformative. For example, for an electrode contact located in the left hemisphere, trials with cued location to the left are considered to be part of the ipsilateral condition.

ERPs Data

Statistical analysis of the sustained responses was performed on the 0.2–15 Hz bandpass-filtered intracranial EEG. To identify for each patient the electrode contacts where this sustained response was emerging, a Wilcoxon test was computed on the mean amplitude of successive 100-ms time-windows between 800 and 1200ms after cue onset, in comparison with a prestimulus baseline (defined between -100 and 0ms). All statistical p-values were FDR-corrected (False Discovery Rate) (Genovese et al., 2002) for multiple comparisons across time. Briefly, this procedure controls the expected proportion of the rejected hypotheses that are falsely rejected. Using the map of p-values computed, the FDR method is used to find appropriate significance level below which all points are considered significant. Only emerging effects that resisted to FDR correction are discussed here. For contacts that showed a significant emerging response, differences between conditions (contralateral, ipsilateral and uninformative cues in relation to the recorded hemisphere) were estimated by Kruskal–Wallis tests applied to the same windows as above. If a significant effect was found, *post-hoc* Mann–Whitney tests were performed to assess 2-by-2 differences. The statistical threshold was set at $p<0.05$.

Time Frequency Data

Modulation of alpha rhythm after cue onset was assessed by Wilcoxon tests comparing the mean power in each frequency (6-16Hz) in successive 200ms windows between 0 and 1200ms after cue onset, in comparison with the prestimulus baseline power (between -800 and -400ms) in the respective frequency (note that the prestimulus baseline is shifted away from 0ms because wavelet analysis tends to stretch out the early poststimulus low frequency components). All statistical p-values were FDR-corrected (False Discovery Rate) (Genovese et al., 2002) for multiple comparisons across time. Only emerging effects that resisted to FDR correction are discussed here. For contacts that showed a significant alpha modulation, differences between conditions (contralateral, ipsilateral and uninformative cues in relation to the hemisphere recorded) were

estimated by Kruskal–Wallis tests applied to the same windows as above. If a significant difference was shown, *post-hoc* Mann–Whitney tests were performed to assess 2-by-2 differences. The statistical threshold was set at p<0.05.

Auditory Cortex Anatomy

In the human brain, auditory information is transmitted from the cochlea in the internal ear to the auditory cortex via several sub-cortical nuclei, following a tonotopic organization. The auditory cortex's organization is complex (Figure 2). In humans, auditory cortices are located in the superior temporal plane, deep in the Sylvian fissure and extends towards the superior temporal gyrus and the adjacent parietal and insular cortices. It is comprised of the primary auditory cortex and associative auditory areas. The primary auditory cortex is located in the deeper part of Heschl's Gyrus. It is surrounded with associative areas either in front: Planum polare or behind: Planum temporale and lateral Superior temporal gyrus (STG). In addition, these regions receive projections from frontal and parietal cortices, known to be involved in attentional control (for review see Corbetta *et al.*, 2008).
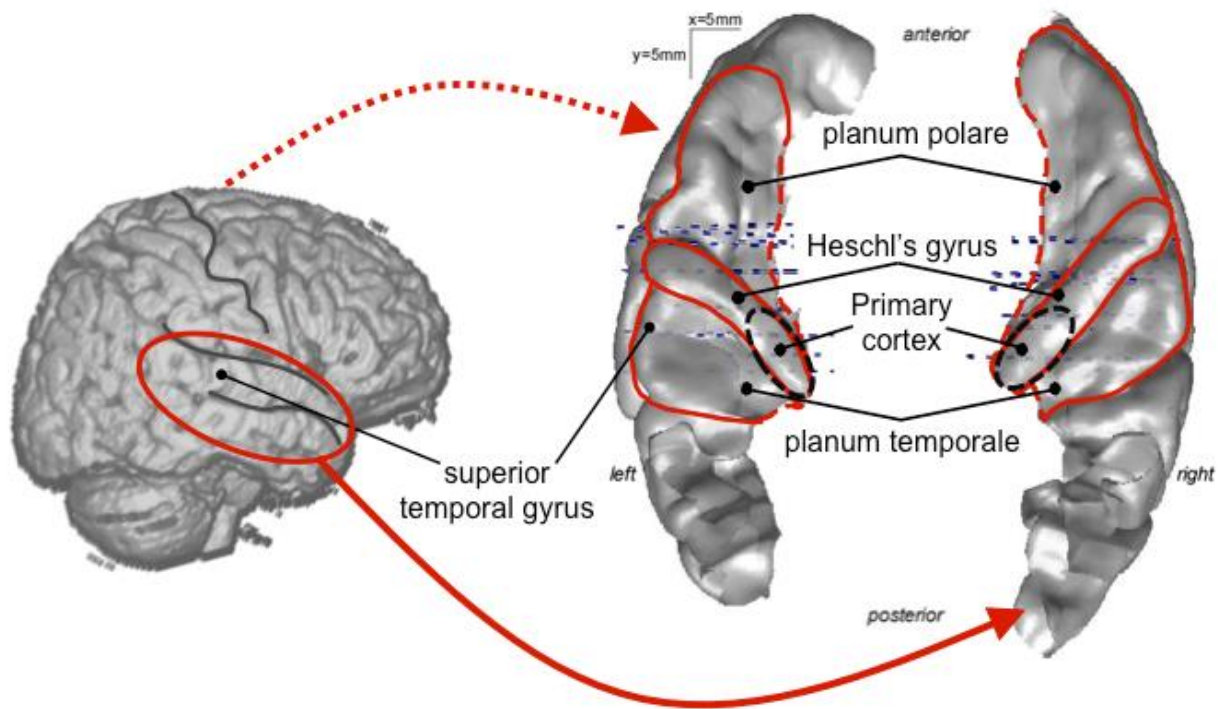

Figure 2 – Main auditory regions. On a top view of the superior temporal plane after 3D rendering of the cortical surface of the Montreal Neurological Institute (MNI) standard brain.

Electrode implantation, anatomical registration and normalization

Depth probes (diameter, 0.8 mm) with 5 to 15 contacts each were inserted perpendicularly to the sagittal plane using Talairach's stereotactic grid (Talairach and Tournoux, 1988). Electrode contacts were 2 mm long and spaced every 3.5 mm (center to center). Numbering of contacts increases from medial to lateral along an electrode track. Electrodes were anatomically localized using a custom software, IntrAnat, (using SPM8 &

BrainVisa), by aligning the preoperative with the postoperative structural MRIs of each patient. This step allows us to localize correctly the implanted electrodes, seen on the postoperative MRI, (Figure 3A) on the preoperative MRI (Figure 3B), which has fewer artifacts.
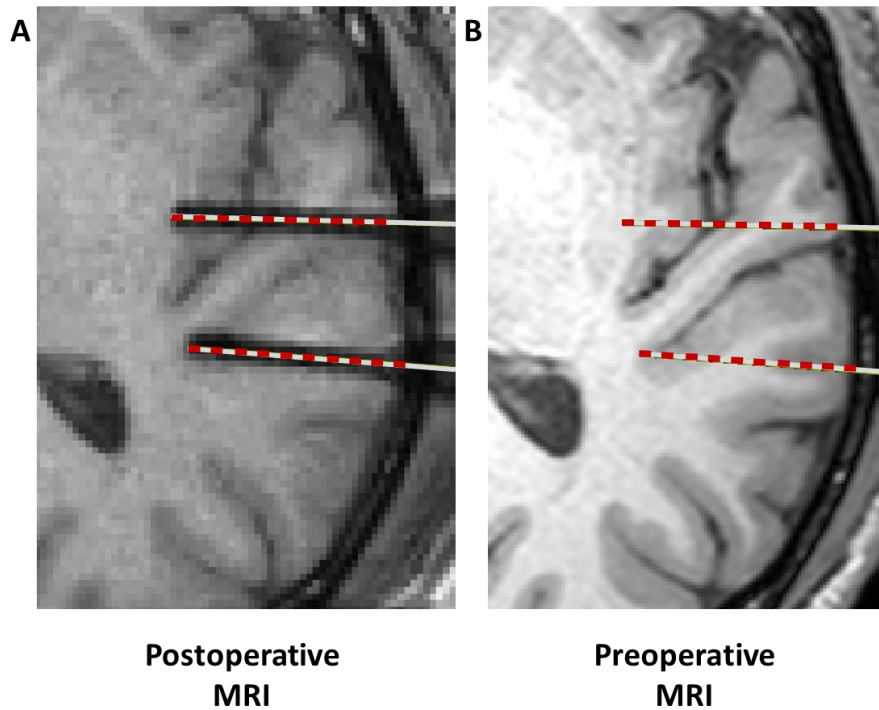

Figure 3 – Electrode localization on axial MRI - Example on one of the patients after alignment of the two MRIs: A) Postoperative MRI with artifacts due to the electrode implantation B) Preoperative MRI with corresponding electrode location. The electrode contacts are represented in red on both MRIs.

Two patients were implanted in the right hemisphere only, five in the left only, and three in both hemispheres. In all implanted hemispheres, at least one electrode track was located in the superior temporal cortex. Electrodes H, H', X, X', I' (prime denoting the left hemisphere) were positioned posteriorly, passing through Heschl's gyrus (HG), the planum temporale (PT), and the superior temporal gyrus (STG), and electrodes T, T' were positioned anteriorly, passing through Heschl's gyrus and the anterior planum temporale, the planum polare (PP) or the superior temporal gyrus. Electrodes G', P', E' were positioned in the frontal cortex just above the auditory cortex. Although intracranial recordings in epileptic patients provide a sparse spatial sampling of the auditory cortex, we could access not only primary auditory areas (posteromedial part of Heschl's gyrus), but also posterior and anterior secondary auditory regions (planum temporale and planum polare).

The electrode coordinates of each patient were converted from the individual Talairach's space to the normalized Talairach's space (Talairach and Tournoux, 1988), and then to the Talairach's space of the Montreal Neurological Institute (MNI) standard brain. Eventually, electrode contacts and experimental effects of all patients were plotted on a schematic representation of the temporal cortices of the MNI standard brain. This procedure facilitated the comparison across patients of the activated sites that could be positioned with respect to the main superior temporal structures that were delineated on the standard brain (Figures 2 & 4).
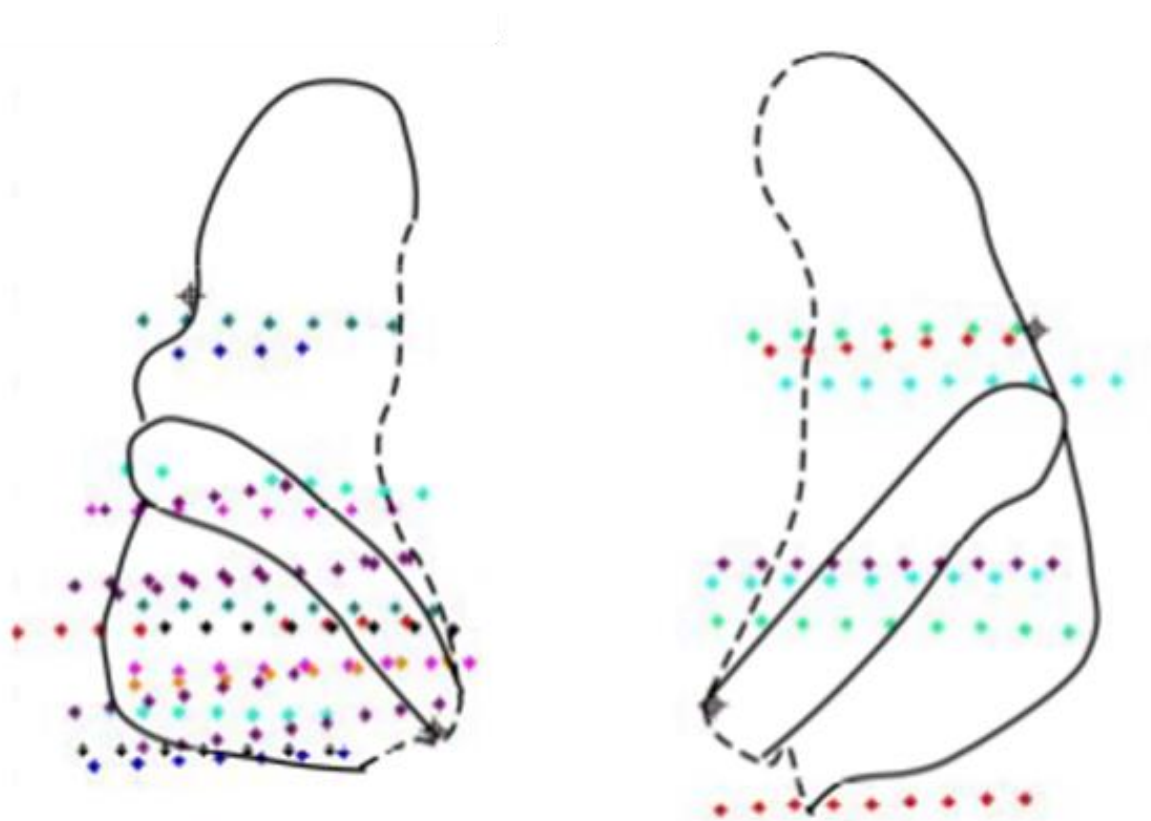
Figure 4 – Electrode implantation in the auditory cortex – Schematic representation of the auditory cortices derived from Figure 2, superimposed with electrode localization from all patients (n=10). Each color is associated with one patient, showing all his electrodes located in the auditory cortices. This schematic representation will be used in Figures 5 – 9.

Internship Progress

Due to prolonged ethics authorization to record scalp EEG of patients with lateral prefrontal cortex, we decided at the end of December to change the M2R internship topic. Using the same paradigm, the Competitive Attention Test to assess both top down and bottom up attention, I would be analyzing intracranial EEG data from 8 patients with epilepsy (already recorded between June 2012 and October 2013). The month of January was devoted to intracranial EEG analysis (artifact rejection, filtering) and behavioral analysis. We decided to remove some blocks from analysis (in order to have only blocks with a reaction time showing a 'Posner effect'). To be able to do this, I learned how to program on Matlab with the help of Aurélie Bidet-Caulet and Romain Bouet. Mid-February, I recorded 2 new patients at the Lyon Neurological Hospital for the study. Unfortunately, due to a problem with the recording software, one patient had to be excluded from analysis due to loss of triggers and false reaction times. For all 9 patients, I computed event-related potentials and time-frequency plots (TF / spatio-temporal / phase locking factor) in order to analyze the responses to the visual cue and the target sound. To have a global view I studied the statistical emergence to the cue, distractor and target onset for each different condition (left, right and uninformative cue) for each electrode contact. In addition, I studied the attentional effect (modulation of the cue: left, right, uninformative) on cue and target responses in the conditions without distractors. The month of March was dedicated to figuring out the new program for

intracranial electrode localization (alignment of the pre and postoperative MRIs, electrode contact coordinates space, loading patients into the database) with the help of Manik Bhattacharjee and Mathilde Petton. At the same time, we developed programs to plot the evolution of the power or phase of oscillations according to reaction time for each trial. I formed these plots for oscillations ranging from the theta to the gamma band. Unfortunately, the results from these plots were inconclusive due to the small difference in reaction time between conditions. Mid-April, after discussion with Oliver Bertrand and Aurélie Bidet-Caulet, we decided to focus on the preparatory mechanisms of auditory attention, portrayed by the evoked sustained response and alpha-band oscillations. At the same time, I recorded the 10th patient included in this study and then computed his event-related potentials and time frequency plots. To improve my Matlab programming skills, I followed the Matlab workshop dispensed by the Lyon Neuroscience Reasearch Center (CRNL). The month of May was reserved to summarize the results of all patients using a program rendering the results on a schematic representation of temporal cortices of the MNI standard brain and to write this thesis.

RESULTS

Behavioral Data

Participants performed the task well with mean accuracies of 94.61 ± 1.8%, 91.6±4.9% and 92.31±4.41% in Uninformative, Left and Right conditions respectively. No significant difference (p=0.7) was found between conditions.

Reaction times were significantly different between conditions (p<0.001). Indeed, reaction times in the uninformative condition (mean reaction time, 382.55 ± 44.4ms) were significantly longer than in both informative (left and right) conditions (mean reaction time, Left: 355.83 ± 45.6ms; Right: 344.37 ± 42.8ms).

Sustained evoked responses

Emergence

We found significant sustained evoked responses in anticipation of the upcoming target sound in all patients at 73 out of 187 contacts of electrodes in different areas of the auditory cortex (Heschl's gyrus, Planum temporale, Planum polare). Figure 5 summarizes the spatio-temporal emergence of the sustained response between 800 and 1200ms after cue onset. In the left hemisphere, this response's polarity is of negative polarity in Heschl's gyrus, with greater amplitude in the posteromedial part (PAC). Responses of positive polarity are localized more laterally in the planum temporale. Few contacts exhibiting this sustained response were observed in the right hemisphere. In general, its amplitude seemed to increase, in absolute value, until the target onset. Looking at the temporal evolution, it seems as though the response is deployed more posteriorly and laterally when closer to the target.
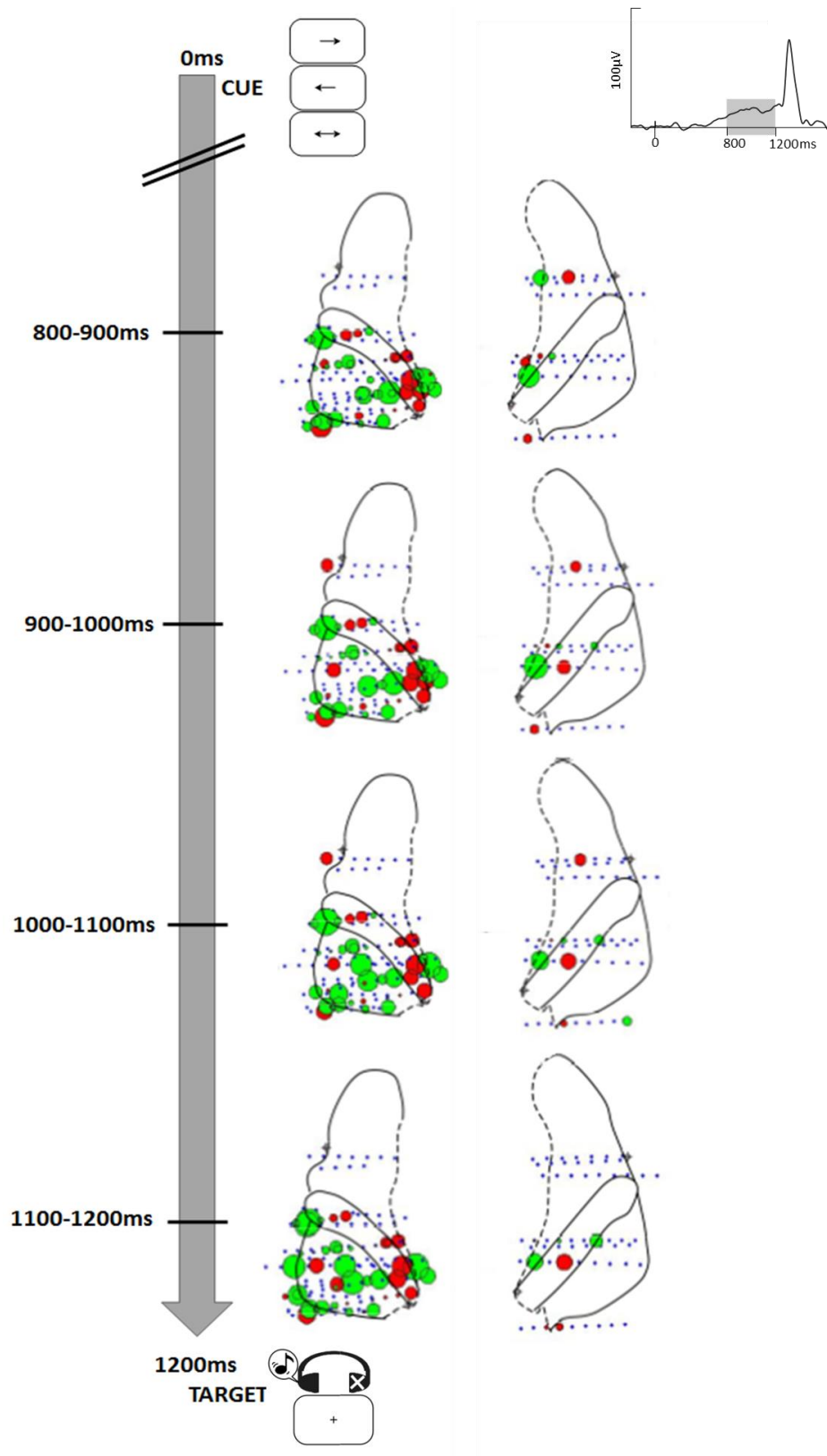
Figure 5 – Emergence of the sustained evoked response between cue and target onset. The significant emergence of this response is indicated by disks (green: positive potentials / red: negative potentials) on the anatomical plots. The diameter of these disks corresponds to the normalized (across each patient, and over a 400ms time period: 800-1200ms) mean amplitude of the sustained response. Only significant responses, after FDR correction, are presented. An example of the time course of this response is shown in the upper-right corner, where the sustained response is shaded in grey. This curve was obtained by averaging the single trials in all conditions without distractors from 0.2-15Hz filtered intracranial EEG and is baseline-corrected with respect to the [-100, 0ms] period preceding the cue onset.

Attention Effects

The sustained response was found significantly modulated by attention in 8 patients at 20 out of the 73 contacts (across 8 patients) presenting a significant emergence between 800 and 1200ms after cue onset. Different modulations were observed according to the type of cue. A greater response was seen at 9 contacts in 5 patients, in the contralateral condition (cued location contralateral to the recorded hemisphere), at 5 contacts in 4 patients in the ipsilateral condition and at 6 contacts in 3 patients both in the ipsilateral and the contralateral conditions (Figure 6). None of the modulations showed greater amplitude in the uninformative condition compared to the ipsilateral or contralateral conditions. Most of the contacts with modulations were located in the left hemisphere, along the Heschl's gyrus and the planum temporale.
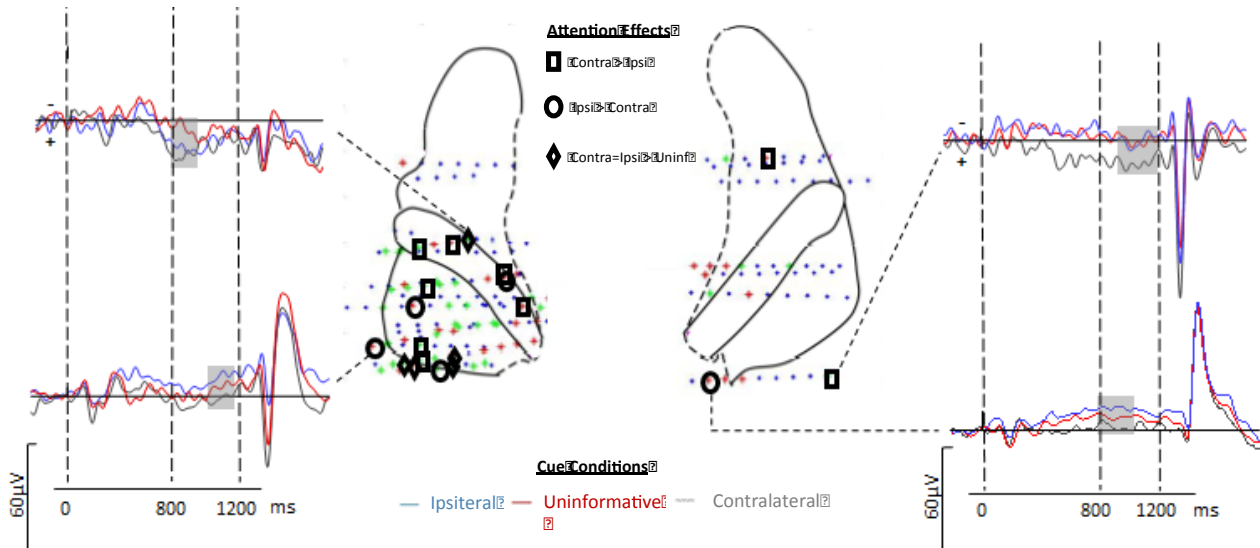
Figure 6 – Attention effects of the sustained evoked response between cue and target onsets. Contacts where the sustained response was significantly emerging between 800 and 1200ms are indicated by stars (green: positive potentials / red: negative potentials) on the anatomical plots. Black squares on the figure correspond to contacts where the sustained response was greater in trials in the contralateral condition. Black ovals on the figure correspond to contacts where the sustained response was greater in trials in the ipsilateral condition. Black diamonds on the figure correspond to contacts where the sustained response was greater in the contra and ipsilateral conditions than in the uninformative condition. The time course of this response is represented on the left and right side of the figure. These curves were obtained by averaging the single trials from 0.2-15Hz filtered intracranial EEG and are baseline-corrected with respect to the [-100, 0ms] period preceding the cue onset (Blue curves: Ipsilateral condition; Red curves: Uninformative condition; Grey curves: Contralateral condition; differences are indicated by grey shaded areas).

Auditory alpha activity

Time profile

Alpha-band oscillations were analyzed using a time-frequency decomposition of the electrophysiological signals. The time frequency power was averaged after wavelet-based transform of each single trial. The time profiles were constructed at 8 and 10Hz from the time-frequency plots. Figure 7 illustrates an example of alpha decrease in response to the cue onset, up until the target onset. In this example, we can see a stronger alpha activity decrease in the 8Hz frequency compared to the 10Hz.
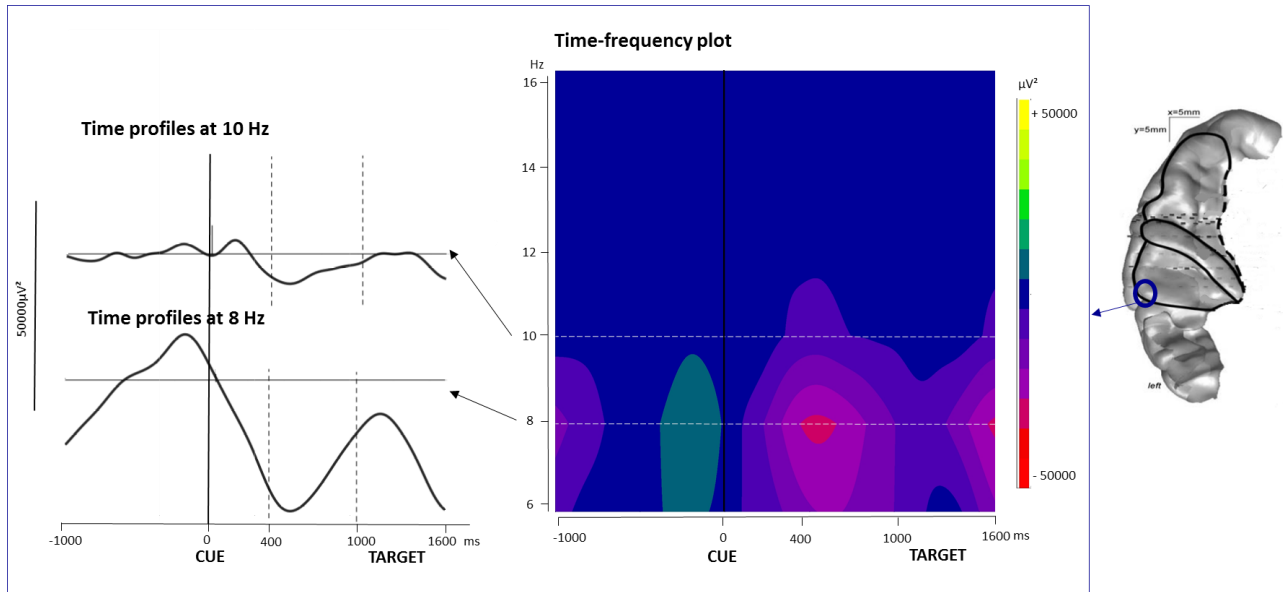
Figure 7- Time profile illustration – Alpha band oscillations were analyzed between 6 and 16Hz. To do so, we based our analysis on the time frequency transformation of electrophysiological activities (time frequency power averaged after wavelet-based transform of each single trial), between -1000 to 1600ms around cue onset, and in all conditions without distractor. The time profiles were constructed at 8 and 10Hz from the time-frequency plots. These responses are baseline corrected with respect to a prestimulus period preceding the cue onset.

Alpha modulation

We found a significant alpha modulation post-cue in anticipation of the upcoming target sound in all patients at 48 out of 187 contacts of electrodes in the different areas of the auditory cortex (Heschl's gyrus, Planum temporale, Planum polare). Figure 8 summarizes the spatio-temporal emergence of alpha activity for 2 frequencies 8 and 10Hz between 400 and 1000ms after cue onset. In the right hemisphere, a decrease in alpha activity is observed only in the planum polare. In the left hemisphere, alpha activity seems to mostly decrease, predominantly in the planum temporale and Heschl's gyrus.
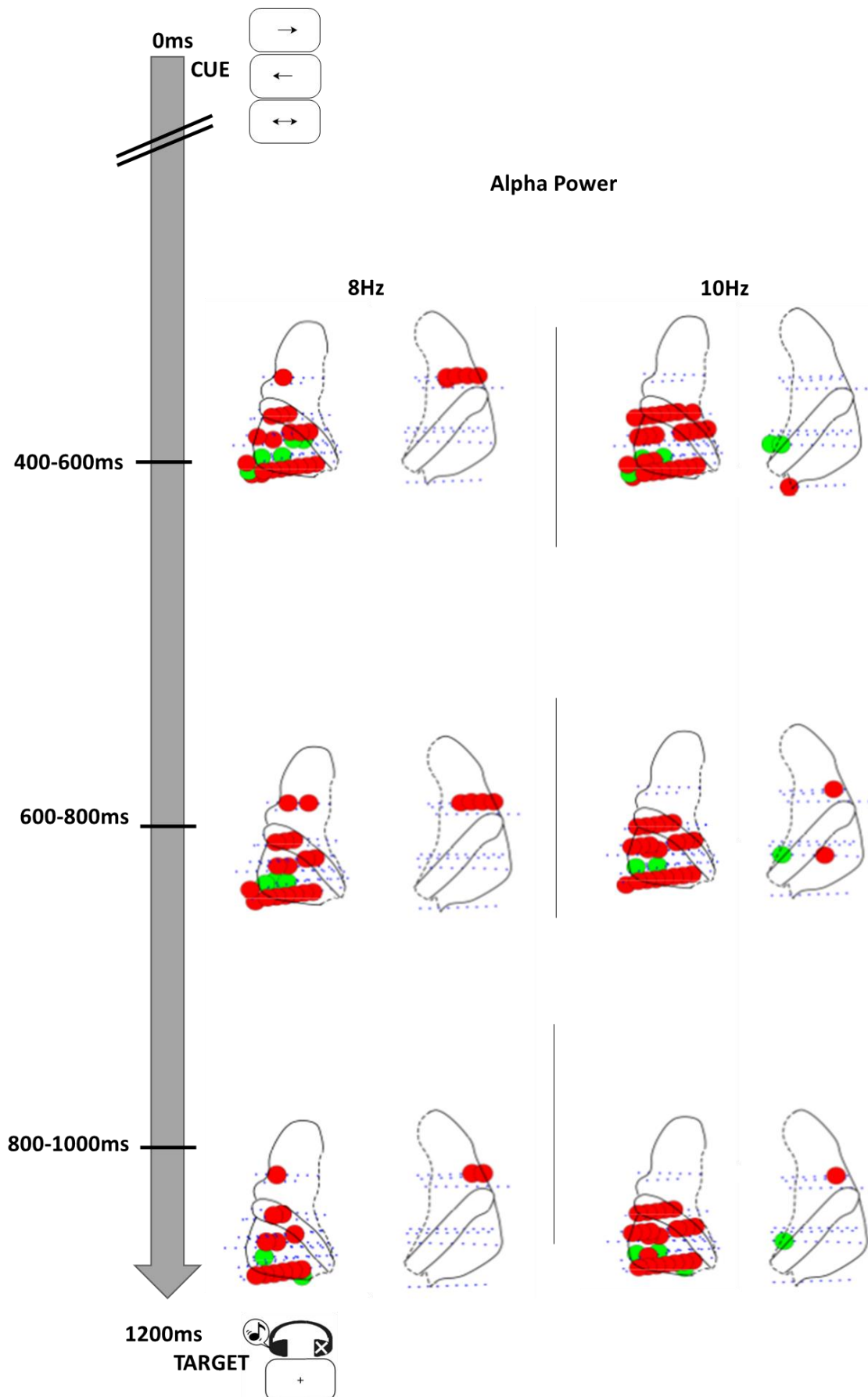
Figure 8 – Modulation of the auditory alpha activity post cue-onset. The significant modulation of this response is indicated by disks (green: increase / red: decrease) on the anatomical plots. These disks correspond to the significant auditory alpha activity at either the 8 or 10Hz frequency (over a 600ms time period: 400-1000ms, after FDR correction).

Attention Effects

The auditory alpha power was found significantly modulated by cue condition in 9 patients at 18 out of the 48 contacts presenting a significant modulation between 400 and 1000ms after cue onset. Different modulations were observed depending on the type of cue. A greater response was seen at 8 contacts in 6 patients in the contralateral condition, at 6 contacts in 3 patients in the ipsilateral condition, at 2 contacts in 2 patients in the uninformative condition and at 2 contacts in one patient both in the ipsilateral and contralateral condition (Figure 9). A majority of the modulations occurred between 600 and 800ms. Most of the contacts with modulations where located posteriorly and laterally to the primary auditory cortex in the left hemisphere. In the right hemisphere, the few contacts modulated were located in the anterior areas of the auditory cortex.
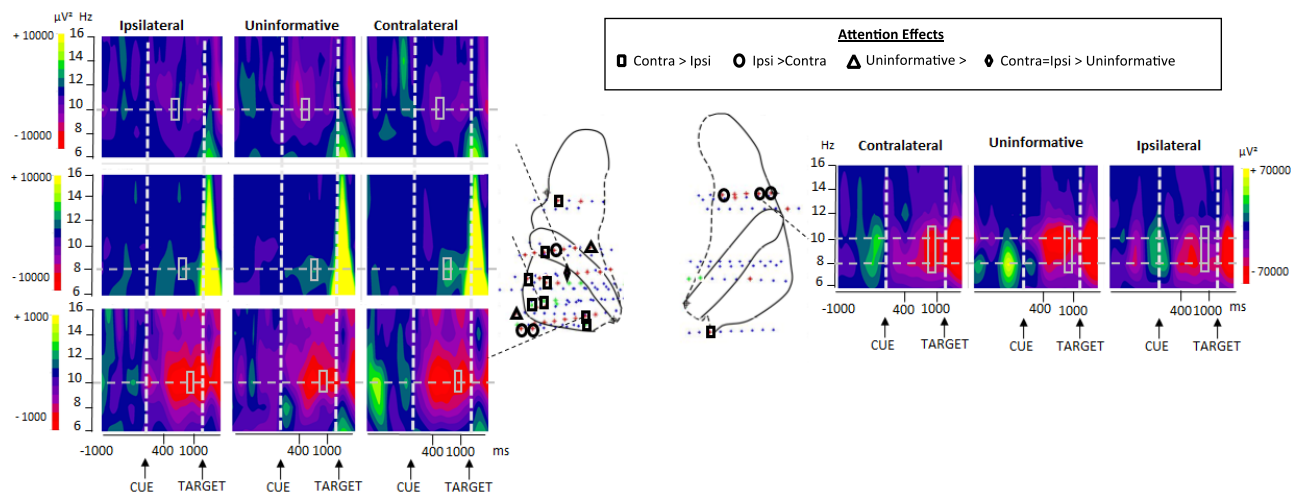

Figure 9 – Attention effects of the auditory alpha activity post cue-onset. The significant emergence of an auditory alpha activity at 8 and 10Hz frequencies between 400 and 1000ms is indicated by stars (green: increase / red: decrease) on the anatomical plots. Black squares on the figure correspond to contacts where auditory alpha activity was greater in the contralateral condition. Black ovals on the figure correspond to contacts where auditory alpha activity was greater in the ipsilateral condition. Black triangles correspond to contacts where auditory alpha activity was greater in the uninformative condition. Black diamonds on the figure correspond to contacts where auditory alpha activity was greater in the ipsilateral and contralateral conditions than in the uninformative condition. Some examples of this response is represented on time frequency plots on the left and right sides of the figure.

DISCUSSION

In this study, the aim was to characterize the mechanisms of preparatory attention in the primary auditory cortex and its associative auditory areas using intracranial recordings in Human. We found that top-down preparatory mechanisms during expectancy of an auditory target are indexed by the deployment of a sustained evoked response and the modulation of alpha oscillations. These responses are modulated by attention, according to the type of cue presented, mostly in associative posterior and lateral areas in the left auditory cortex.

Informative (left and right) cues lead to faster reaction times compared to uninformative cues, as documented in previous studies (Posner, 1980; Hillyard et al., 1998), suggesting an enhanced preparatory attention with informative cues. This effect is more likely to be related to preparatory attention than motor preparation since the motor response was always the same and could be evenly anticipated in informative and uninformative trials.

Sustained evoked response of preparatory attention

Slow sustained evoked responses started around 800ms after cue onset and slowly increased in amplitude up until the target onset. Similar responses have been reported in previous studies, either reflecting the deployment of preparatory attention in frontal regions (CNV, Brunia & Van Boxtel, 2001; Gómez et al., 2007; Bidet-Caulet et al., 2014) or reflecting an enhanced neural activity in modality-specific cortical areas underlying the representation of the to-be-attended location (Green & McDonald, 2006; Jongen et al., 2006; Grent-'t-Jong & Woldorff, 2007).

The present study shows a deployment of this sustained slow wave in the left hemisphere predominantly. First the wave is deployed in the primary auditory cortex and then spreads to auditory associative posterior and lateral areas (Planum temporale and lateral superior temporale gyrus). The left-right asymmetry, reported here, is consistent with previous findings. In an intracranial study, Bidet-Caulet et al. (2007) found that the effect of selective attention was predominant in the left hemisphere. Alcaini (1995) have suggested that the left hemisphere could be preferentially involved in voluntary attention, whereas the right hemisphere would be more engaged in automatic attentional orientation to unexpected stimuli.

Concerning the effects of attention on preparatory mechanisms, the present study reports a larger sustained response after informative cues (both ipsilateral and contralateral to the hemisphere recorded) in comparison with uninformative cues. These effects were observed along Heschl's gyrus and in posterior and lateral associative areas of the left auditory cortex. Furthermore, the sustained response is greater when the cued side is contralateral to the recorded hemisphere. These attentional effects are consistent with previous noninvasive studies, reporting a greater contralateral waveform than the ipsilateral waveform in relation to the to-be-attended side (Green and McDonald, 2006). Furthermore, adding to these studies, the present results confirm the presence of a sustained response reflecting preparatory attention, which is generated in auditory areas. Interestingly, this response is enhanced with increased attentional preparation, in particular when the cue is contralateral to the recorded site, along Heschl's gyrus and in posterior and lateral associative areas of the left auditory cortex.

Alpha oscillations during preparatory attention

During auditory target expectancy, we found, on one hand, a modulation of alpha activity in the auditory cortex between 400 and 1000ms post cue onset, in the 6- to 16Hz frequency band, predominantly in 8 and 10Hz. This modulation is manifested foremost by a decrease in alpha power, mostly in the left hemisphere, posteriorly and laterally to the primary auditory cortex. This alpha decrease during auditory target expectancy is in line with previous non-invasive studies (Lehtelä et al., 1997; Müller and Weisz, 2012; Weisz et al., 2013; Frey et

al., 2014). However, the timing of the alpha decrease varies depending on the studies. Indeed, Müller & Weisz (2012) and Weisz *et al.* (2013) reported that alpha decrease covered approximately 500 to 700ms post cue onset, but Frey *et al.* (2014) reported an alpha decrease along the line of our timing (450-900ms).

The present study reports alpha modulation predominantly in the left auditory cortex. These results are consistent with Frey *et al.* (2014). Indeed, they showed a modulation in the left but not the right auditory cortex of an auditory alpha rhythm. However, the effect of attention on either the left (Frey et al., 2014; Present Study) or the right auditory cortex (Müller and Weisz, 2012; Weisz et al., 2013) remains unclear. In the present study, more electrodes were implanted in the left auditory cortex than in the right. Perhaps the absence of alpha modulation in the right auditory cortex could be due to the less extensive coverage of this region.

On the other hand, the results regarding the attentional effects on preparatory mechanisms are complex. First of all, the effects of attention were found located in posterior and lateral parts of the left auditory cortex. In the present study, the effects of attention showed great variability during expectancy of the auditory target. Nevertheless, the alpha increase appears more predominantly when cued attention was contralateral to the recorded side. However, different attentional effects have been reported in previous noninvasive studies. Indeed, Frey *et al.* (2014) found a decrease in amplitude, when attention was directed to the right (contralateral) compared to the left (ipsilateral) side only. Using MEG, Müller & Weisz (2012) and Weisz *et al.* (2013) found a right hemispheric dominance of auditory attentional modulations. They showed significant increased alpha activity in the right auditory cortex, following ipsilateral visual cues signaling the location of auditory targets. The difference between the present and previous results could be due to a difference in task difficulty. Indeed, in their studies, the task was either to detect a target sound but close to perceptual threshold (Frey *et al.*, 2014) or to discriminate two competing sounds (Müller and Weisz, 2012; Weisz et al., 2013). In addition, the present study focused on trials without distractors. However, these trials were randomly positioned in the midst of trials including auditory distracting sounds, which could have impacted differently the attentional preparation. The difference in complexity observed between visual and auditory studies is possibly due to the uncertain of localization of the primary auditory cortex (Da Costa et al., 2011). In addition, the differences observed with non-invasive technics could be explained by the variability between subjects that needs to be taken into account when comparing power values between conditions (Haegens et al., 2014).

All together, the present results seem to confirm the existence of an alpha rhythm generated in auditory regions separated from occipital alpha band generators. As suggested by non-invasive studies, auditory alpha oscillations seem to have a functional relevance in auditory cognition and in audio-spatial attention. But how the modulation of alpha power impacts (facilitatory or inhibitory) auditory processing is still to debate.

Conclusion

These results show that preparatory auditory attention seems to recruit similar alpha-band oscillatory mechanisms and sustained evoked responses as visuo-spatial attention, in the auditory cortex. Indeed, sustained responses and alpha oscillations are generated in the auditory cortex and modulated by attention. However,

not all contacts showed a modulation of alpha activity and enhanced slow responses contralateral to attended space, as in non-invasive studies. Additional studies would be necessary to have a clearer view.

To further investigate the functional role of the sustained response and alpha oscillations, it would be interesting to correlate their deployment with reaction times and perhaps increased gamma oscillations (>30Hz) or early sensory event related potentials (N1, P2, P3b) to the target sound, reflecting increase target processing (Fries et al., 2008; Bidet-Caulet et al., 2014a). Concerning alpha oscillations, several other studies would be needed to have a clearer view of its mechanisms. First of all, we could study the link between pre- and post-target alpha activity, reported to decrease from baseline levels in task-relevant regions (Jensen and Mazaheri, 2010; Klimesch, 2012). Secondly, adding to the inhibition hypothesis, it would be interesting to investigate local and inter-areal alpha phase dynamics, based on a different hypothesis of the role of alpha oscillations in coordinating task-relevant neuronal processing. Indeed, some studies report that alpha phase synchronization between brain areas could support cognitive function such as attention (for review, see Palva & Palva, 2012). For example, in line with preparatory attention mechanisms in the auditory cortex, it would be interesting to study the synchronization between different areas such as frontal and auditory cortices, or visual and auditory cortices, or between auditory areas.

Even further along the road, the task was aimed at studying the interaction between top-down (anticipatory and inhibitory) and bottom-up (attentional capture) auditory mechanisms of attention, according to the position of the distractor in relation to the target sound. The investigation of evoked potentials and oscillations (low to high frequencies, transient coupling) seem relevant to understand the competition between top-down and bottom up mechanisms of auditory attention.

PERSPECTIVES

Another way to investigate the mechanisms of preparatory attention would be to study the functional impact of a lesion in the lateral prefrontal cortex (lPFC) on the mechanisms deployed during target expectancy. Indeed, the lPFC plays a crucial role in the control of attention. Functional MRI or positron emission tomography studies have found the lPFC to be involved in top-down attention in visual (Corbetta *et al.*, 2008) and auditory (Voisin *et al.*, 2006) modalities. Moreover, patients with lesions of the lPFC have been shown to have impairments in top-down anticipatory attention (Rosahl and Knight, 1995). However the role of lPFC in the deployment of preparatory oscillations remains unknown (Jensen and Mazaheri, 2010; Foxe and Snyder, 2011).

Using the same task as in the present study (Competitive attention test; visual cues and auditory targets), behavioral and scalp EEG data could be collected in patients with lPFC lesions (~n=15 patients and 15 control subjects). We then could explore the neurophysiological mechanisms of preparatory attention during the delay between the visual cue and auditory target, in the auditory cortex, by comparing brain responses to attended and unattended targets, on event related potential and oscillatory measures.

We would expect a disruption in the deployment of preparatory mechanisms when the cue is presented in the hemifield contralateral to the lesion, resulting behaviorally in increased reaction time to the auditory target compared to the control group. Compared to intracranial EEG recordings, this study would have a less precise localization of these components and the signals would be more contaminated by physiological artifacts such as muscles and eye-related activity. However, it would allow us to further understand how the different regions of the cortex participating in auditory preparatory attention are functionally coupled to the auditory cortex.

ACKNOWLEGMENTS

BIBLIOGRAPHIE

Aguera P-E, Jerbi K, Caclin A, Bertrand O (2011) ELAN: a software package for analysis and visualization of MEG, EEG, and LFP signals. Computational intelligence and neuroscience 2011:158970.

Alho K, Rinne T, Herron TJ, Woods DL (2014) Stimulus-dependent activations and attention-related modulations in the auditory cortex: a meta-analysis of fMRI studies. Hearing research 307:29–41.

Bidet-Caulet A, Barbe P-G, Roux S, Viswanath H, Barthélémy C, Bruneau N, Knight RT, Bonnet-Brilhault F (2012) Dynamics of anticipatory mechanisms during predictive context processing. The European journal of neuroscience 36:2996–3004.

Bidet-Caulet A, Bottemanne L, Fonteneau C, Giard M-H, Bertrand O (2014a) Brain Dynamics of Distractibility: Interaction Between Top-Down and Bottom-Up Mechanisms of Auditory Attention. Brain Topography. Epub ahead of print

Bidet-Caulet A, Buchanan K, Viswanath H, Black J, Scabini D, Bonnet-Brilhault F, Knight R (2014b) Impaired facilitarory mechanisms of auditory attention after damage of the lateral prefrontal cortex. Cerebral Cortex. In press

Bidet-Caulet A, Fischer C, Besle J, Aguera P-E, Giard M-H, Bertrand O (2007) Effects of selective attention on the electrophysiological representation of concurrent sounds in the human auditory cortex. The Journal of neuroscience : the official journal of the Society for Neuroscience 27:9252–9261.

Bidet-Caulet A, Mikyska C, Knight RRT (2010) Load effects in auditory selective attention: Evidence for distinct facilitation and inhibition mechanisms. NeuroImage 50:1–18.

Brunia CH, Van Boxtel GJ (2001) Wait and see. International Journal of Psychophysiology 43:59–75.

Corbetta M, Patel G, Shulman GL (2008) Review The Reorienting System of the Human Brain : From Environment to Theory of Mind. Neuron 58:306–324.

Da Costa S, van der Zwaag W, Marques JP, Frackowiak RSJ, Clarke S, Saenz M (2011) Human primary auditory cortex follows the shape of Heschl's gyrus. The Journal of neuroscience : the official journal of the Society for Neuroscience 31:14067–14075.

Foxe J, Simpson G, Ahlfors S (1998) Parieto-occipital~ 1 0Hz activity reflects anticipatory state of visual attention mechanisms. Neuroreport 9:3929–3933.

Foxe JJ, Snyder AC (2011) The Role of Alpha-Band Brain Oscillations as a Sensory Suppression Mechanism during Selective Attention. Frontiers in Psychology 2:13.

Frey JN, Mainy N, Lachaux J-P, Müller N, Bertrand O, Weisz N (2014) Selective modulation of auditory cortical alpha activity in an audiovisual spatial attention task. The Journal of neuroscience : the official journal of the Society for Neuroscience 34:6634–6639.

Fries P, Womelsdorf T, Oostenveld R, Desimone R (2008) The effects of visual stimulation and selective visual attention on rhythmic neuronal synchronization in macaque area V4. The Journal of neuroscience : the official journal of the Society for Neuroscience 28:4823–4835.

Genovese CR, Lazar N a, Nichols T (2002) Thresholding of statistical maps in functional neuroimaging using the false discovery rate. NeuroImage 15:870–878.

Giesbrecht B, Weissman DH, Woldorff MG, Mangun GR (2006) Pre-target activity in visual cortex predicts behavioral performance on spatial and feature attention tasks. Brain research 1080:63–72.

Gómez CM, Flores A, Ledesma A (2007) Fronto-parietal networks activation during the contingent negative variation period. Brain research bulletin 73:40–47.

Green JJ, McDonald JJ (2006) An event-related potential study of supramodal attentional control and crossmodal attention effects. Psychophysiology 43:161–171.

Grent-'t-Jong T, Woldorff MG (2007) Timing and sequence of brain activity in top-down control of visual-spatial attention. PLoS biology 5:114-126.

Haegens S, Cousijn H, Wallis G, Harrison PJ, Nobre AC (2014) Inter- and intra-individual variability in alpha peak frequency. NeuroImage 92:46-55.

Harter M, Miller S, Price N (1989) Neural processes involved in directing attention. Journal of cognitive neuroscience 1:223–237.

Hillyard S, Vogel E, Luck S (1998) Sensory gain control (amplification) as a mechanism of selective attention : electro- physiological and neuroimaging evidence. Phil Trans R Soc Lond B 353:1257–1270.

Hopf JM, Mangun GR (2000) Shifting visual attention in space: an electrophysiological analysis using high spatial resolution mapping. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology 111:1241–1257.

Jensen O, Mazaheri A (2010) Shaping functional architecture by oscillatory alpha activity: gating by inhibition. Frontiers in human neuroscience 4:186.

Jongen EMM, Smulders FTY, van Breukelen GJP (2006) Varieties of attention in neutral trials: linking RT to ERPs and EEG frequencies. Psychophysiology 43:113–125.

Kastner S, Pinsk M a, De Weerd P, Desimone R, Ungerleider LG (1999) Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron 22:751–761.

Kelly SP, Gomez-ramirez M, Foxe JJ (2009) The strength of anticipatory spatial biasing predicts target discrimination at attended locations : a high-density EEG study. European Journal of Neuroscience 30:2224–2234.

Klimesch W (2012) A-Band Oscillations, Attention, and Controlled Access To Stored Information. Trends in cognitive sciences 16:606–617.

Lamarche M, Louvel J, Buser P, Rektor I (1995) Intracerebral recordings of slow potentials in a contingent negative variation paradigm: an exploration in epileptic patients. Electroencephalography and clinical neurophysiology 95:268–276.

Lehtelä L, Salmelin R, Hari R (1997) Evidence for reactive magnetic 10-Hz rhythm in the human auditory cortex. Neuroscience letters 222:111–114.

Müller N, Weisz N (2012) Lateralized auditory cortical alpha band activity and interregional connectivity pattern reflect anticipation of target sounds. Cerebral cortex (New York, NY : 1991) 22:1604–1613.

Palva S, Palva JM (2012) Discovering oscillatory interaction networks with M/EEG: challenges and breakthroughs. Trends in cognitive sciences 16:219–230.

Pfurtscheller G, Stancák a, Neuper C (1996) Event-related synchronization (ERS) in the alpha band--an electrophysiological correlate of cortical idling: a review. International journal of psychophysiology : official journal of the International Organization of Psychophysiology 24:39–46.

Posner MI (1980) Orienting of attention. The Quarterly journal of experimental psychology 32:3–25.

Rihs T a, Michel CM, Thut G (2007) Mechanisms of selective inhibition in visual spatial attention are indexed by alpha-band EEG synchronization. The European journal of neuroscience 25:603–610.

Rosahl SK, Knight RT (1995) Role of Prefrontal Cortex in Generation of the Contingent Negative Variation. Cerebral Cortex 2:123–134.

Sauseng P, Klimesch W, Stadler W, Schabus M, Doppelmayr M, Hanslmayr S, Gruber WR, Birbaumer N (2005) A shift of visual spatial attention is selectively associated with human EEG alpha activity. The European journal of neuroscience 22:2917–2926.

Silver M, Ress D, Heeger D (2007) Neural correlates of sustained spatial attention in human early visual cortex. Journal of neurophysiology 97:229–237.

Sylvester CM, Shulman GL, Jack AI, Corbetta M (2007) Asymmetry of anticipatory activity in visual cortex predicts the locus of attention and perception. The Journal of neuroscience : the official journal of the Society for Neuroscience 27:14424–14433.

Tallon-Baudry C, Bertrand O (1999) Oscillatory gamma activity in humans and its role in object representation. Trends in cognitive sciences 3:151–162.

Thut G, Nietzel A, Brandt S a, Pascual-Leone A (2006) Alpha-band electroencephalographic activity over occipital cortex indexes visuospatial attention bias and predicts visual target detection. The Journal of neuroscience : the official journal of the Society for Neuroscience 26:9494–9502.

Voisin J, Bidet-Caulet A, Bertrand O, Fonlupt P (2006) Listening in silence activates auditory areas: a functional magnetic resonance imaging study. The Journal of neuroscience : the official journal of the Society for Neuroscience 26:273–278.

Weisz N, Hartmann T, Müller N, Lorenz I, Obleser J (2011) Alpha rhythms in audition: cognitive and clinical perspectives. Frontiers in psychology 2:73.

Weisz N, Müller N, Jatzev S, Bertrand O (2013) Oscillatory Alpha Modulations in Right Auditory Regions Reflect the Validity of Acoustic Cues in an Auditory Spatial Attention Task. Cerebral cortex (New York, NY : 1991). Epub ahead of print

Worden MS, Foxe JJ, Wang N, Simpson G V (2000) Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. The Journal of neuroscience : the official journal of the Society for Neuroscience 20:1-6.

Wu C-T, Weissman DH, Roberts KC, Woldorff MG (2007) The neural circuitry underlying the executive control of auditory spatial attention. Brain research 1134:187–198.