Neurophysiological Mechanisms of Auditory Distractibility in the Healthy, Aging or Damaged Human Brain

Hesham Elshafei

N°d'ordre NNT : xxx

THESE de DOCTORAT DE L'UNIVERSITE DE LYON

opérée au sein de

l'Université Claude Bernard Lyon 1

Ecole Doctorale ED476

Neurosciences and Cognitive Sciences

Spécialité de doctorat : Neurosciences

Discipline : Neurosciences

Soutenue publiquement le 22/11/2018, par :

Hesham A. ELSHAFEI

Neurophysiological Mechanisms of Auditory Distractibility in the Healthy, Aging or Damaged Human Brain

---

Devant le jury composé de :

Pr. Stephanie CLARKE	Université de Lausanne	Rapporteure
Pr. Sarang DALAL	Aarhus University	Rapporteur
Dr. Marie GOMOT	INSERM	Examinatrice
Pr. Norbert Nighoghossian	UCBL1	Examinateur
Dr. Aurélie BIDET-CAULET	INSERM	Directrice de thèse
Dr. Olivier BERTRAND	INSERM	Co-directeur de thèse

To Gimmy and Nouaa,

To Zozo,

Acknowledgements

First, I would like to thank my wonderful PhD supervisors. Olivier, thank you for your presence, support and helpful feedback. Aurélie, from day one, you have guided me through this adventure and you have taught me everything I know. I will always cherish the time we have spent together, working, arguing, travelling, and just plain having fun. There are no words to express my gratitude in the couple of languages I know. I would also like to thank everybody in the DYCOG team for their help and support and for just being who they are. Special thanks to:

- My MATLAB guru, Romain with whom we have spent hours and hours dealing with one hell of a messy dataset and with whom I am glad to have had co-authored my first paper;
- Lesly, for her invaluable help with data preprocessing; Anne for her insightful feedback and help with the frontal damage study;
- Catherine for help with patient recruitment; Professor Nighoghossian for opening the doors of his Stroke department.

Thanks to all of the great kids in the lab: Roxane, Marion, Enrico, Stephano, Raphaël, Jelle, Jelena, Oussama, Kristien, Gaëtan, Anne, Remy, Bastien, Salomé, Agathe, Laurianne, Thibaut, Benoit and Florian. You have put fun in fundamental research. I would also like to thank my magnetoencephalography heroes: Sébastien and Claude. Sébastien, you have been through the dozens of participants we have recruited, you have helped more than you were supposed to. MEG forever and for always.

A whole hearted thanks to all of the beautiful people I've shared my life outside of the lab with: Saloni, Judith, Alex, Mélaine, Camille and Elise. Thank you, my loves, for always being there throughout the rollercoaster of emotions this journey has been. And not to forget my (besties): Jimmy, Mr. n'aimes pas les tomates, Beyoncé, BenBen, Isabella and Coco, with whom I have become the person I have always wanted to be.

Last but not least, my family, whose love since my eyes opened to this world have carried me from one continent to another and from one career to another. Thank you for never stopping believing in me.

Finally, special thanks to the two artists who have accompanied and inspired me through the last year of this PhD: David Bowie and RuPaul.

Abstract

Top-down (TD) and bottom-up (BU) mechanisms of attention are supported by dorsal and ventral networks that mainly overlap in the lateral prefrontal cortex (lPFC). A balance between these mechanisms is essential, yet rarely investigated. Increased distractibility observed during ageing or after frontal damage could result from jeopardizing this balance. It has been proposed that distinct oscillatory frequencies support the activation of these two attention networks. Our main aim was to test, in the auditory modality, whether (1) alpha oscillations would coordinate activity within the dorsal TD network, (2) gamma activity would index the activation of the ventral BU network, (3) the lPFC would support the balance between these networks through oscillatory coupling. We also aimed to investigate the oscillatory correlates of the increased distractibility associated with ageing or frontal damage. MEEG data were recorded while participants performed the Competitive Attention Test, which enables simultaneous investigation of BU and TD attention mechanisms. We showed that alpha oscillations indexed facilitatory and suppressive mechanisms of TD attention, and communication within the dorsal network; while gamma oscillations indexed the ventral network activation. Moreover, the lPFC subtended communication in the two networks; with the TD/BU interaction occurring in the medial PFC. We also showed that ageing-related distractibility was of TD deficit origin. Finally, preliminary results suggest that lPFC damage can impact both TD and BU attention. This thesis provides novel insights into the brain oscillatory dynamics of the TD/BU attentional balance supporting distractibility.

Keywords: *Auditory attention; Attentional capture; Alpha oscillations; Gamma activity; Oscillatory coupling; Ageing; Frontal damage; Magnetoencephalography*

Résumé

Les mécanismes volontaires (V) et involontaires (I) de l'attention reposent sur les réseaux dorsal et ventral, convergeant dans le cortex préfrontal latéral (lPFC). La distractibilité accrue liée au vieillissement ou à une lésion frontale pourrait être due à une altération de l'équilibre entre ces mécanismes V et I, essentiel mais rarement étudié. Notre objectif est de tester, dans la modalité auditive, si (1) les oscillations alpha coordonnent l'activité du réseau dorsal, (2) les oscillations gamma celle du réseau ventral, (3) le couplage oscillatoire dans le lPFC maintient l'équilibre entre les deux réseaux. Ce travail vise également à étudier les corrélats oscillatoires de la distractibilité accrue liée au vieillissement ou à une atteinte frontale. Des données MEEG ont été enregistrées alors que des participants réalisaient le Competitive Attention Test, qui permet d'étudier simultanément les mécanismes V et I de l'attention. Nous avons montré que les oscillations alpha reflètent l'activation des mécanismes facilitateurs et suppresseurs de l'attention V, et la communication au sein du réseau dorsal ; alors que les oscillations gamma indexent l'activation du réseau ventral. De plus, le lPFC serait impliqué dans la communication au sein des deux réseaux, et le PFC médian dans l'équilibre attentionnel V/I. Nous avons également montré que la distractibilité accrue était liée à un déficit d'attention V au cours du vieillissement, et à une altération des processus V et I après lésion frontale. Ce travail de thèse offre donc une meilleure compréhension de la dynamique cérébrale oscillatoire sur laquelle repose l'équilibre attentionnel V/I, et donc la distractibilité.

Mots-clés : Attention auditive ; Capture attentionnelle ; Oscillations alpha ; Activité gamma ; Couplage Oscillatoire ; Vieillissement ; Lésion frontale ; Magnétoencéphalographie

Résumé Substantiel

L'attention est une fonction cérébrale qui permet, volontairement ou non, de faciliter le traitement de certaines informations de l'environnement tout en ignorant les autres. Le traitement des informations par le cerveau est contrôlé par deux types de processus : des processus volontaires et involontaires. D'une part, l'attention volontaire permet de sélectionner les informations pertinentes pour réaliser efficacement la tâche en cours. L'attention volontaire peut agir par différents mécanismes tels que des mécanismes facilitateurs ou inhibiteurs et des mécanismes de préparation ou d'anticipation attentionnelle. D'autre part, l'attention peut être capturée involontairement par un stimulus saillant inattendu, et donc détournée de la tâche en cours. Cette forme involontaire de l'attention est nécessaire pour pouvoir réagir à un évènement potentiellement important mais non pertinent pour la tâche en cours (ex. une alarme au feu). La tendance au détournement involontaire de l'attention est communément dénommée distractibilité. Un bon équilibre entre l'attention volontaire et l'attention involontaire est crucial pour être efficace dans une tâche donnée, tout en étant réactif à l'environnement, sans être distrait en permanence. Un manque de distractibilité pointe vers une dominance de l'attention volontaire, alors qu'une distractibilité accrue peut être due soit à une réduction de l'efficacité de l'attention volontaire, soit à une facilitation du déclenchement de la capture attentionnelle involontaire. Cet équilibre précaire est souvent altéré dans des pathologies psychiatriques ou neurologiques, et même au cours du vieillissement normal.

L'attention volontaire reposerait sur un réseau dorsal comprenant les régions frontales postérieures et intra-pariétales, alors que la capture attentionnelle involontaire activerait un réseau ventral incluant les la jonction temporo-pariétale et le cortex frontal ventral. Ces deux réseaux convergent au niveau du cortex préfrontal latéral (lPFC). Par ailleurs, l'exploration des activités oscillatoires est une approche idéale pour étudier la dynamique des mécanismes attentionnels. En effet, des études chez l'animale et l'humain suggèrent que l'activité oscillatoire refléterait non seulement l'activation mais aussi la communication au sein des réseaux ventral et dorsal de l'attention.

Ce travail de thèse a pour objectif de tester les hypothèses suivantes. (1) Un couplage longue distance dans les basses fréquences alpha (8-14 Hz) coordonnerait l'activité au sein du réseau dorsal de l'attention volontaire. (2) Les activités dans les hautes fréquences gamma (>

30 Hz) reflèteraient l'activation du réseau ventral de l'attention involontaire. (3) Le couplage des oscillations haute et basse fréquence dans le lPFC permettrait la communication entre les deux réseaux et sous-tendrait l'équilibre entre l'attention volontaire et l'attention involontaire. Ce travail a également pour but de comprendre l'origine cérébrale de la distractibilité exacerbée associée au vieillissement sain ou à une altération du cortex frontal en étudiant cette hiérarchie oscillatoire.

Des données MEG / EEG ont été simultanément enregistrées alors que des participants réalisaient le Competitive Attention Test. Ce paradigme permet d'évaluer, sur les plans comportemental et neurophysiologique, les processus d'attention volontaire (anticipation et inhibition attentionnelles) et involontaire (capture attentionnelle). Nous avons montré que les oscillations alpha reflétaient l'action de mécanismes facilitateurs et suppresseurs de l'attention volontaire dans les cortex auditifs (pertinents pour la tâche) et les cortex visuels (non pertinents pour la tâche), respectivement, via des sous-bandes d'alpha distinctes. La synchronisation de phase dans la bande alpha pourrait sous-tendre la communication entre les cortex auditifs et des régions distantes du réseau dorsal de l'attention volontaire. Nous avons aussi montré que les oscillations gamma reflétaient l'activation du réseau ventral de l'attention involontaire. De plus, le lPFC serait impliqué dans la communication cérébrale, via synchronisation de phase, au sein des deux réseaux ; tandis que l'équilibre attentionnel volontaire/involontaire reposerait sur le PFC médian et le cortex cingulaire antérieur. Nous avons également observé que la distractibilité au cours du vieillissement était liée à un déficit d'attention volontaire plutôt qu'à une altération du réseau ventral de l'attention involontaire. Enfin, les résultats comportementaux préliminaires que nous avons obtenus après accident vasculaire cérébral indiquent que des lésions du lPFC entraineraient à la fois des altérations de l'attention volontaire et de l'attention involontaire.

Ce travail de thèse offre donc une meilleure compréhension de la dynamique oscillatoire de l'équilibre attentionnel volontaire/involontaire qui conduit à un bon niveau de distractibilité chez l'adulte jeune sain ou à une distractibilité accrue au cours du vieillissement sain ou pathologique.

Table of Contents

List of Figures

List of Acronyms

APF: Alpha Peak Frequency

BU: Bottom-up

CAT: Competitive Attention Task

CFC: Cross-frequency coupling

CMV: Contingent Magnetic Variation

CNV: Contingent Negative Variation

CSD: Cross-spectral density

DICS: Dynamical Imaging of Coherent Sources Beamformer

dlPFC: Dorsolateral Prefrontal Cortex

dmPFC: Dorsomedial Prefrontal Cortex

EEG: Electroencephalography

ERP: Event-Related Potential

FEF: Frontal Eye Fields

fMRI: Functional Magnetic Resonance Imaging

IPS: Intraparietal Sulcus

LC-NE: locus Coeruleus-Norepinephrine

LCMV: Linearly Constrained Minimum Variance Beamformer

lPFC: Lateral Prefrontal Cortex

MEG: Magnetoencephalography

MMN: Mismatch negativity

PAC: Phase-Amplitude Coupling

PCC: Partial Cannonical Correlation Beamformer

PET: Positron Emission Tomography

RON: Reorientation Negativity

RT: Reaction Time

TD: Top-down

TFR: Time-Frequency Representation

TMS: Transcranial Magnetic Stimulation

TPJ: Temporoparietal Junction

VFC: Ventral Frontal Cortex

vlPFC: Ventrolateral Prefrontal Cortex

vmPFC: Ventromedial Prefrontal Cortex

NB: Acronyms are always first defined in the text before being used as abbreviations.

Preamble

"Sand was dribbling out of the bag of her attention, faster and faster."

— Sarah Blake

Our environment contains far more information than we can process at one time. Thus, we depend on our attention to orient our limited resources towards relevant items. Attention can be oriented endogenously (top-down), in anticipation of a stimulus, a red light turning green for example; or it can be captured exogenously (bottom-up), e.g. by a telephone ringing. A dynamic balance between top-down and bottom-up mechanisms of attention is essential to carry out day-to-day tasks, and the tendency to have one's attention captured is commonly referred to as distractibility.

"Any distraction tends to get in the way of being an effective gangster."

— Terence Winter

Top-down and bottom-up mechanisms of attention are supported by distinct brain networks that overlap mainly in the lateral prefrontal cortex. Nevertheless, these mechanisms have been mostly explored in the visual domain and in separate experiments, with few attempts to investigate the balance between them. Moreover, several questions have been raised concerning the paradigm which has been used to investigate auditory distractibility i.e. the oddball paradigm.

Brain oscillations refer to the rhythmic activity generated spontaneously or in response to stimuli by neurons in the central nervous system. More and more, the role of brain oscillations as functional building blocks in sensory-cognitive processes such as attention is being established. Moreover, there is a growing hypothesis that activity in different oscillatory band, alpha and gamma, support different mechanisms of attention, top-down and bottom-up, respectively.

Throughout the work presented here in this thesis, we have adapted, The Competitive Attention Test, a novel paradigm recently proposed to investigate (1) the oscillatory orchestra underlying top-down and bottom-up auditory attentional mechanisms, and the balance between them; (2) how this balance changes with healthy ageing and frontal lobe damage.

In the first four chapters, the theoretical context of this work shall be laid out, followed by a description of the main methodological techniques used throughout the thesis work. Afterwards, four studies shall be presented highlighting our main results, followed by a synthesis and a discussion of these results.

Part I: Theoretical Context

1 Attention as a Concept

1.1 What We Talk About When We Talk About Attention

"The world is too much with us [..] Little we see in Nature that is ours"
— William Wordsworth

Imagine a modern-day PhD student listening to a tutorial on how to write a thesis. The time he would make it from the beginning to the end of the audio, a mobile phone has beeped, a colleague giggled over a cat photo and many other external and internal events have competed for neural representation (Ruff 2013). Facing these numerous events is our brains' limited processing capacity. Thus, we rely on our attention to prioritize the processing of only a fragment of these incoming stimuli (Desimone and Duncan 1995; Reynolds and Heeger 2009), but what do we talk about when we talk about attention? While according to William James: "Everyone knows what attention is…" (James 1890), more than a century of psychology, psychophysics and neurosciences research have provided us with numerous views of what attention could be.

First, attention was viewed as a "filter" or a "bottleneck" through which all physical properties of incoming stimuli would be first extracted, then based upon task-relevant properties, irrelevant (unattended) stimuli would be selectively filtered out while relevant (attended) stimuli would pass for further processing (Broadbent 1958; Duncan 1980). This model was updated, where attention was regarded rather as a "buffer" where relevant and irrelevant stimuli would be processed but to different extents i.e. processing of irrelevant (unattended) stimuli would be much attenuated in comparison to that of the augmented processing of attended stimuli (Treisman 1964). Later on, attention would be considered as "glue" which combines singleton features of attended stimuli that are pre-attentively extracted and separated (Treisman and Gelade 1980; Treisman 1988).

However, a more compelling view of attention is that rather than being a unitary phenomenon, attention should be regarded as a multi-component system that involves several cognitive processes and relies on different brain networks (Posner and Petersen 1990; Posner and Fan 2008; Petersen and Posner 2012). In their seminal review, Posner and Petersen (1990) have proposed that attention is sustained by three main systems/networks: the

alerting system, the executive system and the orienting system. The latter is the main focus of this thesis; however, the other two systems shall be discussed here briefly.

Alerting, phasic alertness or phasic arousal can be understood as a rapid increase of vigilance (readiness) from resting baseline that could be triggered in response to warning signals or in anticipation of upcoming stimuli (Kahneman 1973; Posner and Petersen 1990; Petersen and Posner 2012). It is distinguishable from **tonic (intrinsic) alertness (arousal)** which fluctuates in the order of minutes to hours and refers to a more general form of wakefulness control (Sturm et al. 1999; Degutis and Van Vleet 2010). It has been demonstrated that alertness is associated with several physiological responses, such as an increase in cardiac rhythm (Kahneman 1973; Oken et al. 2006). In addition, behaviorally it manifests as a reduction in reaction times when a target event is preceded by a warning signal in comparison to the absence of such signal (Marrocco et al. 1994; Marrocco and Davidson 1998; Beane and Marrocco 2004). The activation of the alerting system has been associated with the locus coeruleus-norepinephrine (LC-NE) system, a neuromodulatory system in the midbrain which could influence the cortical control of attention through noradrenergic innervation to cortical regions such as the right inferior and superior frontal gyri and the parietal cortex (Marrocco et al. 1994; Coull et al. 1996; Raz and Buhle 2006; Sara and Bouret 2012; Masson and Bidet-Caulet 2018).

Executive attention or executive control is another major component of the attentional framework (Petersen and Posner 2012). This system is essential for complex situations that requires planning, decision making, conflict resolution among competing cognitive elements, process switching, and novelty detection (Bush et al. 2000; Botvinick et al. 2001). The application of such system could be demonstrated in tasks such as the Stroop task where participants are required to indicate the written color name (e.g. green), that could be congruent (e.g. green) or not (e.g. blue) with the actual color of the word (Stroop 1935; Fan et al. 2009). The activation of the executive system has been associated with two main frontal regions: the anterior cingulate cortex and the lateral prefrontal cortex (Damasio and Sutherland 1994; Anderson et al. 2000; Ochsner et al. 2001; Stuss 2011).

The third component in the aforementioned taxonomy is the **orienting system**. Orienting refers to the allocation of attention to a specific perceptual input thus prioritizing the processing of such attended input (Eriksen and Hoffman 1972; Posner 1980; Hawkins et al. 1988). Orienting could englobe various modalities, e.g. visual, auditory or somatosensory,

and could involve attentional allocation to specific points in space i.e. spatial attention (Posner 1980) or in time (Coull and Nobre 1998). Spatial auditory attention is the main focus of this thesis.

Orienting can occur in two different modes: **top-down** or **bottom-up** (Posner and Petersen 1990; Petersen and Posner 2012). For example, going back to our PhD student, on one hand, while listening to the tutorial, he is actively orienting (allocating) his attention to the lecturer's voice in an endogenous top-down manner. On the other hand, the colleague's audible giggle would orient the student's attention in an exogenous bottom-up manner. In a laboratory setting, one of the main paradigms that has been used to disentangle these two modes of attentional orienting is the Posner Spatial Cuing Paradigm (Posner 1980). Typically, participants are first presented with a visual or an auditory cue that indicates the spatial location of an upcoming visual or auditory target.

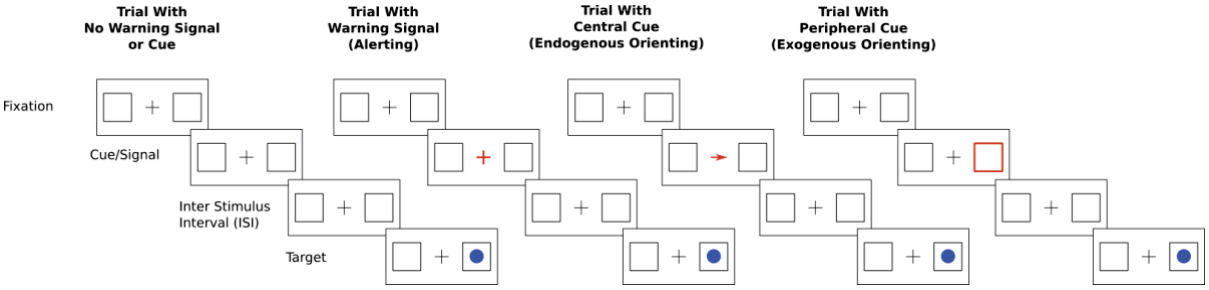


Figure 1. Representative frames of four different trials of the Posner Cueing Paradigm. Participants are often required to press a button as soon as they detect the target (Adapted from Chica et al. 2013).

As shown in **Figure 1**, in the Posner paradigm, attention could be oriented either endogenously, using a spatially central cue which informs the participant on the potential location of the target. Attention could also be oriented exogenously, using a spatially peripheral cue, which automatically captures the participant's attention to the possible location of the target (Posner 1980). These cues could be either valid i.e. the target location would match the location indicated by the cue or invalid i.e. the target location would not match the location indicated by the cue.

In order to disentangle the orienting component of attention from the alerting component, one could add trials where either (1) the cue is substituted by a warning signal (or an uninformative cue) or (2) no cue nor warning signals are present. Thus, by subtracting the uninformative cue, from the no cue condition, we could obtain a measure of the alerting

system. Moreover, by subtracting the uninformative cue from the informative cue condition, we could obtain a measure of the top-down or bottom-up orienting system, with central or peripheral cues, respectively (Petersen and Posner 2012).

We've described the different components of attention which should be regarded as a multicomponent system: alerting, orienting and executive control. Now let's delve into the underlying neurophysiological correlates of the two orienting mechanisms of attention (top-down and bottom-up) and the interplay between them.

1.2 Ground Control to Major Tom: Top-Down Attentional Mechanisms

Top-down, or endogenous, attentional orienting is a voluntary, goal-driven process that enables the efficient performance of an on-going task by selecting relevant information (Posner and Petersen 1990; Berger et al. 2005; Petersen and Posner 2012). It has been thoroughly investigated using the Posner paradigm with a central visual or auditory cue that either indicates (informative) or not (neutral/uninformative) the spatial location of an upcoming visual or auditory target. By comparing informative and uninformative cue-trials, investigators could shed light onto the deployment of top-down attentional orienting mechanisms using various behavioral and neurophysiological measures.

Behaviorally, reaction times to targets preceded by an informative cue are shorter than those preceded by an uninformative cue. In other words, when participants are informed of the location of the upcoming target, they are faster to detect or discriminate these targets (Müller and Findlay 1988; Müller and Rabbitt 1989; Golob et al. 2002; Hayward and Ristic 2013; Bidet-Caulet et al. 2014; ElShafei et al. 2018).

The neural correlates of this orienting (cueing) effect has been investigated using either neuroimaging techniques such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI) or electrophysiological techniques such as Electroencephalography (EEG), Magnetoencephalography (MEG) or intracranial EEG recordings. The deployment of top-down attention can be investigated via cue-locked activity during the time-interval between the cue and the target. In addition, the impact of top-down attention on target processing can be investigated via target -locked activity.

1.2.1 Top-Down Attention

Before the presentation of the target, several studies highlighted the presence of cue-related evoked activity usually arising (500-600ms) after cue presentation: the Contingent Negative Variation (CNV: Brunia and van Boxtel 2001) and it's magnetic counterpart: the Contingent Magnetic Variation (CMV: Gómez et al. 2004). For example, as seen in **Figure 2**, using an adaptation of the Posner paradigm, Bidet-Caulet and colleagues (2014) reported an enhanced amplitude of the CNV in trials with cues informative of an upcoming auditory target, compared to trials with uninformative cues. This has led to the suggestion that the CNV represents a reliable index of top-down attention deployment (Brunia 1999; Brunia and van Boxtel 2001; Gómez et al. 2004, 2007, Bidet-Caulet et al. 2012, 2014).

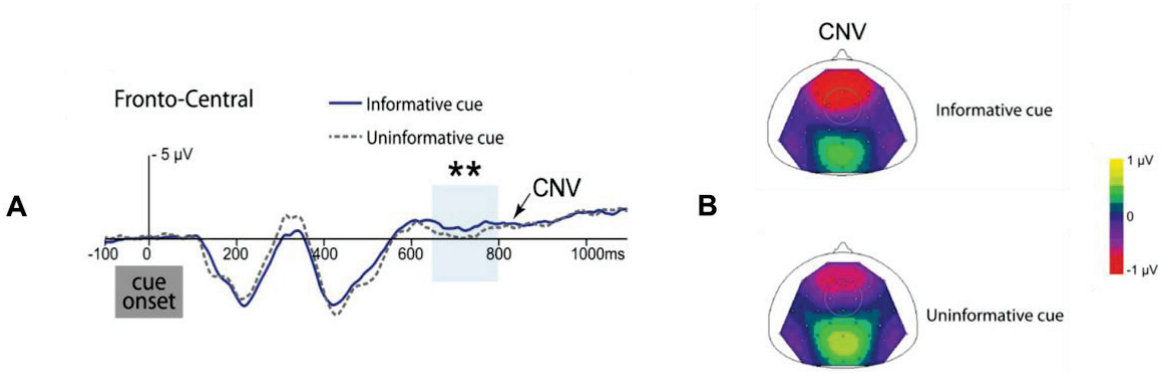


*Figure 2. Cue-Related Potentials. A. Mean cueRPs at the fronto-central group of electrodes as a function of the cue category (informative or uninformative). B. Scalp topographies of the CNV, in trials with informative or uninformative cue in the 650–800 ms window after cue onset. **P<0.01. (Adapted from Bidet-Caulet et al. 2014).*

However, concerns have been raised on which process the CNV represents: anticipatory attention or motor preparation. It has been proposed that the CNV represents both however on two different time scales. In other words, the CNV can be divided into an early and a late phase (Brunia and van Boxtel 2001), where the early phase of the CNV would primarily reflect anticipatory attention, and the late phase of the CNV would principally index (but not necessarily uniquely) motor preparation (Brunia and van Boxtel 2001; Hart et al. 2012).

In addition, studies using fMRI have demonstrated pre-activation of brain sensory regions relevant for processing the upcoming target. For example, task-relevant visual (Kastner et al. 1999; Liu et al. 2014), auditory (Voisin et al. 2006; Bueti and Macaluso 2010) or somatesnesory (Langner et al. 2011) regions have been shown to be pre-activated according to the modality of the expected target. Thus top-down attention increases sensory activity

and would subsequently improve the processing of anticipated relevant input, acting as a facilitatory mechanism.

1.2.2 Top-Down Modulation of Target processing

After the presentation of the target, studies using electrophysiological techniques, have utilized target-related evoked activity to investigate the impact of the deployment of top-down attention on target processing. Target sound presentation has been associated with three main canonical evoked responses: the fronto-central N1 negative response (80—110 ms post target onset), the central P2 positive response (150—200 ms post onset) and the parietal P3 positive response (250—450 ms post onset) (Hillyard et al. 1973; Caporello Bluvas and Gentner 2013).

On one hand, numerous studies have demonstrated that top-down attention enhanced the amplitude of the early N1/P2 components (see **Figure 3**), reflecting an enhanced processing of the attended stimuli in comparison to the non-attended stimuli in the auditory (Picton and Hillyard 1974; Hansen and Hillyard 1980; Näätänen and Picton 1987; Neelon et al. 2006; Bidet-Caulet et al. 2007) and the visual (Eason et al. 1969; Mangun and Hillyard 1991; Guerreiro et al. 2010; Mittag et al. 2013; Slagter et al. 2016) modalities.

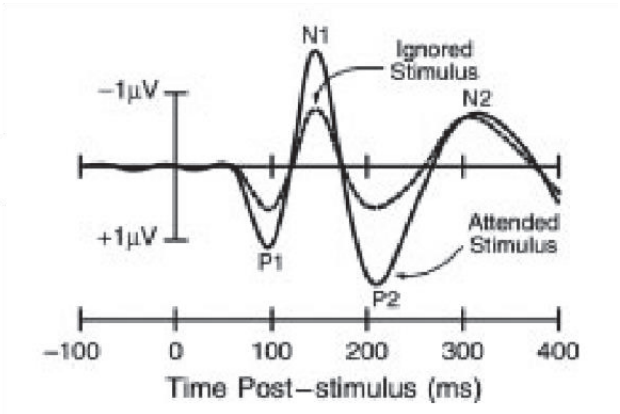


Figure 3. The Event-Related Potential (ERP) elicited by a visual stimulus typically consists of early sensory evoked components including the N1 wave followed by higher-level cognitive components such as the P3. ERPs shown here are in response to left field stimuli. The early sensory evoked component N1 are typically found to be larger when a stimulus is presented at an attended location as compared with an unattended location. (Adapted from Hillyard et al. 1998).

On the other hand, several studies have demonstrated an opposite effect of top-down attention on the amplitude of the P3 component (Hugdahl and Nordby 1994; Golob et al. 2002; Ofek and Pratt 2004; Bidet-Caulet et al. 2014). For example, Bidet-Caulet and colleagues (2014) demonstrated a reduced P3 component to auditory targets preceded by an informative cue in comparison to those preceded by an uninformative cue (see **Figure 4**). This reflects the functional relevance of the P3 component as a tracker of the probabilities of possible events with its amplitude reflecting target certainty rather than attentional relevance (Duncan-Johnson and Donchin 1977; Suwazono et al. 2000; Mars et al. 2008; Bidet-Caulet 2014).

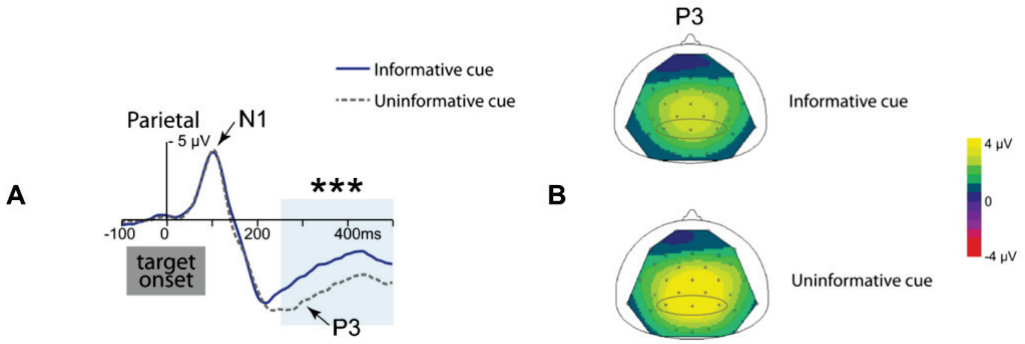


*Figure 4. ERPs to targets (targetRPs). A. Mean at the parietal group of electrodes as a function of the cue category. B. Scalp topographies of the target-P3, in trials with informative or uninformative cue in the 250–500 ms window after target, *** P<0.001. (Adapted from Bidet-Caulet et al. 2014).*

1.2.3 Top-Down Modulation of Selection

Thus far, we have described how top-down anticipatory attention would modulate brain activity during the expectation of a unimodal target, but what if we are faced with other targets in a different or same modality as that of the expected target? In the auditory modality, in order to investigate top-down auditory attention, investigators have used the dichotic-listening paradigm which requires the subject to attend to an auditory stream presented to one ear while ignoring an auditory stream presented to the other ear (Cherry 1953; Broadbent 1958). This form of top-down selective attention promotes the processing of attended (relevant) stimuli, resulting in reduced brain responses to unattended (irrelevant) inputs and enhanced processing of relevant information (Hillyard et al. 1998).

In addition, using imaging techniques such as fMRI and PET (see **Figure 5**), it has been demonstrated that attention to one modality during presentation of asynchronous streams of auditory and visual objects enhances activity in the sensory cortex of the attended modality and decreases activity in the sensory cortex of the unattended modality (Ghatan et al. 1998;

Kastner and Ungerleider 2000; Laurienti et al. 2002; Johnson and Zatorre 2006; Salmi et al. 2007; Serences and Yantis 2007; Salo et al. 2013, 2017). This suggests that there exits two distinct sub-systems within the top-down selective attentional system: a facilitatory system which increases brain activity to task-relevant input and a suppressive system which decreases brain activity to task-irrelevant input (Pinsk et al. 2004; Gazzaley et al. 2005; Bidet-Caulet et al. 2007, 2010; Chait et al. 2010). However, while modulations of an anticipated target processing suggest the deployment of distinct facilitatory and suppressive attentional mechanisms during target expectancy, little is known about the genuine activation of these mechanisms during anticipation of an upcoming stimulus.

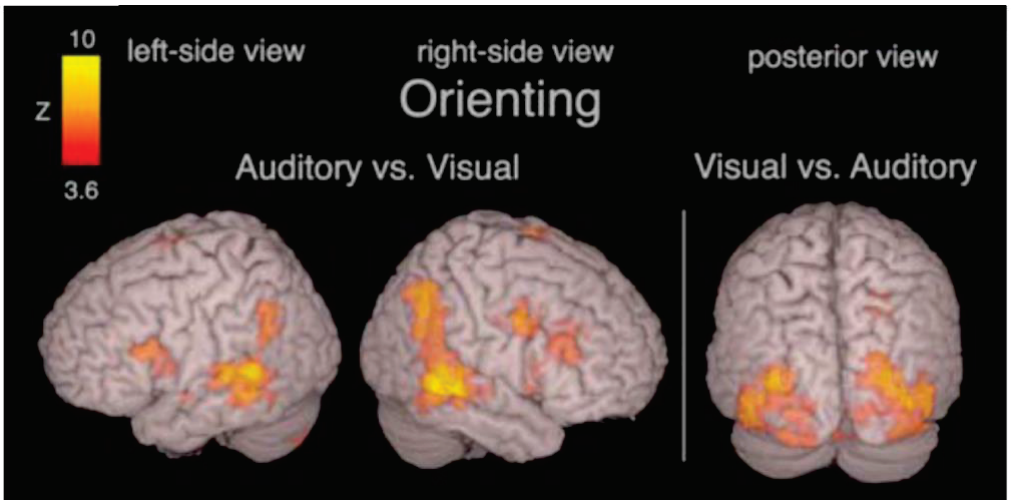


Figure 5. Comparison of auditory versus visual orienting tasks revealed auditory and visual modality- specific attention-related modulations. (Adapted from Salmi et al. 2007)

In summary, we have described behavioral, electrophysiological and functional neural correlates of top-down anticipatory mechanisms of attention. We have demonstrated how top-down anticipatory attention would modulate both cue- and target-related activity. Finally, we have provided evidence that top-down attention would comprise two systems: a facilitatory system and a suppressive system. However, the activation of these systems during stimulus anticipation remains barely investigated.

1.3 Major Tom to Ground Control: Bottom-Up Attentional Mechanisms

1.3.1 Bottom Up Attentional Mechanisms: Definitions & Key Aspects

Above, we have discussed how attention can be oriented in an endogenous top-down manner. Attention can also be oriented in an exogenous (bottom-up) manner, as when captured by task-irrelevant salient stimuli (such as luminosity change or a car break screech) that are not in our initial intentions or goals (James 1890; Jonides 1981). In comparison to top-down mechanisms, bottom-up attentional mechanisms are externally-driven, less voluntary, and more automatic.

The involuntary allocation of attention away from one's goal directed behavior is denoted distraction, and the tendency to have one's attention captured in such fashion is denoted distractibility. Distraction has been studied in the visual and auditory modalities using different approaches and here, a special focus shall be on distraction by sound due to the fundamental differences in how information is registered and processed in the two modalities. For example, whereas the spatial selectivity of the visual system provides a strong selection mechanism, the auditory system does not appear to allow such an extreme focus i.e. our ears cannot be easily shut to avoid registering sound, unlike the eyes in relation to light (Hughes 2014).

Distraction as a behavioral phenomenon underlies two distinct mechanisms: interference-by-process and attentional capture (Hughes 2014). For example, in a seriall recall task, participants are required to memorize (encode) and then recall a series of digits (e.g. Jones et al. 1992; Jones and Macken 1993; Neath 2000). If for example, a distracting sound is played during either the memorization or recalling phases, the negative behavioral impact of such sound would stem from its interference with the ongoing process and not necessarily due to an allocation of attention towards it (Hughes 2014).

A distracting sound could also impact behavioral performances primarily due to its physical saliency and its capability to momentarily disengage attention away from the focal task, regardless of the particular processing involved in the ongoing task (Escera et al. 1998; Parmentier 2008; Parmentier et al. 2008). We shall focus more on the latter mechanism of distraction: attentional capture which, in turn, could be categorized into two separate forms according to the nature of the distracting sound and the ongoing task.

First is the transition-related attentional capture which corresponds to the occurrence of "transients" in an ongoing stimulation such as a sudden onset of a sound during silence or

even the reverse, a sudden offset of a long-lasting sound (Wetzel and Schröger 2014). Second is the deviance-related attentional capture, which is associated with the predictive modeling of regularities in the acoustic environment. In other words, a distracting sound violates an established model of auditory regularities (Schröger et al. 2014; Wetzel and Schröger 2014). In the literature, the latter has received much more "attention" and thus we shall discuss the main paradigm that has been used for that line of work and afterwards we shall discuss the pitfalls of the use of such paradigm and then discuss a relatively more recent line of work investigating mainly the transition-related form of attentional capture.

1.3.2 Bottom Up Attentional Mechanisms: The Oddball Paradigm

Deviance-related attentional capture has been investigated using variations of the reaction time-based oddball paradigm. In this paradigm, participants are required to respond (detect or discriminate) to a specific target stimulus. Meanwhile, they are presented with a sequence of repetitive regular (standard) stimuli which are sporadically interrupted by a rare (deviant or oddball) stimulus that breaks this repetitive sequence and potentially captures the participants' attention. It has been proposed that attentional capture could be measured as the difference between the time taken to respond to a target stimulus in the presence and absence of the rare deviation (Dalton and Hughes 2014).

One variation of this paradigm (see **Figure 6**) has been used by Schröger and colleagues (1996). In this paradigm, participants were presented with a pair of tones (S1 in the left ear followed by S2 in the right ear). They were instructed to ignore sounds in the left ear (S1) while attending to the other (S2) in order to perform a Go/NoGo task. In the unattended ear, S1 was either a standard sound (played 88% of the time) or a deviant sound with a carrier frequency that deviates from the standard sound by a small or large magnitude. Participants were slower when S2 was preceded by a small deviant S1, even more so when it was preceded by a large deviant S1, when compared to trials where it was preceded by a standard S1. The authors have related this RT effect to the attentional capturing effect of the deviant sounds.

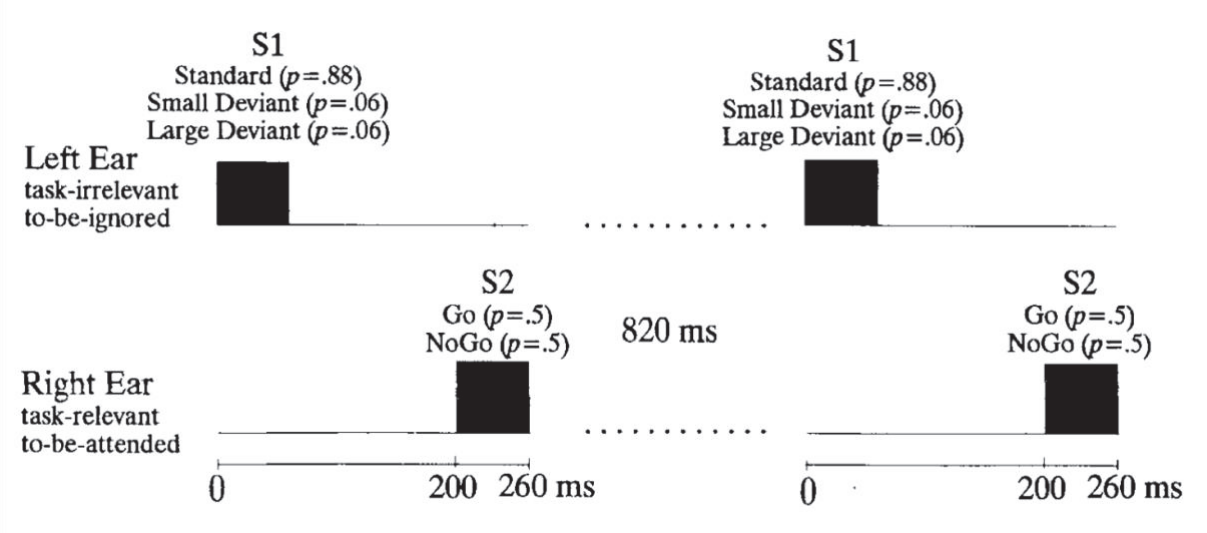


Figure 6. Pairs of tones (S1 and S2) were presented and subjects were instructed to ignore S1 (left ear) and make a Go/NoGo response to S2 (right ear). SI had a standard frequency of 700 Hz occasionally deviating by a small (p = 0.06; Af = 50 Hz) or large (p = 0.06; Af = 200 Hz) amount. S2 were presented with an intensity of 70 (Go; p = 0.5) or 80 (NoGo; p = 0.5) dB SPL The S1-S2 interval was 200 msec. (Adapted from Schröger 1996).

Another variation (see **Figure 7**) has been proposed by Escera and colleagues (Escera et al. 1998). In this paradigm, participants were instructed to perform a visual discrimination task while ignoring a sequence of sounds that contained standard tones (80%), deviant tones (10%), and novel natural sounds (10%). Reaction times to visual stimuli preceded by a deviant tone were longer compared to those preceded by a standard tone. Moreover, reaction times to visual stimuli preceded by novel sounds were even more prolonged in comparison to standard and deviant tones. Several studies have replicated these results using different versions of these two paradigms (Parmentier et al. 2008; Parmentier and Hebrero 2013).

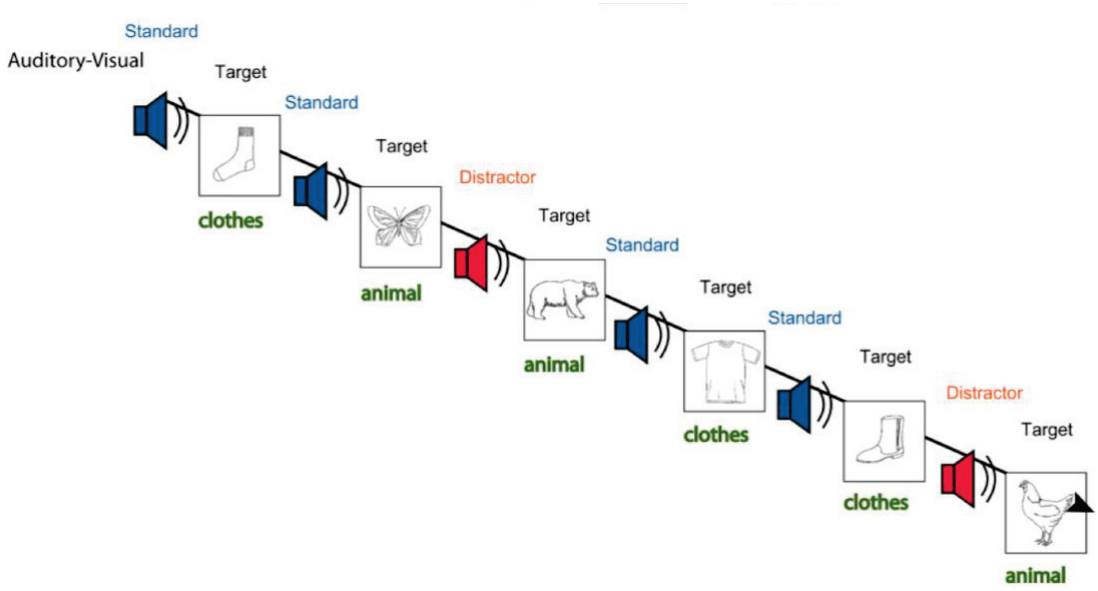


Figure 7. A variation of the auditory-visual oddball paradigm, in which standard and oddball (deviant or novel) sounds are presented while the participant is engaged in a visual task not related to the distinction between standard and oddball sounds. All sounds are followed by a picture of animals or clothes. Subjects are instructed to distinguish animal and clothes by button press. (Adapted from Wetzel and Schröger 2014).

Alongside these behavioral effects, a triumvirate of electrophysiological responses to deviant sounds has been extensively reported: the mismatch negativity, the P3a and the reorientation negativity (RON) (Schröger 1997, 2005; Escera et al. 1998; Jacobsen et al. 2003; Winkler 2007; Berti 2008; Berti et al. 2013).

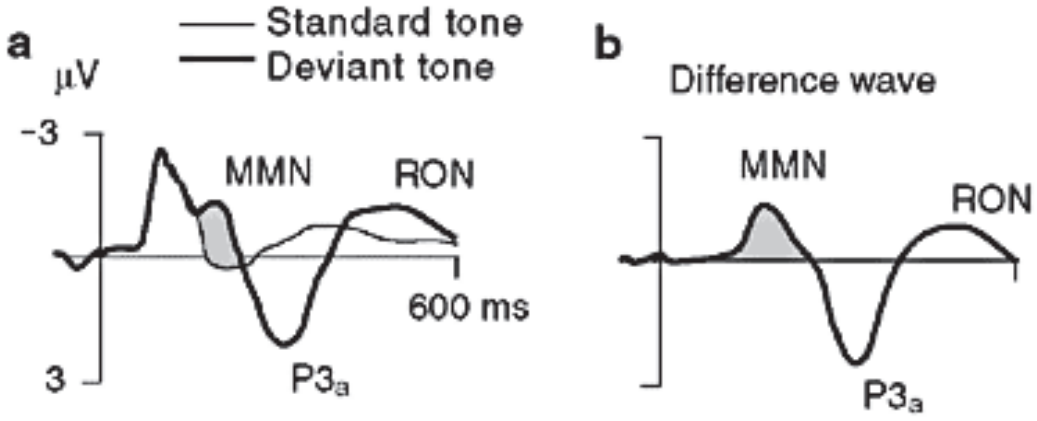


Figure 8. Idealized illustration of (a) Event-Related Potentials to standard and deviant tones in an oddball paradigm. (b) Difference waves between standard and deviance tones highlighting the deviant-related triumvirate responses: the mismatch negativity (MMN), the P3a and the reorientation negativity (RON). (Adapted from Kahkonen and Ahveninen 2002).

According to these studies, each component represents a stage in the three-stage model of distraction. First the MMN would represent the automatic detection of the deviant sound, then the P3a would index novelty detection and involuntary orienting of attention towards novel sounds (review in Escera et al. 2000). Finally, the RON would reflect the reorienting of attention to task-relevant information (Escera et al. 2003; Escera and Corral 2007; Horváth et al. 2008).

1.3.3 Bottom Up Attentional Mechanisms: How odd is the ball?

Nevertheless, recently, the use of the reaction-time based oddball paradigm has received several critiques. First, target stimuli in this paradigm are always preceded by a sound. Thus, one might wonder if these irrelevant sounds act as warning signals rather than true distractors. Indeed, Parmentier and colleagues (2010) demonstrated that varying the relationship between the deviant sound and the probability/onset of the target sound could abolish distraction effects or even result in facilitation effects. Second, attentional capture (distraction) is measured by comparing reaction times in trials with novel sounds and trials with standard sounds, while there is no comparison with the reaction times in the absence of any sound (Bidet-Caulet et al. 2014). Third, the sounds are embedded in sequences that could be inhibited by top-down mechanisms of selective attention similarly to the unattended stream in a classic dichotic paradigm i.e. listening to different acoustic stimuli presented to each ear simultaneously (Hillyard et al. 1973). Interestingly when distracting sounds are not presented within a sequence the cost in reaction time is highly reduced (Berti 2013).

In summary, we have described behavioral and electrophysiological correlates of bottom-up attentional capture which have been almost uniquely investigated using the oddball paradigm. Finally, we have reviewed recent critiques to this paradigm. In the following section, we shall discuss alternative paradigms to investigate not only bottom-up mechanisms of attention but also the interaction of such mechanisms with top-down mechanisms.

1.4 Let's Dance: Interaction Between Top-Down & Bottom-Up Attentional Mechanisms

As seen above, top-down and bottom-up mechanisms have been mostly investigated in separate experiments (Corbetta and Shulman 2002). Only few studies have explored how an unexpected stimulus outside the focus of attention can disturb top-down attentional mechanisms necessary to the good performance of the ongoing task, and how these top-down mechanisms can modulate the bottom-up mechanisms of attentional capture triggered by the unexpected stimulus.

For example, Miller and colleagues (2011) investigated distraction through presentation of rare isolated environmental sounds while subjects were playing a video game: Tetris. The authors could show that enhancing top-down attention, by increasing the game difficulty, resulted in reduced brain responses to distracting sounds. This was in accordance with previous evidence that the electrophysiological P3a response to deviant distracting sounds could actually be altered (amplitude reduction) by attentional load or task demand leading to reduced attentional orienting towards the distracting sound (Harmony et al. 2000; Zhang et al. 2006; SanMiguel et al. 2008; Lv et al. 2010). Unfortunately, in their study Miller and colleagues could not measure the impact of the distracting sounds on the game performance neither at the behavioral nor at the electrophysiological level.

In 2014, Bidet-Caulet and colleagues proposed a novel paradigm, the Competitive Attention Task (CAT), that allows the assessment of bottom-up and top-down mechanisms of auditory attention in a more ecological setting. This paradigm shall be discussed in length in the Material and Method section but to summarize, it is an adaptation of the Posner cueing paradigm using visual cues and monaural auditory targets. In this task, top-down (TD) anticipatory attention is measured by comparing trials with informative cues to trials with uninformative cues. Bottom-up (BU) attentional capture is triggered by a binaural distracting sound played during the delay between the cue and the target in only 25 % of the trials. Distraction is assessed as the impact of distracting sounds on task performance and the balance between TD and BU mechanisms can be measured by comparing responses to distracting sounds following informative vs. uninformative cues.

Using scalp EEG recordings, they were able to show that, on the one hand, increasing the load in top-down anticipatory attention decreases distracting sound processing at early stages (as reflected by N1 to distracting sounds), but seemed to fail to reduce the behavioral distraction effect. On the other hand, bottom-up attentional capture by distracting sounds

could disturb top-down mechanisms by lengthening target processing (as reflected by N1 to targets) and detection (see **Figure 9**).

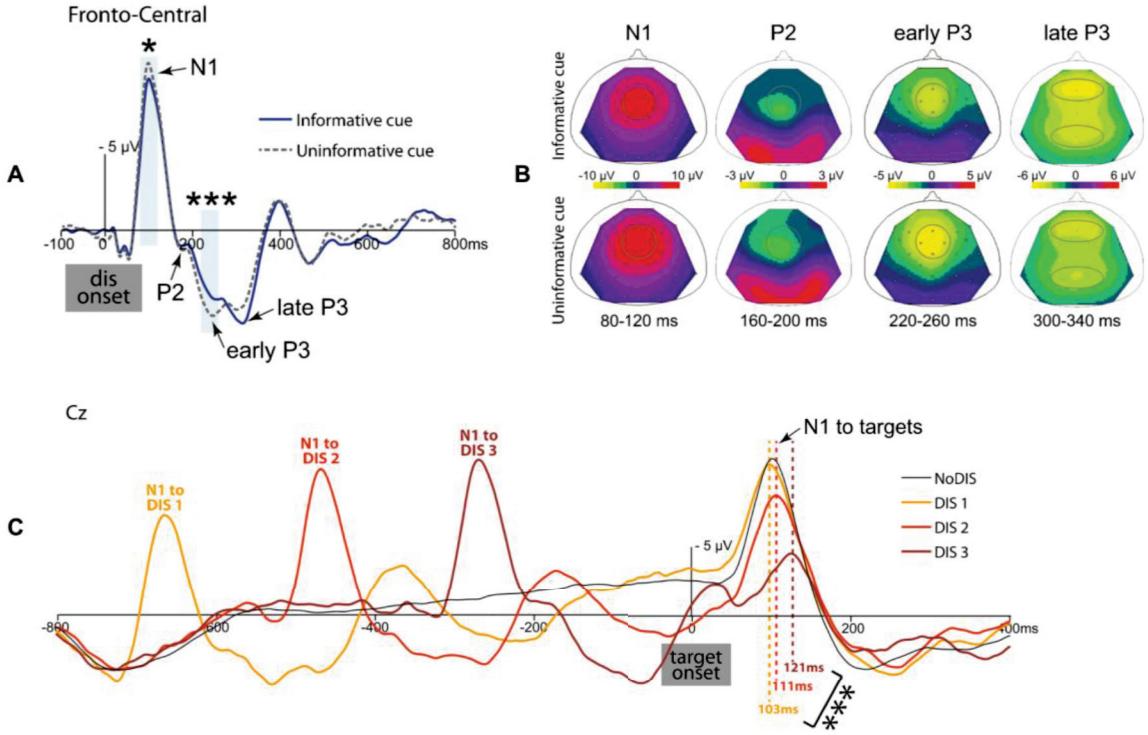


*Figure 9. A. Mean ERPs to distracting sounds at the fronto-central group of electrodes as a function of the cue category (informative or uninformative). B. From left to right, scalp topographies of the N1, P2, early P3 and late P3, in trials with informative or uninformative cue after distractor onset, respectively. C. Mean ERPs to targets according to distractor onset time at Cz electrode (NoDIS, DIS1, DIS2, DIS3). *P<0.05, ***P<0.001. (Adapted from Bidet-Caulet et al., 2014).*

In summary, while several endeavors have been undertaken to investigate bottom-up and top-down mechanisms of attention separately, there have been fewer attempts to investigate the interaction between the two mechanisms. In the light of the concerns about the oddball paradigm's adequacy, we believe that the CAT would be more particularly suitable to investigate the underpinnings of such interaction.

2 Attention as a Network

"Invisible threads are the strongest ties."
— Friedrich Nietzsche

In the previous chapter, we have attempted to define top-down and bottom-up attentional mechanisms in a phenomenological sense. We have also presented electrophysiological and fMRI markers of these mechanisms. In this chapter, we discuss how these mechanisms are supported by distinct yet overlapping brain networks. Since much of the knowledge about such networks stems from studies investigating visual attention, we shall be discussing studies from visual and auditory modalities.

2.1 Networks Supporting Top-Down Attentional Mechanisms

In their seminal review, Corbetta and Shulman (2002) identified two major brain networks supporting top-down (endogenous) and bottom-up (exogenous) attentional mechanisms: a **dorsal** fronto-parietal network and a **ventral** fronto-parietal network, respectively. In the visual domain (see **Figure 10**), two main hubs for top-down signals have been highlighted: The Frontal Eye Fields (FEF) and the Intraparietal Sulcus (IPS). The visual top-down orienting system has been investigated in both the human (Kastner et al. 1999) and the non-human primate (e.g. Wardak et al. 2006) brain using several techniques such as PET (Corbetta et al. 1993; Nobre et al. 1997; Vandenberghe et al. 1997) and fMRI (Gitelman et al. 1999; Kastner et al. 1999; Shulman et al. 1999; Wojciulik and Kanwisher 1999; Corbetta et al. 2000, 2002; Hopfinger et al. 2000; Wardak et al. 2006). A recurrent finding in these studies is an enhanced activation of both the FEF and IPS when participants direct their attention endogenously towards a visual hemifield.

Activity in these regions have also been found to dynamically track the locus of attention in the visual field (Serences and Yantis 2007). Moreover, using techniques such as single-pulse transcranial magnetic stimulation (TMS) that could interfere with signal propagation across cortical regions, it has been demonstrated that temporary abruption of FEF/IPS activity impeded participants to successfully orient their attention to anticipated targets (Szczepanski and Kastner 2013). However, there is evidence that FEF and IPS might play slightly different roles in top-down attention. In two separate studies, Hung and

colleagues demonstrated that disruption of the IPS functioning (Hung et al. 2005) led to an impaired top-down attention control only in the visual hemifield contralateral to the upcoming target (responsible for processing an upcoming target). However, disruption of the FEF (Hung et al. 2011) functioning, impaired top-down control in both contralateral and ipsilateral hemifields.

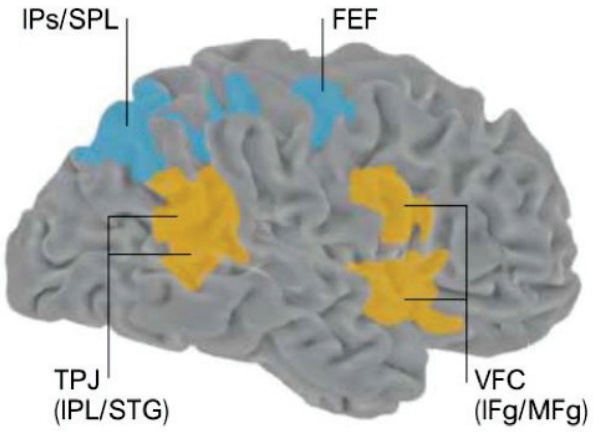


Figure 10. Dorsal and ventral fronto-parietal networks. Areas in blue indicate the dorsal fronto-parietal network. FEF, frontal eye field; IPs/SPL, intraparietal sulcus/superior parietal lobule. Areas in orange indicate the stimulus-driven ventral fronto-parietal network. TPJ, temporoparietal junction (IPL/STG, inferior parietal lobule/superior temporal gyrus); VFC, ventral frontal cortex (IFg/MFg, inferior frontal gyrus/middle frontal gyrus). (Adapted from Corbetta and Shulman 2002).

In the auditory domain, there is a growing number of neuroimaging studies suggesting that top-down endogenous orienting of auditory attention engages cortical circuitry that is highly similar (see **Figure 11**) to that engaged during visual attention e.g. the FEF and the IPS (Rosano et al. 2002; Shomstein and Yantis 2004; Mayer et al. 2006; Wu et al. 2007; Smith et al. 2010; Kong et al. 2012; Lee et al. 2013). However, several studies have reported the activation of other regions during top-down orienting of auditory attention such as the inferior frontal gyrus (Voisin et al. 2006; Salmi et al. 2009), the dorso- (Voisin et al. 2006; Salmi et al. 2009) and ventro-lateral (Kong et al. 2012) prefrontal cortex, suggesting a more widespread dorsal network of top-down auditory attention. Moreover, Kong and colleagues (2012) demonstrated that even within the common (supramodal) regions of top-down attention such as the IPS, visual and auditory attention recruit different neuronal subpopulations (Kong et al. 2012).

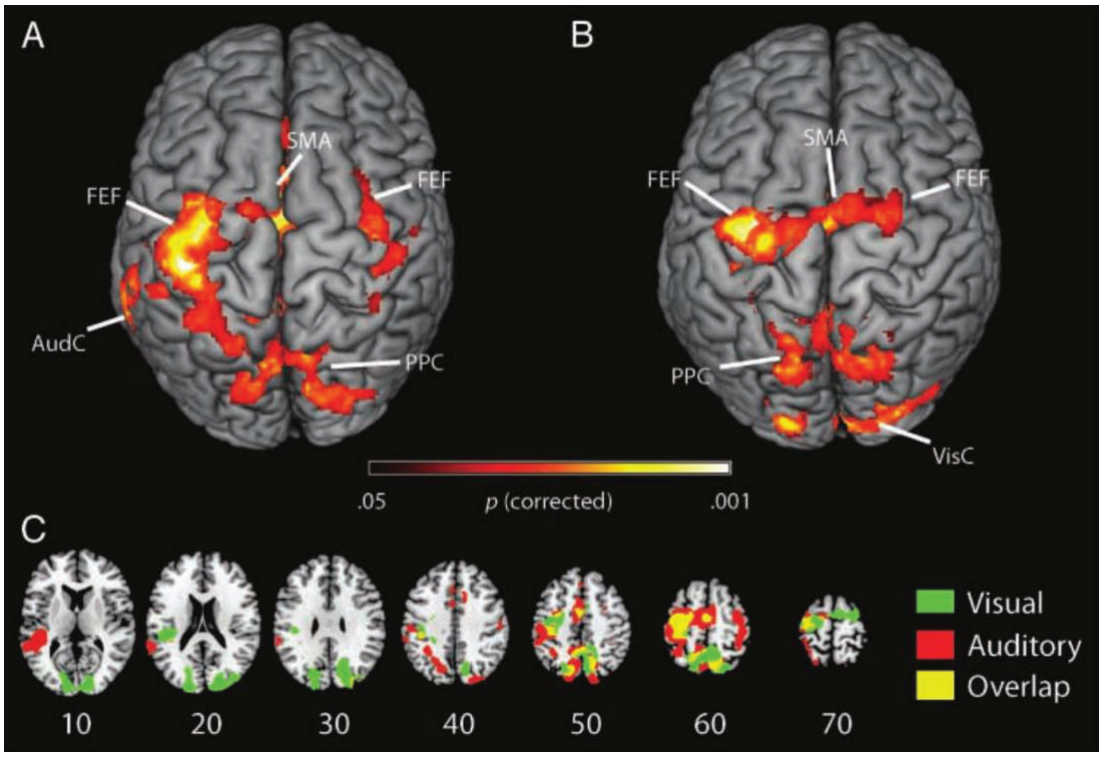


Figure 11. Auditory and visual attention evoke similar patterns of brain activation. (A) Neural basis of audiospatial attention (spatial cues versus non-spatial cues). (B) Neural basis of visuospatial attention. (C) Statistical maps from both conditions (auditory and vision) on the same background image. FEF: Frontal Eyes Fields, PPC: Posterior Parietal Cortex, SMA: Supplementary Motor Area, AudC: Auditory Cortex, VisC: Visual Cortex. (Adapted from Smith et al. 2010).

2.2 Networks Supporting Bottom-Up Attentional Mechanisms

Supporting the bottom-up (exogenous) attentional mechanisms is the ventral fronto-parietal network comprising the temporoparietal junction (TPJ) and the ventral frontal cortex (inferior and middle frontal gyri) (Corbetta and Shulman 2002; Corbetta et al. 2008; Chica et al. 2013; Ruff 2013). In the visual domain, various studies have demonstrated the activation of these regions in response to rare (low-frequency) stimuli and/or during attentional capture by task-irrelevant stimuli (Robinson et al. 1995; Steinmetz and Constantinidis 1995; Downar et al. 2000, 2001; Kirino et al. 2000; Marois et al. 2000; Serences et al. 2002).

Although often investigated separately, neural networks supporting visual and auditory bottom-up attentional mechanisms appear to be highly similar (Mayer et al. 2009; Salmi et al. 2009; Huang et al. 2012; Larson and Lee 2013a). For example, in a meta-analysis of more than 70 studies investigating brain activation during an oddball paradigm, revealed that the ventral (bottom-up) network was almost identical in both modalities, except for a more right-lateralized TPJ activation in the visual modality in comparison to a bilateral

activation in the auditory modality (Kim 2014). Thus, it has been suggested that ventral (and dorsal) networks supporting bottom-up (and top-down) attentional mechanisms are potentially supramodal systems (Macaluso et al. 2003; Macaluso and Driver 2005; Macaluso 2010; Vossel et al. 2014).

Finally, it's important to note that while so far we have outlined distinct regions for dorsal and ventral networks, some investigations in the visual domain demonstrated that such distinction between the two networks might not be as clear as we would like to believe (Serences and Yantis 2007). This common activation has been reported even more in the auditory domain (Salmi et al. 2009; Alho et al. 2014). For example, Alho and colleagues reported activations of the FEF/IPS and the TPJ to both top-down and bottom-up orienting of attention. However, the activation of the IPS was more prominent in the top-down orienting task.

2.3 Prefrontal Cortex (PFC)

It has been shown that while the dorsal and ventral networks are anatomically segregated, there exists some overlap between them in the visual (Buschman and Miller 2007; Corbetta et al. 2008; Katsuki and Constantinidis 2014) and auditory (Salmi et al. 2009; Alho et al. 2014) domains. A recurrent candidate for this overlap is the lateral prefrontal cortex (Chao and Knight 1995; Kim et al. 1999; Miller and Cohen 2001; Fox et al. 2006; He et al. 2007). Below, we shall first detail the various structures (see **Figure 12**) that constitute the prefrontal cortex and their role in cognition. Then, we shall highlight how the lateral prefrontal cortex, in particular, could support the dynamic balance (interaction) between top-down and bottom-up networks attention.

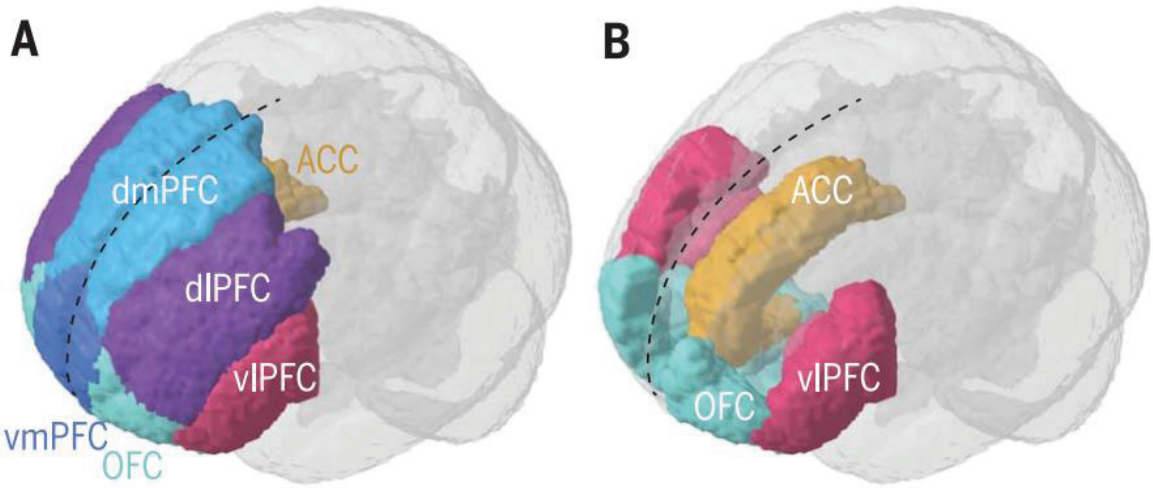


Figure 12. Functional division of the human prefrontal cortex. (A and B) Tilted frontal-side view (left) of the human brain with illustration of common functional divisions of the prefrontal cortex. dlPFC: dorsolateral prefrontal cortex, dmPFC: dorsomedial prefrontal cortex, vmPFC: ventromedial prefrontal cortex, vlPFC: ventrolateral prefrontal cortex, OFC: oribital frontal cortex, ACC: anterior cingulate gyrus. (Adapted from Carlen 2017).

The prefrontal cortex can be subdivided into a medial and a lateral part. The medial prefrontal cortex (comprising the ventro- and dorso- medial prefrontal cortices), along with the anterior cingulate cortex, is a component of the cognitive control system, with higher activation of these regions corresponding to enhanced active suppression of irrelevant stimuli (Rule et al. 2002; Badre 2008; Salmi et al. 2009). The lateral prefrontal cortex (comprising the ventro- and dorso- lateral prefrontal cortices) also plays a major role in cognitive task control (Cole et al. 2013). Interestingly, the auditory modality is richly represented in the prefrontal cortex more than any other modality i.e. the auditory modality impinges on prefrontal cortices on the lateral, medial, and orbital surfaces with almost every area of the prefrontal cortex having some connections with auditory association cortices (Barbas et al. 2012a). In addition to this role in cognitive control, the prefrontal cortex seems to play an important role in balancing top-down a bottom-up attentional mechanisms.

On one hand, it has been demonstrated, in both visual (Kastner and Ungerleider 2000) and auditory (Bushara et al. 1999; Zatorre et al. 1999; Lewis et al. 2000; Voisin et al. 2006) modalities, that the lateral prefrontal cortex (lPFC) plays a role in supporting top-down attention by activating the pathway of the relevant sensory modality (Barceló et al. 2000; Esterman and Yantis 2010) and inhibiting the irrelevant sensory modality pathway (Caclin and Fonlupt 2006). In other words, lPFC could be involved in the top–down control of attention by

means of biasing sensory processing in favor of information that is behaviorally relevant (Miller and D'Esposito 2005; Rossi et al. 2007). In addition, studies using transcranial magnetic stimulation (TMS) have demonstrated a causal role of lateral prefrontal top-down signals in modulating the neural processing of relevant stimuli (Johnson et al. 2007; Miller, Vytlacil, et al. 2011; Zanto et al. 2011). Taken together, these findings suggest that the lateral prefrontal cortex plays a crucial role in the top-down control of attention.

On the other hand, lPFC seems to also play an important role in bottom-up attentional mechanisms. fMRI studies suggest that the lPFC is involved in attentional capture in both auditory (Watkins et al. 2007) and visual (Han and Marois 2014) modalities. lPFC activation has been associated with the inhibition of responses to distracting stimuli (Dolcos et al. 2007; Clapp et al. 2010; Suzuki and Gottlieb 2013). In addition, reduced activity in the lPFC has been linked to impaired distraction processing (Gaebler et al. 2015), while increased connectivity between the lPFC and task-relevant regions reduces external interference (Takeuchi et al. 2015). Finally, Cosman and colleagues (2015) decreased susceptibility to attentional capture by utilizing transcranial direct-current stimulation (tDCS) to stimulate the lPFC. However, it remains unclear whether lPFC is actually involved in the attentional capture itself and/or in controlling reorientation of attention towards the initial task.

In summary, these results highlight the implication of the lPFC in both top-down and bottom-up attentional mechanisms. Based upon these findings, we hypothesize that the lPFC would support the interaction (balance) between these two mechanisms. A promising way of probing this dynamic interaction is to explore oscillatory brain activities. In the following, we shall define brain oscillations and how they could shed more light to this role of lPFC.

3 Attention as a Wave

"Sit in reverie and watch the changing color of the waves
that break upon the idle seashore of the mind."
— Henry Wadsworth Longfellow

In 1929, Hans Berger described continuous waves (oscillations) in the electroencephalogram, specifically a large-amplitude rhythm induced by eye closure, the "alpha" rhythm (1929). While Berger was (allegedly) attempting to investigate their role in telepathic communication (Buzsaki 2006), brain oscillations have been assigned a much more essential role in cognitive functions.

Briefly, oscillations are described by three pieces of information: frequency, power, and phase. Frequency is the speed of the oscillation (number of cycles per second) and according to this speed, oscillations are clustered into frequency bands, including delta (1–4 Hz), theta (4–8 Hz), alpha (8–14 Hz), beta (15–30 Hz), gamma (>30 Hz). Power is the amount of energy in a frequency band and phase is the position along the sine wave at any given time point (see **Figure 13**). Here we shall focus mainly on oscillations in the alpha and gamma bands and how modulations in their power (amplitude) and phase might orchestrate attentional mechanisms.

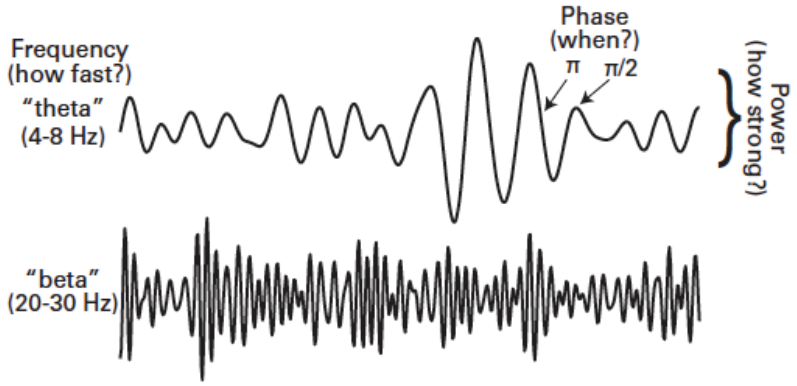


Figure 13. The three dimensions that define oscillations: frequency, power and phase. (Adapted from Cohen 2014).

3.1 Oscillatory Activity in The Alpha Band

3.1.1 You Shall Not Pass: Alpha Oscillations as The Gate Keeper

Being more prominent when awake participants close their eyes, oscillations in the alpha band (8 and 14Hz) were first considered as a marker of cortical idling (Pfurtscheller et al. 1996). However, this idea has been recently challenged with hypotheses that alpha activity actually reflects neuronal excitability, namely, the inhibition-timing hypothesis by Klimesch and colleagues (2007) and the gating by inhibition hypothesis by Jensen and Mazaheri (2010).

The inhibition-timing hypothesis assumes that alpha oscillations are induced by inhibitory cells and reflect rhythmic changes between phases of maximal and minimal inhibition. Thus, a neuron might (a) in a high excitation level, fire in a tonic manner and subsequently overrides the inhibitory influence of the oscillatory activity (**Figure 14**A), or (b) in a lower excitation level fire rhythmically (entrained to the oscillation: **Figure 14**B). In other words, increases in alpha power (alpha synchronization) reflects a state of low excitability i.e. inhibition, whereas decreases in alpha power (alpha desynchronization) reflects a state of rather high excitability i.e. release of inhibition (Klimesch et al. 2007). More importantly, the inhibition-timing hypothesis assumes that since this increase in amplitude leads to an increased rhythmic activity thereby it allows a more precise timing of neural activity by providing a small time-window for firing for many neurons. For example, in **Figure 14**B, one can note that the neuronal rhythmic firing is regulated by alpha oscillations in a way that it occurs solely in phases of low alpha activity.

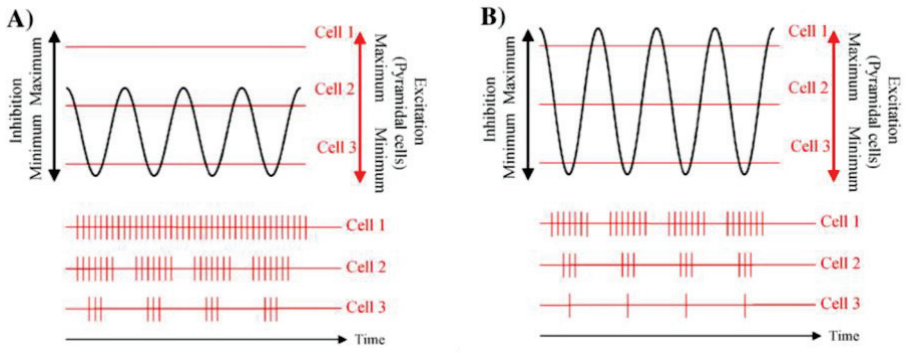


Figure 14. The inhibition–timing hypothesis assumes that depending on the amplitude of the oscillation (and the excitation level of single cells), two different firing patterns can be distinguished. (A) If the amplitude of the oscillation is small, cells with a high level of excitation fire tonically, not entrained to the phase of the oscillation. (B) If the amplitude is large even cells with a high level of excitation will fire rhythmically, entrained to the phase of the oscillation. (Adapted from Klimesch et al. 2007).

The gating by inhibition hypothesis (see **Figure 15C**) implements this inhibitory role of alpha oscillations in the functional architecture of the different brain networks. According to this hypothesis, in a certain task, neural pathways could be either task-relevant or irrelevant: through GABAergic interneurons, alpha power would increase in task-irrelevant pathways (regions), blocking information processing in a pulsed manner, along this pathway, and subsequently gating the information flow to task-relevant pathways (Jensen and Mazaheri 2010).

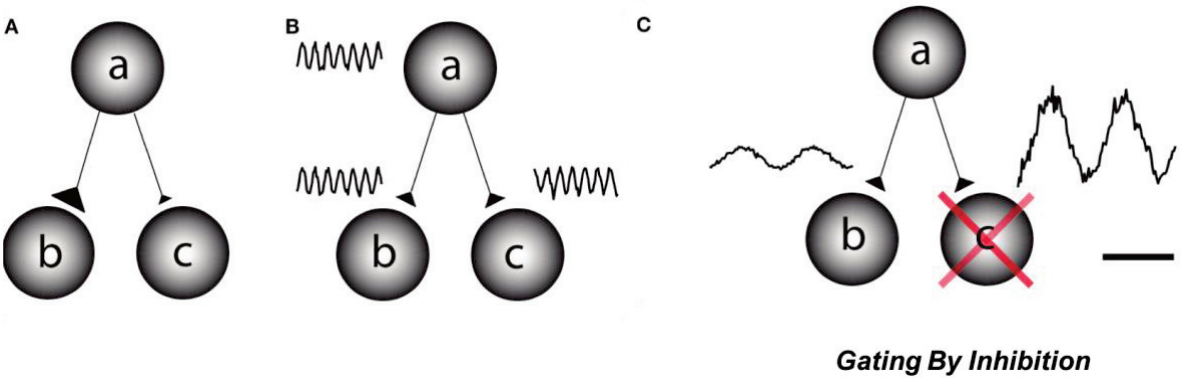


Figure 15. Consider a situation in which information is supposed to be routed from node a to node b but not from node a to node c. (A) One possibility is that the synaptic connections from node a to b are strengthened on a fast time scale and weakened from node a to c. This would require a mechanism for synaptic plasticity that works on a fast time scale. (B) Information might be gated through neuronal phase-synchronization between node a and c. The information flow from node b to c is blocked by adjusting the phase difference. (C) Gating by inhibition. Node c is actively suppressed by functional inhibition. This serves to gate the information flow from a to b. The functional inhibition is reflected in the 9–13 Hz alpha band.(Adapted from Jensen and Mazaheri 2010).

3.1.2 Alpha in Your Eyes, Alpha in Your Ears: Alpha Oscillations and Sensory Modulations

In support of these hypotheses, in the visual domain (see **Figure 16**), it has been demonstrated that during the expectation of visual targets in a specific hemifield, alpha power decreases in contralateral visual areas responsible for processing the attended space, while alpha power increases in ipsilateral visual areas responsible for processing the unattended space (Worden et al. 2000; e.g. Kelly et al. 2006; Thut 2006; Rihs et al. 2007, 2009; Marshall, Bergmann, et al. 2015; Doesburg et al. 2016). Not only does alpha activity display a retinotopic specificity, but also visual feature specificity. For example, Snyder and Foxe (2010) used a paradigm in which participants were required to attend to either the color or the motion of a visual stimulus, and

they demonstrated that alpha power increased in regions responsible for color-processing when color was cued, and similarly for motion-processing regions when motion was cued.

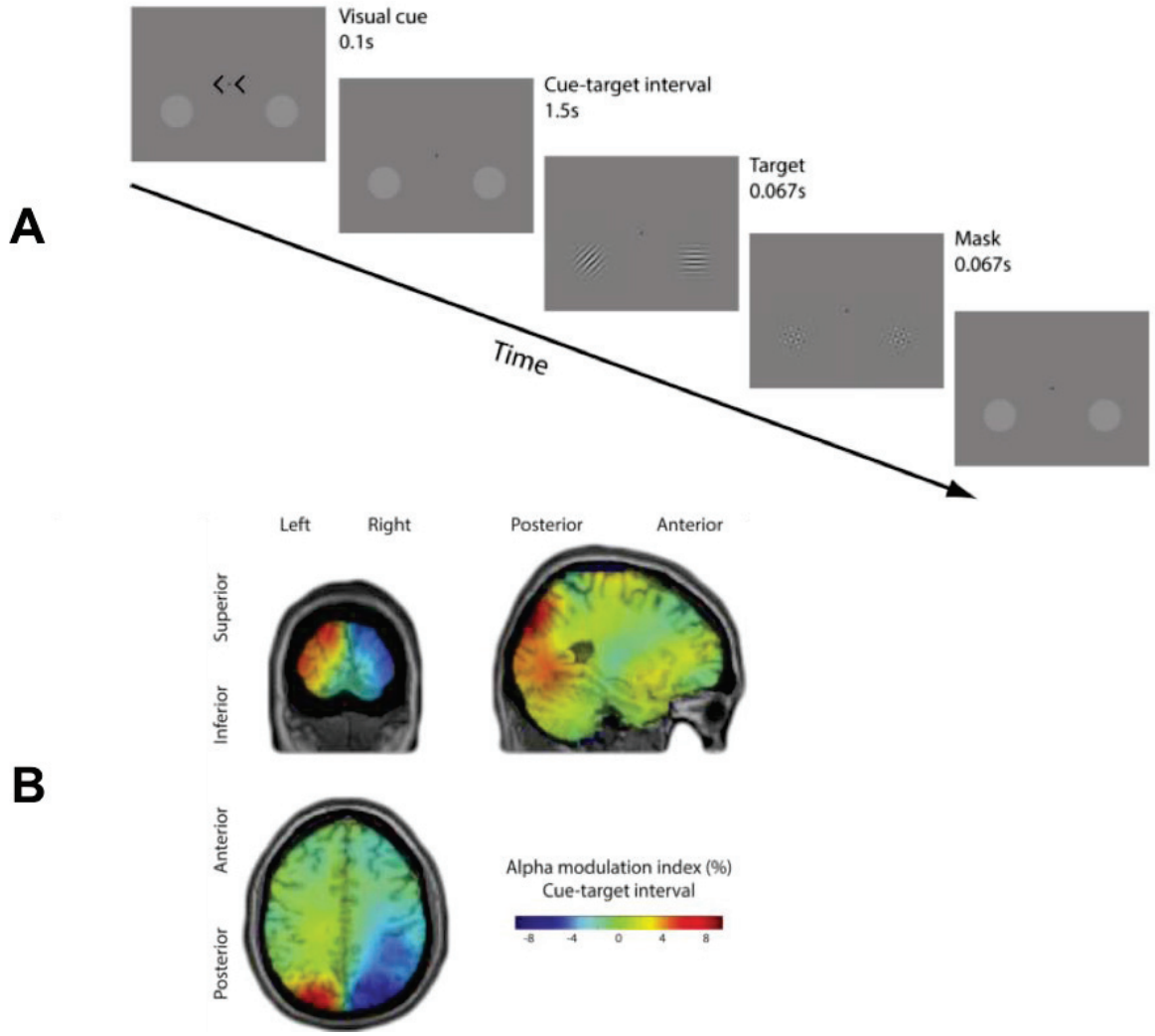


Figure 16. (A) Experimental paradigm. Each trial began with one of four visual cues, instructing subjects either to attend to the left, right or both luminance pedestals. (B) Grand average alpha modulation index (attention left versus attention right) calculated for cue-target interval (350–1,350 ms post-cue). (Adapted from Marshall, Bergmann, et al. 2015).

These results also extend to the somatosensory domain (Haegens et al. 2010, 2011, 2012; Cheyne 2013) and even to cross-modal domains, where alpha power increases in regions processing the unattended modalities and decreases in regions processing the relevant modality (e.g. Foxe et al., 1998; Fu et al., 2001; Gomez-Ramirez et al., 2011; Jiang et al., 2015). Based upon all these evidences combined, alpha oscillations would be a suitable

candidate for supporting facilitatory and suppressive mechanisms of top-down anticipatory attention. But what about auditory alpha?

Contrary to the visual domain, only a handful of studies investigated the impact of anticipatory attention on alpha modulations in the auditory cortices. This relative scarcity in the literature is probably due to doubts in the existence of independent generators of auditory alpha activity due to the inferior visibility of auditory alpha activity in raw electrophysiological data, in comparison to the visual and motor alpha activity probably due to the orientation of such generators which might impede their visibility in EEG signals, for example (Weisz et al. 2011). However, in 2012, Muller and Weisz provided compelling evidence for the existence of auditory generators of alpha activity. In their study, using magnetoencephalography (MEG), they have demonstrated an increase in alpha power, solely in the right auditory cortex, when attention was directed towards the ipsilateral right ear compared to when directed towards the contralateral ear. This has been followed by several reports of auditory alpha modulations (Mazaheri et al. 2013; Frey et al. 2014; Weisz and Obleser 2014; Weise et al. 2016; van Diepen and Mazaheri 2017).

Importantly, alpha power was also found to correlate with behavioral performances. For example, in a study by Mazaheri and colleagues (2013), participants performed a cross-modal discrimination task, where according to an attentional cue, they were required to discriminate a feature of either a visual or an auditory stimulus. They have demonstrated that in anticipation of a visual target, reaction times positively correlated with alpha power in the occipital cortex, while in anticipation of an auditory target similar positive correlation pattern were noticed in the vicinity of the auditory cortex. In other words, the more alpha power decreased (desynchronized) in the relevant regions, the faster participants were. Similar correlation patterns have been demonstrated in visual (Thut 2006; Händel et al. 2011; Bonnefond and Jensen 2012; Payne et al. 2013; Myers et al. 2014), somatosensory (Haegens et al. 2011) and cross-modal (Weise et al. 2016) tasks.

3.1.3 Power Is Not Everything: A Role for the Phase of Alpha Oscillations

So far, we have discussed how top-down attentional mechanisms would modulate alpha oscillations in task (ir)relevant sensory regions, and throughout this section we have affirmed the inhibitory role played by alpha oscillations. However, it is important to note that alpha oscillations could reflect other processes rather than cortical inhibition e.g. active processing

(Palva and Palva 2007, 2011). In both of their reviews, Palva and Palva have pointed out the discrepancy between the assigned "inhibitory" role of alpha oscillations and evidence of increases in alpha power in frontal and parietal regions as well as in sensory regions high up in the processing hierarchy i.e. regions that are task-relevant (Jensen et al. 2002; Palva et al. 2005, 2011; Haegens et al. 2011).

In their framework, they have suggested two main ideas. First, that the amplitude of alpha oscillations might not always reflect the same processes: While the amplitude of alpha oscillations in sensory regions might reflect "inhibition" or "inhibition release", the amplitude of alpha oscillations in other higher-level regions, might in fact reflect active processing (active processing hypothesis: Palva and Palva 2007). Second, amplitude data is not sufficient to draw a complete physiological picture of alpha oscillations. Thus, more light should be shed on the phase dynamics of these oscillations. Indeed, on a sensory level, it has been shown that the phase of alpha oscillations in sensory regions plays a role, in stimuli detection, where stimuli coinciding with a certain phase of ongoing alpha oscillations are more likely to reach sensory awareness (Busch et al. 2009; Mathewson et al. 2010).

So far, we have discussed alpha modulations in sensory cortices. However, empirical evidence highlights the fact that alpha activity is also modulated in frontal and parietal regions (e.g. Capotosto et al. 2009). Thus, it has been proposed that the alpha phase dynamics would orchestrate long-range inter-areal communication through phase synchrony or coherence between the different nodes of a given task-related neural network (Palva et al. 2005; Klimesch et al. 2007; Palva and Palva 2007, 2011).

Following this thread of thought, during a task that manipulates top-down attentional mechanisms, might one expect alpha activity to be modulated in different nodes of the dorsal fronto-parietal network supporting top-down attention mechanisms? Could the alpha rhythm pave the way for modulatory signals to travel from fronto-parietal regions of the dorsal attentional network, such as the IPS and the FEF, to task-relevant sensory regions such as the visual or auditory cortices?

3.1.4 Alpha Oscillations & Top-Down Attentional Networks

It has been proposed that fronto-parietal regions could control spatial attention through the modulation of ongoing alpha rhythms (Capotosto et al. 2009). In their study, Capotosto and colleagues (2009), targeted the IPS and the FEF, using repetitive transcranial magnetic stimulation (rTMS), while participants performed a posner-based visual discrimination task. Interference with either the FEF or the IPS, impaired participants' behavioral performances, i.e. they were slower to discriminate the visual targets. More interestingly, this behavioral effect was accompanied by (and correlated to) a disruption of anticipatory alpha (power) desynchronization in the occipital cortex. Thus, providing preliminary evidence to the causal role of the dorsal fronto-parietal network in the control of human visuo-spatial attention via alpha oscillations in visual regions.

Combining neuroimaging techniques such as EEG, MEG and fMRI and advanced connectivity measures such as partial directed coherence, phase locking, and granger causality, several reports in the somatosensory (Sacchet et al. 2015), the visual (Sauseng et al. 2005; Capotosto et al. 2009, 2011, 2015, 2016, Doesburg et al. 2009, 2016; Zumer et al. 2014; Lobier et al. 2018) and the auditory (Muller and Weisz 2012; Huang et al. 2014; Weisz et al. 2014) domains have established that synchrony in the alpha rhythm could play a role in coordinating and regulating neuronal processing across fronto-parietal and visual/auditory systems. For example, in tasks of auditory spatial attention, while attending to a monaural target, stronger phase synchrony (connectivity) has been observed between the contralateral auditory cortex and nodes of the dorsal attentional network (IPS: Huang et al. 2014; intraparietal lobule: Weisz et al. 2014).

3.1.5 How Many Alpha(s) Are There: Alpha Oscillations & Peak Frequency

One final key characteristic of alpha oscillations that we shall discuss is the alpha peak frequency. While earlier studies demonstrated that alpha could be divided into three alpha sub-bands: a lower band, reflecting phasic alertness, an intermediate band, reflecting expectancy and an upper band reflecting task performance (Klimesch et al. 1993, 1998; Klimesch 1999), currently, studies regard alpha activity in between 8 and 14 Hz as a monolithic entity, i.e. alpha band is often regarded as a single band.

Nevertheless, recent evidence suggests that rather than representing random fluctuations alpha peak frequency (APF) might represent the nature and activation level of the

neural population and task demands (Kawasaki et al. 2010; Nir et al. 2010; Haegens et al. 2014; Hülsdünker et al. 2015; Mierau et al. 2017). According to these studies, the APF should be regarded as a "trait" and/or "state" variable.

APF could be considered as a "trait" or a "characteristic" variable that changes across (1) individuals and varies as a function of age, neurological diseases or behavioral performances (Klimesch 1999; Başar 2012), and (2) cortical regions, as found for example, during resting state, where parietal and occipital regions displayed different APFs (Haegens et al. 2014).

APF could also be considered as a "state" variable that would index performance fluctuations, cognitive demands and probably the functional task-relevance of a specific cortical region (Klimesch 1999; Başar 2012; Haegens et al. 2014). For example, studies in the working memory (Haegens et al. 2014), sensorimotor control (Hülsdünker et al. 2015) and pain perception (Nir et al. 2010) domains have shown that APF increases with increasing task demands. While the role of such APF variability remains unclear we believe that such phenomenon should be further investigated in studies of alpha activity.

In summary, we have described how alpha activity (power) would reflect top-down modulations of cortical sensory activity. In addition, we have also described how alpha activity (phase) would support long-range interareal communication between these sensory regions and nodes of the dorsal top-down attentional network. Now, let's shift gears to a faster rhythm: Gamma!

3.2 Oscillatory Activity in The Gamma Band

3.2.1 Gamma Oscillations: Music or noise?

Oscillations with frequency over 30–40Hz are denoted gamma. These fast oscillations became "visible" or "detectable" with the advent of digital EEG whose recording capacity (>200Hz) surpassed that of its analogue counterpart (<25Hz; Hughes 2008). In comparison to the larger and slower rhythms, these oscillations were originally considered as noise but later on, a critical role for gamma oscillations in perceptual binding has been highlighted (review in Singer 2001). Perceptual binding refers to the phenomenon of grouping features representing the same object so that they could be processed (perceived) as a coherent whole. This role of gamma oscillations in perceptual binding has been demonstrated by several studies in the animal (Eckhorn et al. 1988; Aston-Jones and Cohen 2005) and the human (Kristeva-Feige et al. 1993; Desmedt and Tomberg 1994; Jokeit and Makeig 1994; Tallon et al. 1995; Tallon-Baudry et al. 1996, 1997) brain in response to different auditory, visual and somatosensory stimuli.

This gamma-binding hypothesis proposes that by synchronizing assemblies of neurons that process distinct features of an object, the "fractured" features of the object are linked into a unified, coherent percept (Tallon-Baudry and Bertrand 1999). Gamma oscillations have also been related to attentional processes. However, it is important to note that the term "gamma" has been an umbrella term for different types of fast oscillatory activity. In the following, we shall different types of gamma oscillations according to their (a) temporal relationship to their eliciting stimuli and (b) frequency bandwidth.

3.2.2 Gamma Oscillations: One Gamma Fits all?

First, in relation to stimulus onset, there are three different types of gamma activity: evoked, induced and steady-state responses (Galambos 1992). The steady-state response is often elicited to periodically modulated stimulus (auditory, visual or somatosensory) at the driving frequency of the stimulus (Tallon-Baudry and Bertrand 1999; Bertrand and Tallon-Baudry 2000). Evoked and induced gamma oscillations are seen in response to transient stimuli (Tallon-Baudry and Bertrand 1999). However, they differ in their phase-locking to the stimulus (see Figure 17). Evoked gamma is characterized by precise phase-locking to the stimulus onset whereas induced gamma is not phase-locked to the stimulus onset, i.e. its temporal relationship with stimulus onset is fairly loose, and of the three types, induced gamma seems

to have the most relevance with perceptual binding (review in Tallon-Baudry and Bertrand 1999; Bertrand and Tallon-Baudry 2000).

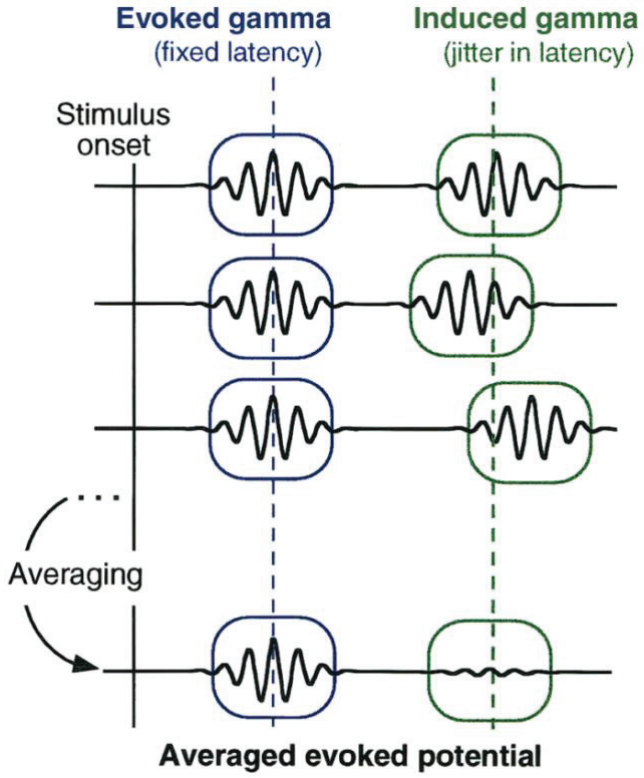


Figure 17. Schematic representation of evoked and induced gamma oscillatory responses. An evoked response (blue boxes) appears at the same latency and phase in each single trial and hence can be detected in the averaged evoked potential. An induced response (green boxes) appears with a jitter in latency from one trial to another, centered around a given latency (green line). It therefore tends to cancel out completely in the averaged evoked potential. (Adapted from Tallon-Baudry and Bertrand 1999).

Second, within the gamma band, two types of "gamma" need to be distinguished: narrowband and broadband gamma (Sedley and Cunningham 2013). On one hand, narrowband gamma (2–5 Hz bandwidth oscillations close to 60 Hz) has been mainly reported in the animal visual cortex (review in Saleem et al. 2017). Yet, the function of this narrowband activity is unclear, with hypotheses that it could represent cortical idling (Jia et al. 2011; Saleem et al. 2017). On the other hand, broadband gamma extends from (30 -90 Hz) rhythms and seems to play a more active role in perception (Fries et al. 2001; Fries 2005; Lachaux et al. 2005; Sedley and Cunningham 2013) that will be discussed in the following. It is important to note, however, that within broadband gamma there exist "true" oscillations occupying a specific frequency band (albeit a broad one) and other indefinite spectral activity that is considered to represent leakage from multi-unit activity (Sedley and Cunningham 2013). Thus,

in this section we shall be concerned only with broadband gamma oscillations with a specific frequency range.

3.2.3 Gamma Oscillations Reflect Attentional Mechanisms

Gamma oscillations have been associated with attention, where, following an opposing pattern to that of alpha activity (see **Figure 18**), attention to a visual or an auditory stimulus enhances gamma power in the visual (Fries et al. 2001, 2008, Fries 2005, 2009; Taylor et al. 2005; Womelsdorf and Fries 2007; Siegel et al. 2008; Popov et al. 2017) or auditory (Debener et al. 2003; Schadow et al. 2009) cortices, respectively.

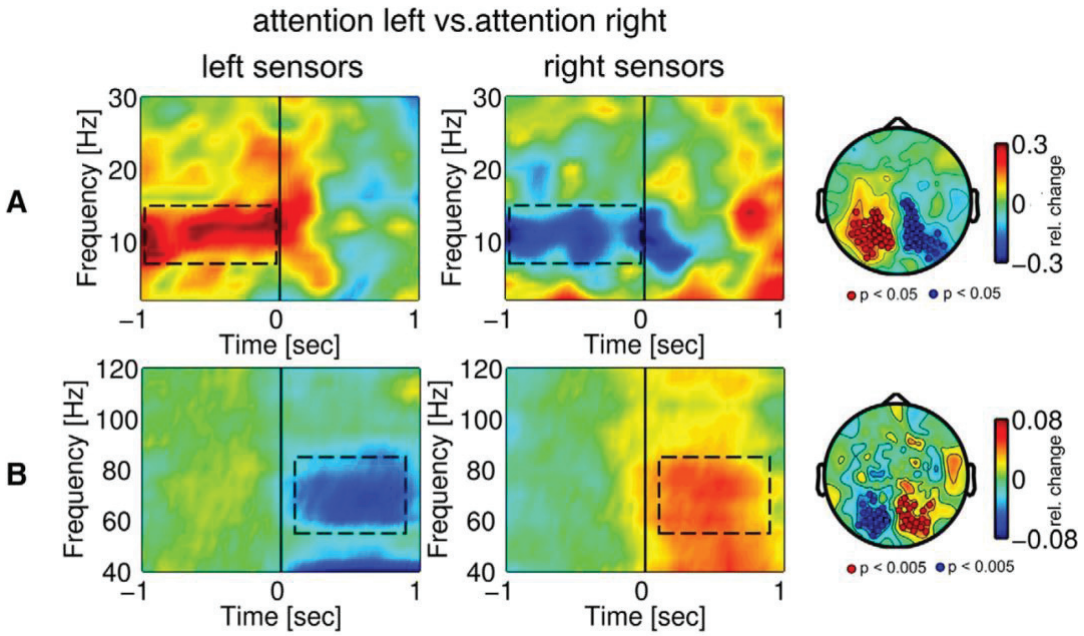


Figure 18. Time-frequency representations (TFRs) of target-locked oscillatory power for left versus right cued trials during visual target expectancy. (A) Pre-target alpha power increased in sensors ipsilateral to the cue direction, whereas it decreased in contralateral sensors. (B) Post-target gamma power decreased relatively in sensors ipsilateral to the cue direction, whereas it increased in contralateral sensors. (Adapted from Popov et al. 2017).

Gamma oscillations have also been observed in regions other than sensory regions in Stroop (Shinichiro Koga et al. 2012; Oehrn et al. 2014), visual search (Ossandon et al. 2012), object categorization (Ramot et al. 2012), reading (Jung et al. 2008), working memory (Michels et al. 2010), Go/No-Go (Swann et al. 2013), visual (Akimoto et al. 2013, 2014) and auditory (Lee et al. 2007; Ahveninen et al. 2013) oddball tasks. Thus, gamma oscillations seem to promote the activation of task-relevant processes across the entire brain and not only in the sensory cortices.

Moreover, similarly to alpha oscillations, it has been demonstrated that gamma band activity correlates with behavioral performances. There is broad evidence for an association of amplitude (and phase) of gamma oscillations with faster (Gonzalez Andino et al. 2005; Fründ et al. 2007; Martinovic et al. 2007, 2008; Schadow et al. 2009; Ahveninen et al. 2013), and better (Kaiser et al. 2006, 2009; Kaiser, Heidegger, and Lutzenberger 2008; Kaiser, Heidegger, Wibral, et al. 2008; Ahveninen et al. 2013) performances. Finally, gamma power in lateral prefrontal cortex was shown to predict attentional performances (Rouhinen et al. 2013).

3.2.4 Does the Brain Speak Gamma? Gamma Synchrony Reflect Interareal Communication

Phase synchrony in gamma oscillations seems to subtend communication between different brain regions (the communication through coherence hypothesis: Fries 2005). According to this framework (see **Figure 19**), communication between sending and receiving neuronal pools is dependent on the phase synchrony between them in the gamma band i.e. communication is dependent on whether gamma oscillatory activity between two neuronal pools is coherent or not. Thus, the coherent phase of gamma oscillations would govern signal transmission across neuronal connections (Fries 2005). This might be achieved by the sending neuronal pool entraining the gamma phase in the receiving pool thus rendering their interconnection more powerful (Fries 2009).

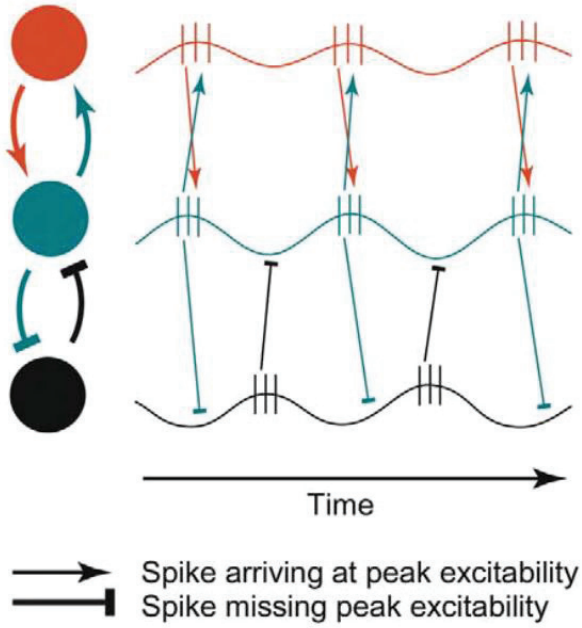


Figure 19. Red and green filled circles illustrate a sending and a receiving neuronal group, respectively. The small vertical lines illustrate action potentials of neurons in the two groups and the arrows illustrate those action potentials traveling along the connecting axons. Spikes that arrive at excitability peaks of the receiving neuronal group have pointed arrowheads. Spikes that miss excitability peaks have blunt arrowheads. The red and green neuronal groups undergo coherent excitability fluctuations and their communication is therefore effective. The black neuronal group however undergoes excitability fluctuations that are not coherent with the green neuronal group and therefore communication between the green and the black neuronal group is prohibited. (Adapted from Fries et al., 2005).

In the attention domain, it has been demonstrated that top-down attention increases gamma synchrony between frontal regions and task-relevant regions (Gregoriou et al. 2009; Baldauf and Desimone 2014). For example, Baldauf and Desimone (2014) using MEG recordings in human subjects demonstrated that synchrony (coherence) in the gamma band (70-100Hz) increased between the inferior frontal junction and (1) the fusiform face area when participants attended to face, or (2) the parahippocampal place area when participants attended to places.

3.3 Different waves for different networks

Previously, we have discussed how alpha oscillations could be involved in feedback signaling. In a similar manner, there is ample evidence that fast gamma oscillations are involved in cortical feedforward signaling (von Stein et al. 2000; Buzsaki et al. 2004; Kaiser and Lutzenberger 2005; Buschman and Miller 2007; Arnal et al. 2011; Bastos et al. 2012, 2015; Xiao-Jing Wang 2013; van Kerkoerle et al. 2014; Buschman and Kastner 2015; Fries 2015; Kornblith et al. 2016; Michalareas et al. 2016).

In what might be the first demonstration of such phenomenon von Stein and colleagues (2000) demonstrated that, in the rat visual system, gamma oscillations predominated in bottom-up interactions, while top-down interactions evolved mainly in the middle frequency (4–12 Hz) oscillations. These findings have been replicated in the macaque (Buschman and Miller 2007) and the human visual (Michalareas et al. 2016) and auditory cortices (Fontolan et al. 2014), where bottom-up and top-down propagation (influences) predominated in gamma and delta/alpha/beta bands, respectively. Moreover, causal evidence of such propagation has been provided from a study by van Kerkoerle and colleagues (2014) using laminar recordings in the monkey brain. In this study, microstimulation in the V1 elicited gamma-oscillations (40-90Hz) in V4, whereas microstimulation in V4 elicited alpha-oscillations (5-15Hz) in V1, thus providing causal evidence for the opposite propagation of these rhythms. Therefore, at least on a signal processing level, there is a growing hypothesis that slow oscillations, namely alpha oscillations, would be involved in cortical feedback signaling while faster oscillations, namely gamma oscillations, would be involved in cortical feedforward signaling. Could such reasoning be applied to attentional mechanisms?

In their seminal study, Buschman and Miller (2007), using electrodes implanted in the monkey brain, found that coupling between prefrontal and parietal cortex differed depending on whether attention was being externally captured (bottom-up/pop out) or internally directed (top-down visual search). When attention was externally captured, and information flowed in a ‘‘bottom- up’’ manner (from parietal cortex to prefrontal cortex), coupling (coherence) was observed in the gamma-band (35-55Hz). In contrast, when attention was internally controlled, and information flowed in a “top-down” manner from prefrontal to parietal cortex, synchrony between prefrontal and parietal cortex was at a lower-frequency beta-band (22-34Hz). Furthermore, several studies using intracranial EEG demonstrated that bottom-up feedforward attentional influences are carried by the gamma-band while top-

down feedback attentional influences are carried by the beta-band either within the primate (Bastos et al. 2015) or the human (Richter et al. 2017) brain.

Based upon these results, we have constructed a working hypothesis on the mechanisms supporting the bottom-up/top-down balance of attention: high frequency oscillations would support bottom-up mechanisms of attention and index the activation of the ventral bottom-up network, whereas long-range coupling in lower frequencies would coordinate activity within the dorsal top-down network.

Earlier we have discussed how bottom-up and top-down attentional networks might overlap then how would their two oscillatory indices (alpha and gamma) interact?

3.4 Alpha-Gamma Coupling

Traditionally, oscillatory activity has been binned into separate frequency bands that have been investigated separately, giving the impression of a lack of interaction between these bands. However, there has been evidence, stemming from both animal and human studies, that oscillatory activity in various bands interact with one another in what is termed cross-frequency interaction or cross-frequency coupling (CFC), which could involve either power-to-power, phase-to-power or phase-to-phase interactions (Onslow et al. 2011). In this section, we shall focus on phase-to-power or phase-amplitude interactions (see **Figure 20**).

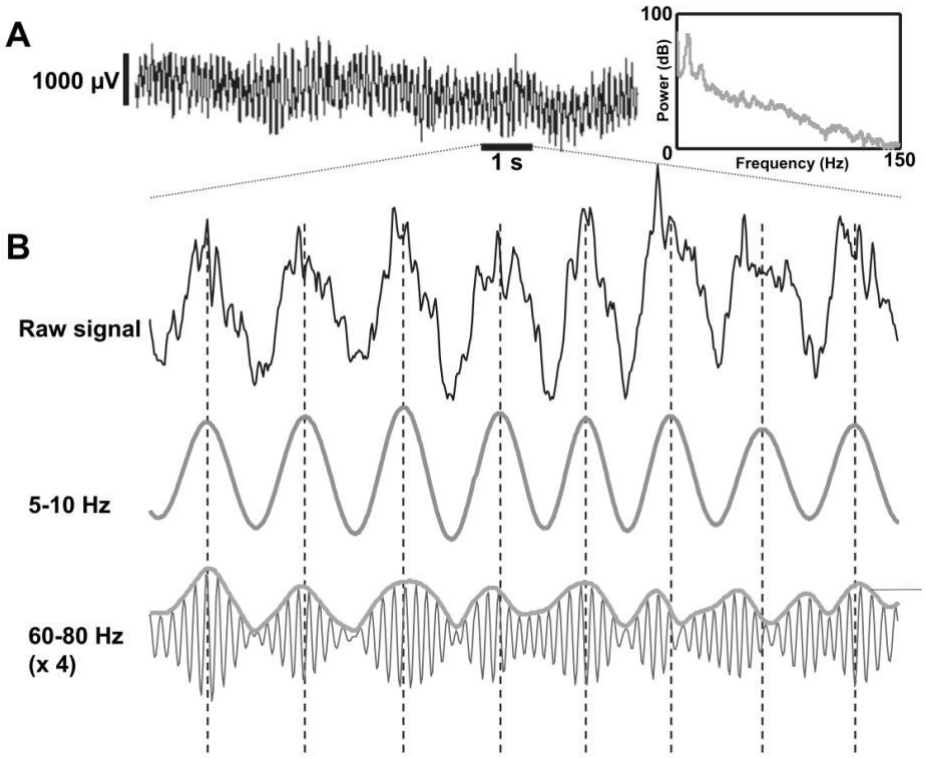


Figure 20. Local field potential data showing theta-gamma phase-amplitude coupling in CA1 of rat hippocampus. (A) 10 s of broadband LFP and corresponding power spectrum (right) showing predominant theta-frequency power whilst a rat actively explores its home cage. (B) Expanded 1 s segment showing raw signal (top) and bandpass filtered theta and gamma (lower) rhythms. The thick grey line over the gamma signal shows the amplitude envelope and dashed horizontal lines mark timing of theta cycle peaks; note alignment of theta peaks and gamma envelope during the first half of the trace. (Adapted from Onslow et al. 2011).

For example, in the rat hippocampus, it has been demonstrated that the power of gamma oscillations were modulated by the phase of theta (Chrobak and Buzsáki 1998) and theta/alpha (Bragin et al. 1995) oscillations. In other words, power of fast oscillations was determined by the phase of slower oscillations. Later on, Lakatos and colleagues showed that in the primary auditory cortex of awake macaque monkeys, during rhythmic auditory stimulation, the amplitude of gamma oscillations (30–70 Hz) was modulated by the phase of slower theta (4–10 Hz: Lakatos et al. 2005) and delta (1—4Hz: Lakatos et al. 2008) oscillations. Later on, this phenomenon was replicated in several modalities, in the macaque and the human brain, highlighting an important role of phase-amplitude coupling (PAC) in the control of neuronal processing and communication generally and attentional selection more specifically (Jensen and Colgin 2007; Lakatos et al. 2008; Bahramisharif et al. 2013; Szczepanski et al. 2014; Bonnefond and Jensen 2015; Esghaei et al. 2015; Chacko et al. 2018).

PAC has also been found to correlate with human behavioral performances. For example, Szczepanski and colleagues (2014), using human intracranial recordings demonstrated that during a task of visuospatial attention, the strength of delta/theta (2–5Hz) phase to high-gamma (70–250Hz) amplitude coupling in visual and dorsal-attention-network regions negatively correlated with reaction time (RT) i.e. the higher PAC, the lower (faster) RTs. Similar results have been obtained by Chacko and colleagues (2018), using electrocorticography (ECoG) recordings while participants performed a visually cued spatial attention task. However, RT negatively correlated with the strength of theta/alpha (6–9 Hz) phase to beta/low-gamma (25-45 Hz) amplitude coupling.

PAC could also be involved in communication within neural networks such as the dorsal and ventral attentional networks. Imagine three neural populations A, B and C, it is required to (1) enhance communication between A and C, and (2) to reduce communication between B and C (see **Figure 15**). In this example, C could be the Frontal Eye Fields (FEF), B could be the auditory cortex ipsilateral to an upcoming target and A could be the contralateral auditory cortex.

Bonnefond and colleagues (2017) proposed a model for such communication with several assumptions. First, long distance interareal communication (A→C and B→C) is established through inter-areal phase synchrony in the alpha band. Thus, for neurons in pool A and C to communicate, they oscillate coherently (phase synchrony) in the alpha band in conjunction with a decrease in alpha power that would allow information transfer between the two regions. However, between B and C communication would be interfered by (a) stronger alpha power in B or (b) phase asynchrony between B and C.

Second, gamma oscillations are nested within alpha oscillations, i.e., they should occur only during the excitability phase of alpha oscillations. Thus, in pool A, the low magnitude of alpha oscillations allows for longer-duty cycles, i.e., longer time windows for the gamma activity during the excitability phase of the alpha cycle. As the excitable phase of the alpha oscillations will be aligned between the two relevant pools of neurons, gamma activity in A will be able to impact the neurons in C and gamma oscillations in A and C will consequently be correlated and possibly coherent. Meanwhile, in pool B, the high magnitude of alpha oscillations will reduce the duty cycle and the asynchrony of alpha oscillations in B and C will prevent gamma activity in B to drive cells in C.

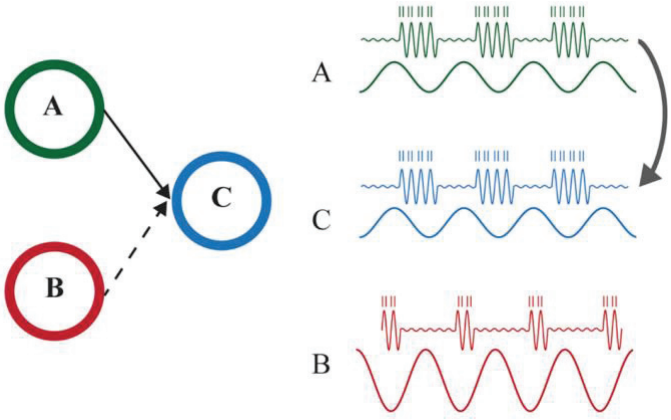


Figure 21. The synchronization in the alpha-band establishes the functional connection between A and C. This allows for representational specific neuronal firing reflected by the gamma band activity to flow to region C. The blocking of communication between B and C is achieved by high alpha power in B and an asynchrony between B and C. Therefore, both modulations in alpha-band power, as in gating by inhibition, and phase synchronization between the regions, as in CTC, are determining the routing of information between regions. Note that phase synchronization is assumed in the alpha band and the information transfer is reflected by gamma-band activity. (Adapted from Bonnefond et al, 2017).

In summary, this model proposes that inter-regional (global) communication could be established through alignment (synchrony) in the phase of alpha oscillations which is (1) concomitant to local modulations in alpha power and (2) coupled to the local power (not the phase) of gamma oscillations. However, while global synchrony or coherency could be established in the gamma band, it is not essential.

This model, in part, fits with the growing literature ascribing slow oscillations a role in communicating top-down attentional signals. However, it is incompatible with evidence from the same studies demonstrating that bottom-up attentional influences are communicated through synchrony within fast gamma oscillations (Buschman and Miller 2007; Bastos et al. 2015; Richter et al. 2017). In our opinion, in order to describe the dynamic communication between cortical regions during specific cognitive processes such as top-down and bottom-up attention, the timing aspect of such processes should be considered.

3.5 A New Model in Town

Here, we propose an oscillatory framework of top-down and bottom-up mechanisms of auditory attention and the interaction between them. First aspect of this framework is that top-down anticipatory signals would modulate the amplitude of alpha oscillations in the auditory cortices (auditory alpha). In this top-down prepatory setting occurring in a relatively

long time-window, such modulation would be possible through phase synchronization between auditory alpha on one side and fronto-parietal (FEF and/or IPS) and prefrontal alpha (lPFC) on the other side. Power of auditory gamma being coupled to the phase of auditory alpha (Lakatos et al. 2005; Canolty and Knight 2010; Bonnefond et al. 2017) would also be modulated by the anticipatory signals.

The second aspect of this framework is that the propagation and regulation of attentional capture-related bottom-up signals would be supported predominantly by gamma activity (power and phase) in the ventral fronto-parietal network of attention and in prefrontal regions (lPFC) as well. We posit that given the rapid nature of attentional capture, it would be more efficient for the brain to rely on information transfer through fast gamma oscillations while alpha oscillations would be more suitable for communication over relatively longer periods of time.

Third aspect of this framework is that we propose a crucial role played by the lateral prefrontal cortex in subtending (1) top-down long-range alpha and bottom-up gamma synchrony, and (2) the interaction between the two mechanisms indexed by gamma power modulations and/or fluctuations in the alpha-gamma coupling magnitude. In order to establish such role, we have planned to investigate two populations that demonstrate prefrontal impairments: healthy ageing individuals and patients with frontal lesions.

4 Attention as a Difficulty

So far, we have attempted to paint a clear picture, in the healthy brain, of the different top-down and bottom-up attentional mechanisms. Now, in order to characterize the role of the lPFC in attentional mechanisms, we shall discuss two conditions that have been associated with attentional difficulties: healthy ageing and frontal damage

4.1 Ageing & Attention

"Age is an issue of mind over matter. If you don't mind, it doesn't matter"
—Mark Twain

Aging is characterized by a decline in many cognitive processes such as working memory, executive function, language and attention (Drag and Bieliauskas 2010). In this section, we shall discuss how ageing impacts top-down and bottom-up attentional mechanisms on behavioral and functional levels.

4.1.1 Ageing & Top-Down Attention

Behaviorally, top-down attentional orienting has been shown to be preserved in ageing. Indeed, it has been demonstrated that in attentional cueing tasks, once age-related general slowing and sensory processing declines are accounted for (Zanto and Gazzaley 2014), older participants take advantage of spatial cues in a similar manner to younger participants to respond faster to upcoming visual (Nissen and Corkin 1985; Hartley et al. 1990; Gottlob and Madden 1998; Talsma et al. 2006) and auditory (Robin and Rizzo 1992) targets. This preserved performance, however, is accompanied by somewhat impaired neural markers of the deployment of top-down attention. For example, ageing has been associated with a reduction in the amplitude of the contingent negative variation (CNV: see **Figure 2** and **section 1.2.1**), an electrophysiological marker of preparatory behavior (Zappoli et al. 1988, 1992; Onofrj et al. 2001).

Another marker recently used to elucidate the influence of ageing upon TD attentional mechanisms is alpha oscillations. With aging, TD attentional facilitatory processes, indexed by alpha desynchronization, have been found to be either reduced (Deiber et al. 2013; Hong et al. 2015; van der Waal et al. 2017), reserved (Leenders et al. 2018; Tune et al. 2018) or even enhanced (Heideman et al. 2018). However, TD suppressive processes indexed by alpha

synchronization seem to deteriorate (Vaden et al., 2012) with ageing. In summary, ageing seems to primarily impact suppressive processes of top-down attention, while facilitatory ones seem to be relatively unaffected.

4.1.2 Ageing & Distraction

Behaviorally, ageing is characterized by a reduced capability to inhibit irrelevant information in visual and auditory modalities (Chao and Knight 1997; Alain and Woods 1999; Gazzaley et al. 2005; Andrés et al. 2006; Fabiani et al. 2006; McGinnis 2012; Wais et al. 2012; Getzmann et al. 2013). However, this heightened susceptibility to distraction could be related to either, an atypical attentional capture response to irrelevant stimuli (scenario 1) or impaired inhibitory mechanisms of top-down attentional control (scenario 2, Gazzaley 2013).

Electrophysiologically, there is evidence supporting both scenarios. On one hand, studies using the oddball paradigm often demonstrated that elder participants display either delayed (Getzmann et al. 2013; Cid-Fernández et al. 2014) or attenuated (Kok 2000; Andrés et al. 2006) responses (MMN-P3-RON) to novel stimuli (evidence for scenario 1). On the other hand, using fMRI, Peiffer and colleagues (2009) demonstrated that visual cortex deactivation during an auditory discrimination task was reduced with ageing. In addition, using fMRI, it has been shown that older adults demonstrated a prominent deficit in the suppression of cortical activity associated with task-irrelevant representations, whereas enhancement of task-relevant activity was preserved (Gazzaley et al. 2005).

Finally, Guerreiro and colleagues (2010; 2013) have demonstrated that modality of both task-relevant and task-irrelevant stimuli determine the extent of distractibility of older adults (see **Figure 22**). In summary, they have hypothesized that, age-related differences in attention are modality dependent. Specifically, this hypothesis predicts that age-related deficits are most likely to arise in tasks that require suppressing unimodal rather than cross-modal distraction and in tasks that require suppressing visual distraction, regardless of the relevant modality (Guerreiro and Van Gerven 2011; Guerreiro, Anguera, et al. 2013; Guerreiro, Murphy, et al. 2013; Guerreiro et al. 2015; Van Gerven and Guerreiro 2016).

In summary, ageing is associated with an exacerbated distractibility that is reflected both behaviorally and electrophysiologically (evoked potentials). Thus, given the potential role of gamma oscillations in bottom-up attention, one might expect oscillatory activity to be involved in such behavioral deficit.

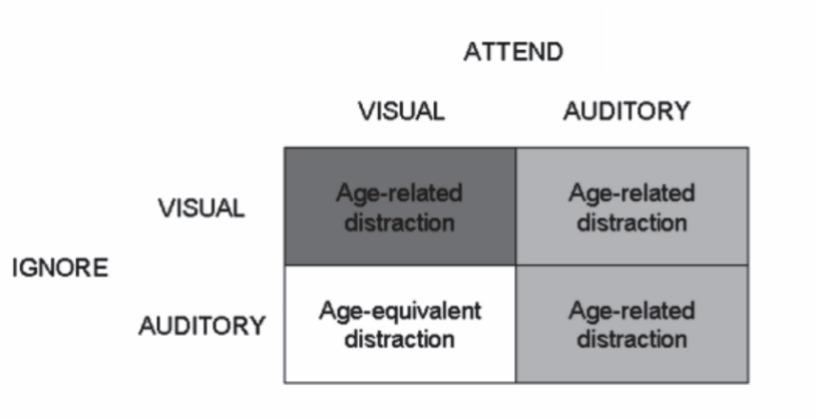


Figure 22. Pattern of age-related differences in selective attention by sensory modality of to-be-attended and to-be-ignored information. Shades of gray indicate graded probability of finding age-related distraction (i.e., darker shades indicate higher probability. (Adapted from Guerreiro, Murphy, et al. 2013).

4.1.3 Ageing & Frontal Integrity

Several theories have been proposed to account for attentional deficits during healthy ageing e.g. the generalized slowing theory (Salthouse 1996), the neural noise (Crossman and Szafran 1956; Welford 1981), the load theory (Maylor and Lavie 1998), the posterior to anterior shift in ageing theory (PASA: Davis et al. 2008), the compensation-related utilization of neural circuits hypothesis (CRUNCH: Reuter-Lorenz and Lustig 2005), the scaffolding theory of ageing and cognition (STAC: Park and Reuter-Lorenz 2009) and the cognitive reserve hypothesis (Stern 2002). However, here we shall focus only on the inhibitory deficit hypothesis (Hasher and Zacks 1988) and the frontal hypothesis of aging frontal lobe (West 1996).

According to the inhibitory deficit hypothesis (Hasher and Zacks 1988) ageing is associated with inhibitory impairment, and, as a result, older adults exhibit disproportionate interference from irrelevant information (Lustig and Hasher 2001). Recent developments to the theory regards inhibition as a three-facet process that (a) controls access to attention's focus, (b) deletes irrelevant information from attention, and (c) suppresses or restrain strong but inappropriate responses (Lustig et al. 2007). Accordingly, during a given task, age-related reduction in inhibitory control might lead to a reduced ability to (a) ignore concurrent task-irrelevant distraction, (b) delete information that is no longer relevant to the current task, and (c) restrain responding when a preponderant response is inappropriate (Friedman and Miyake 2004; Lustig et al. 2007; Guerreiro et al. 2010; Stothart and Kazanina 2016). This hypothesis received validation from studies demonstrating that older adults might not be able to suppress

activity in irrelevant cortical regions (e.g. Mund et al. 2010; Clapp et al. 2011; Chadick et al. 2014). For example, in their study, Chadick and colleagues (2014), using fMRI, demonstrated that ageing was associated with reduced suppressive activity in visual regions (see **Figure 23**) representing irrelevant information in addition to altered functional coupling between these cortical regions and the suppression network including the medial prefrontal cortex.

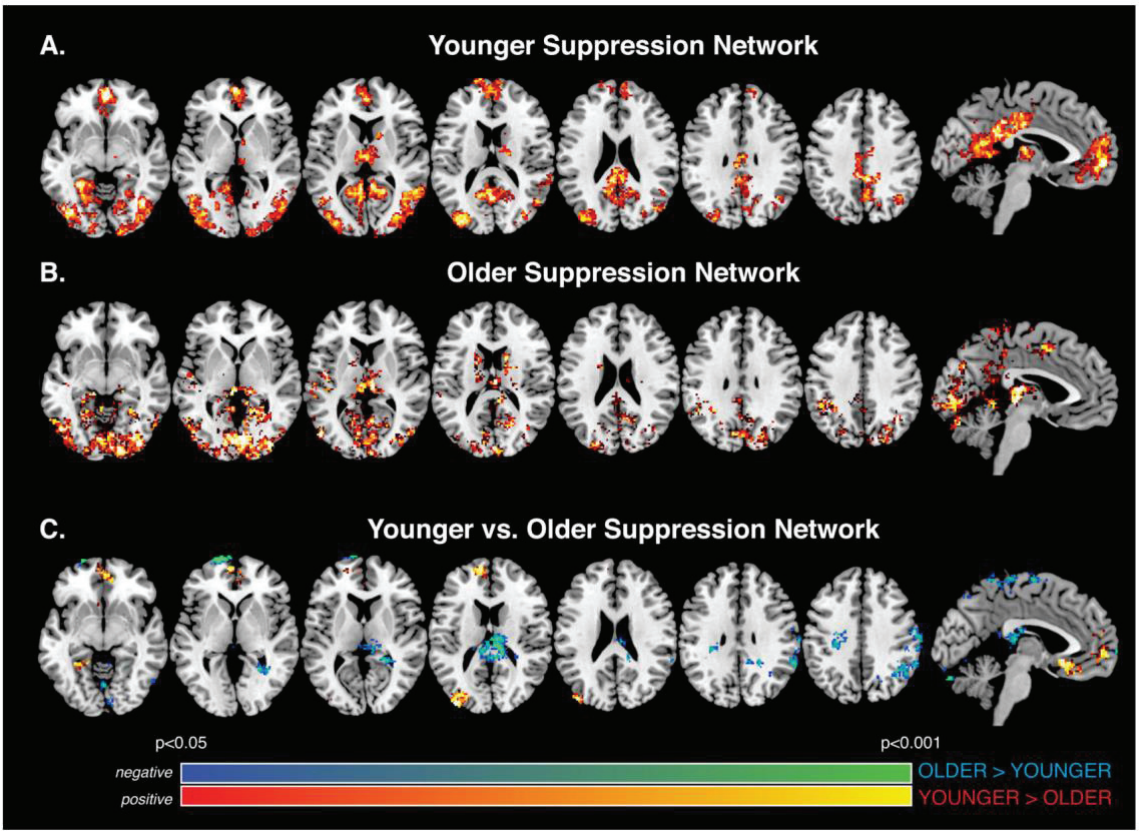


Figure 23. Younger versus Older Suppression Network. A) Functional connectivity map for younger participants using a left parahippocampal place area seed, contrasting face-memory-Overlap > passive-view-overlap (i.e., suppression network). B) Same as A, but for older participants. C) Contrast between younger and older suppression network maps. All images thresholded at p < 0.05 and corrected for multiple comparisons using cluster method. (Adapted from Chadick et al. 2014).

Another leading hypothesis is the frontal hypothesis of aging (West 1996) which speculates that the frontal lobes are particularly sensitive to the aging process and that declines in frontal efficiency can account for several deficits associated with aging including increased distractibility. The frontal lobe is particularly sensitive to the ageing process with age-related declines in frontal anatomy including: decreased gray matter thickness, reduced activity and connectivity (review in Gazzaley and D'esposito 2007; Fabiani and Gratton 2012).

The frontal hypothesis has been supported by studies demonstrating that older adults demonstrate reduced functional connectivity (e.g. Chao and Knight 1997; Campbell et al. 2012; Li and Zhao 2015) and overall activity (Chao and Knight 1997; Solbakk et al. 2008) in prefrontal regions such as the anterior cingulate and the lateral prefrontal cortex that normally would act to reduce interference from distraction. However, in our opinion these two hypotheses are closely-related to each other since most of the regions assigned an inhibitory (control) role are located in the (pre)-frontal cortex, pointing to a possible reconciliation between both hypotheses (Gazzaley and D'esposito 2007).

4.2 Attention & Frontal damage

Every year, around 6.5 million people die from stroke worldwide, making it the second major cause of disability in the world (Lecoffre et al. 2017) with around one in five strokes occurring in the frontal lobe (Bogousslavsky 1994). Anatomically speaking, frontal strokes could be delineated into either prefrontal, premotor, superior medial, orbital-medial, basal forebrain or white matter (Bogousslavsky 1994). In section 2.3 we have discussed that the lateral prefrontal cortex (lPFC) is part of both the ventral and dorsal networks and plays a crucial role in the control of visual (Buschman and Miller 2007; Corbetta et al. 2008; Katsuki and Constantinidis 2014) and auditory (Salmi et al. 2009; Alho et al. 2014) attention. In our working hypothesis, the lPFC plays an important role in subtending the oscillatory interaction between top-down and bottom-up attention. Thus, in this section, we shall narrow our focus to patients with lesions in the lateral prefrontal cortex (lPFC) and provide a summary of the impact of their lesion upon attentional mechanisms.

4.2.1 Prefrontal Lesions & Top-Down Attention

In section 2.3, we have reviewed how the lPFC seems to play a role in supporting top-down attention either by (1) activating the pathway of the relevant sensory modality, (2) inhibiting the irrelevant sensory modality, or even (3) driving oscillatory coupling between frontal and sensory regions in attentional tasks. Interestingly, lPFC lesions have often been associated with impaired top-down selective attentional mechanisms in both the auditory (Knight et al. 1981; Woods and Knight 1986; Bidet-Caulet et al. 2015) and visual (Knight et al. 1981; Barceló et al. 2000; Yago et al. 2004; Sinnett et al. 2009; Miller, Vytlacil, et al. 2011) modalities. This has been demonstrated in the human as well as the macaque brain (Rossi et al. 2007).

However, whether it's the facilitatory (as evidenced by Bidet-Caulet et al. 2015) component or the inhibitory component (as evidenced by Godefroy and Rousseaux 1996) that lies behind this top-down attention deficit remains unclear.

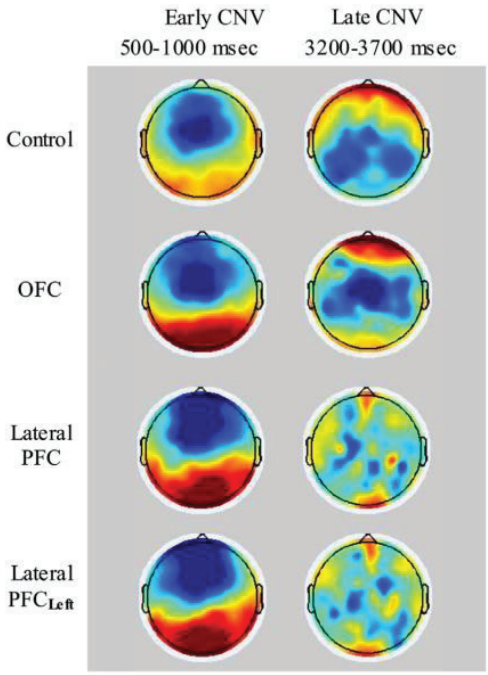


Figure 24. Topography plots of the early and late CNV components for the three group. Lateral PFC_{Left} represent the lateral PFC group when right and left electrodes are exchanged for the patients with right hemisphere lesions so that for the all the lateral PFC patients left hemisphere electrodes are synonymous with lesioned hemisphere. PFC: lateral prefrontal cortex; OFC: orbitofrontal cortex; CNV: contingent negative variation. (Adapted from Funderud et al. 2013).

lPFC lesions have also been associated with deficiencies in preparatory processes indexed by reduction of the contingent negative variation (CNV, see Figure 24) to visual (Funderud et al. 2013) or auditory (Rosahl and Knight 1995; Zappoli et al. 2000) stimuli. However, to our knowledge, no study has investigated how lPFC lesions would impact top-down modulation of ongoing alpha oscillations during a task of spatial orienting.

4.2.2 Prefrontal lesions & Bottom-up Attention

We have also reviewed how lPFC would play an important role in bottom-up attention with lPFC activation being associated with the inhibition of brain responses to distracting stimuli. Behaviorally, stroke lesions to the lPFC have been accompanied by increased distractibility with lPFC patients performances deteriorating in presence of distracting stimuli (Chao and

Knight 1995; Gehring and Knight 2002). These deteriorations correlated with decreased brain activity in the lPFC (Chao and Knight 1998).

Electrophysiologically, it has been demonstrated that, for patients with lPFC lesions, novel stimuli elicited a reduced novelty P3a, which reflects reduced attentional capture. (Knight and Scabini 1998; Solbakk and Løvstad 2014). Novel stimuli also elicited enhanced early P50 responses, whichs reflect reduced suppression of distractor processing even at early stages (Knight et al. 1989; Bolton and Staines 2014). Finally, in response to novel stimuli, lPFC patients present an enhanced sustained negative slow wave, indicating prolonged resource allocation to task-irrelevant stimuli (Løvstad, Funderud, Lindgren, et al. 2012). The ensemble of these results highlights a crucial role of the lPFC in controlling the detection, processing and the disengagement away of the distracting stimuli. Thus, investigating the impact of lPFC damage on distraction in an ecological setting, seems to be rather important. In addition, to our knowledge, no study has investigated the impact of lPFC lesions on bottom-up gamma oscillations.

4.3 The Lateral Prefrontal Cortex: Roads Untraveled

In this chapter, we have reviewed evidence of impaired top-down and bottom-up mechanisms of attention that could be directly (prefrontal stroke) or indirectly (ageing) linked to reduced integrity of the lateral prefrontal cortex. This gives more support to the idea that the lPFC could represent the interaction hub between these mechanisms. However, among the studies reviewed here, very few utilized paradigms that permit the simultaneous investigation of top-down and bottom-up attention mechanisms and the interaction (balance) between them. Thus, the dynamic role of the lPFC in attention remains to be uncovered. Precisely, the following questions remain unanswered:

- What is the impact of frontal “malfunctioning” upon the facilitatory and suppressive mechanisms of top-down anticipatory attention, indexed by modulations in the alpha band?
- What is the brain origin of the exacerbated distractibility associated with frontal malfunctioning: An impaired bottom-up attentional system or a reduced top-down attentional control?
- How would this frontal dysfunction impact the balance between top-down and bottom-up attentional mechanisms?

Answering such question would not only help us to better characterize attentional difficulties within these populations but also, would further our understating of the dynamic balance between attentional processes.

Hypothesis & Objectives

As an action or a reaction to our environment, attention can be oriented either in an endogenous (top-down) or an exogenous (bottom-up) manner. Both orienting mechanisms are supported by two partially segregated networks, the dorsal and ventral fronto-parietal attention networks, with the lateral prefrontal cortex lying at the crossroad between these networks. Brain oscillatory activities have been shown to play an important role in supporting communication within bottom-up and top-down attentional networks in both sensory and higher-level cognitive regions. Ageing and frontal damage are associated with attentional difficulties that could be related to an exacerbated bottom-up attentional capture and/or reduced top-down attentional control.

Regarding the literature of bottom-up and top-down attention, three points could be raised: **First**, studies investigating attention in the visual domain, by far, outnumber those from the auditory domain in spite of the richer representation of the auditory modality in the prefrontal cortex, which could help shed more light onto the architecture of attentional systems. **Second**, and more importantly, few attempts have been made to investigate both top-down and bottom-up attentional mechanisms in the same study and, so far, not so much light has been shed upon the dynamic balance between these mechanisms. In other words, only few studies explored how an isolated unexpected task-irrelevant stimulus outside the attention focus can disturb the top-down attentional mechanisms and, reversely, how top-down mechanisms can modulate the bottom-up mechanisms of attentional capture triggered by an unexpected event. **Finally**, in the oscillatory domain, several investigations highlight the fact that at least on a signal propagation level, slow (alpha) and fast (gamma) oscillations seem to reflect feedback and feedforward signaling, respectively. However, while few studies point out to the existence of such “division” in the attention domain (low and high oscillations supporting top-down and bottom-up attention), it seems to be barely investigated.

Briefly, in this thesis work we sought to provide new insights into the brain mechanisms of distractibility by investigating the oscillatory dynamics supporting the balance between bottom-up and top-down auditory attention in the healthy young, ageing and damaged brain. This work has been constructed on the following hypothesis based on the literature presented in the previous chapters: Long-range coupling in lower frequencies would coordinate activity between the nodes of the dorsal top-down network, whereas high

frequency oscillations would support bottom-up mechanisms of attention and index the activation of the ventral bottom-up network. High frequency oscillations and their coupling to low rhythms in the lateral prefrontal cortex, a brain region common to both ventral and dorsal networks, would regulate the dynamic interplay between these two networks.

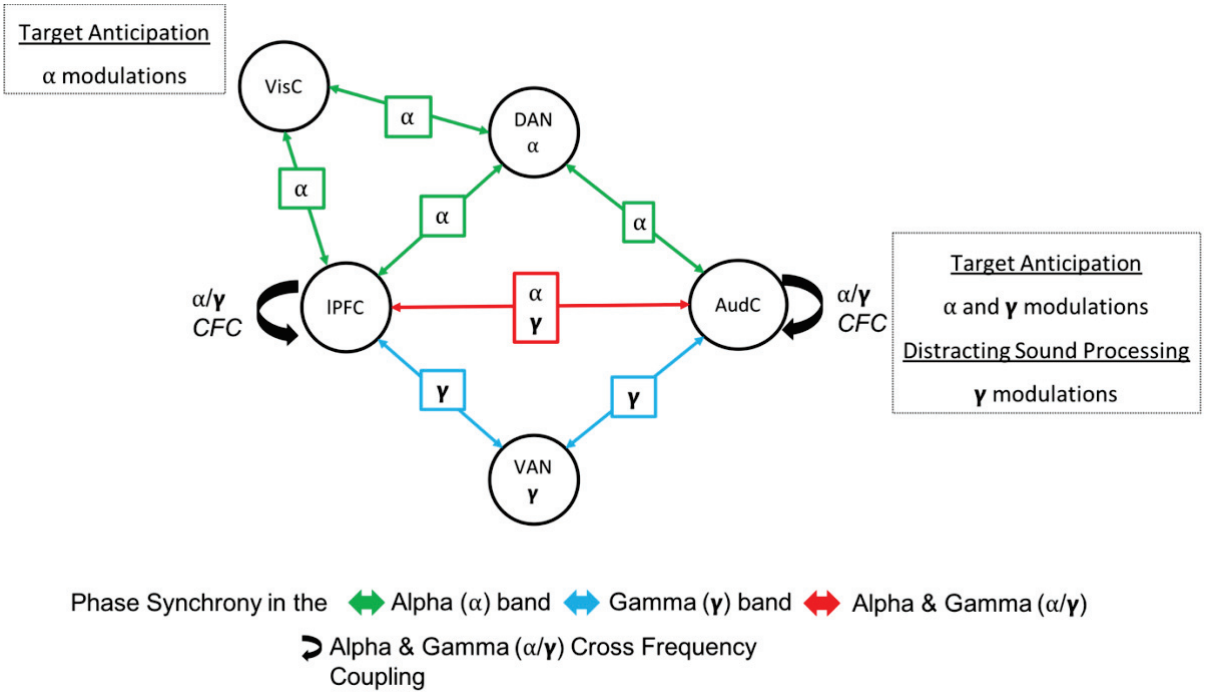


Figure 25. Schematic representation of the oscillatory framework used in this thesis work. DAN: dorsal attentional network, VAN: ventral attentional network, lPFC: lateral prefrontal cortex, AudC: auditory cortex, VisC: visual cortex, CFC: cross-frequency coupling.

This work has been based upon a novel paradigm proposed by Bidet-Caulet and colleagues (2014): The Competitive Attention Test (CAT). It is worth mentioning that for the work presented here, this paradigm has been updated twice and we shall be referring to both versions as CAT2.0 and CAT3.0. In summary, the CAT is an adaptation of the Posner cueing paradigm using visual cues and monaural auditory targets. Top-down anticipatory attention is measured by comparing trials with informative cues to trials with uninformative cues. In only 25 % of the trials, bottom-up attentional capture is triggered by a binaural distracting sound played during the delay between the cue and the target. Distraction is assessed as the impact of distracting sound on task performance and the balance between both mechanisms could be measured by comparing responses to distracting sounds following informative and uninformative cues.

Combining the CAT with behavioral assessment, simultaneous MEG and EEG recordings, we had three aims.

I. Investigating the oscillatory dynamics supporting top-down and bottom-up attention and the interaction between them. For that end, we hypothesized that:
   (1) Low-frequency alpha oscillations would support top-down anticipatory attention in the dorsal top-down network. Further, we hypothesized that during the anticipation of an auditory target:
      a. In the auditory cortex, alpha oscillations would reflect both facilitatory and suppressive mechanisms of top-down attention (Study I: CAT2.0).
      b. Long-range communication between nodes of the dorsal top-down network (e.g. the Frontal Eye Fields) and the auditory cortex would be established through inter-areal phase synchrony in the alpha band (Supplementary study I: CAT2.0).
      c. Based upon evidence of phase-amplitude coupling (Canolty and Knight 2010), gamma oscillations, presumably nested upon alpha oscillations, in the auditory cortex would reflect modulations of top-down attention before and after target presentation (Supplementary study II: CAT2.0).
   (2) High frequency gamma oscillations would support bottom-up attentional mechanisms in the ventral bottom-up network (Study II: CAT3.0).
   (3) The interplay (balance) between the ventral and dorsal attentional networks would be supported by the lateral prefrontal cortex, at the crossroad between the two networks, through modulations of either alpha phase-gamma amplitude coupling or modulations of gamma amplitude (Study II: CAT3.0).

II. Characterizing the neural correlates of the ageing-associated exacerbated distractibility by investigating the impact of ageing on oscillatory activities supporting the balance between top-down and bottom-up attentional mechanisms. We hypothesized that ageing would be characterized by (1) exacerbated behavioral distractibility, (2) reduced top-down filtering of irrelevant information, indexed by alterations in the alpha band, and (3) impaired responses to distracting sounds indexed by alterations in the gamma band (Study III: CAT3.0).

III. Investigating the role of the lateral PFC in supporting the dynamic of top-down and bottom-up attention, and further specifying the brain dysfunction leading to increased distractibility in these patients (Study IV: CAT3.0).

Part II: Material and Methods

5 Experimental Paradigm & Protocol

5.1 The Competitive Attention Test: First Iteration (CAT 1.0)

"By three methods we may learn wisdom: First, by reflection, which is noblest;
Second, by imitation, which is easiest;
and third by experience, which is the bitterest"
— Confucius

The main paradigm used for all of the experiments in this thesis is the Competitive Attention Test (CAT). This paradigm has been proposed by Bidet-Caulet and colleagues in 2014 to investigate the deployment of top-down and bottom-up mechanisms of attention and the balance between them (CAT 1.0: see Figure 26). Please note that this version of the paradigm has not been used in this thesis work.

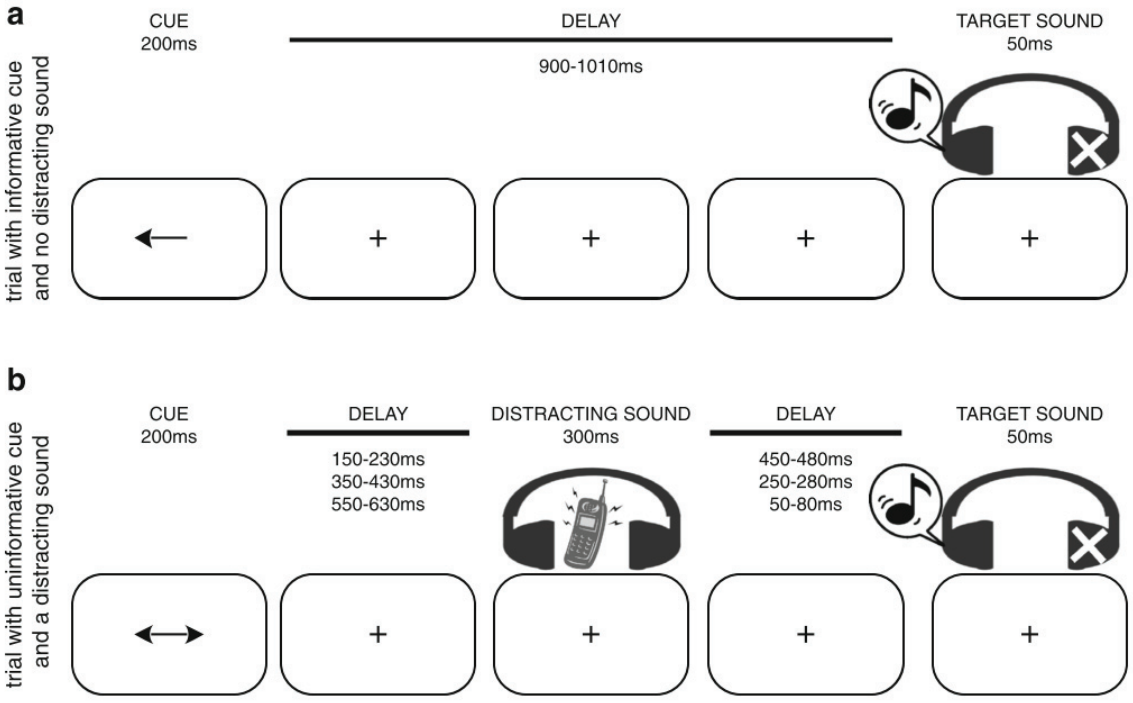


Figure 26. The Competitive Attention Test (CAT1.0). (A) In informative trials, a one-sided visual cue (200 ms duration) indicated in which ear (left or right) the target sound will be played (50 ms duration) after a random delay (900–1,010 ms). (B) In uninformative trials, a two-sided visual cue (200 ms duration) did not provide any indication in which ear (left or right) the target sound will be played. In 25 % of the trials a binaural distracting sound (300 ms duration), such as a phone ring, was played during the delay between cue and target. The distracting sound could equiprobably onset in three different time periods after the cue offset: in the 150–230 ms range, in the 350–430 ms range, or in the 550–630 ms range. (Adapted from Bidet-Caulet et al., 2014).

In 75 % of the trials, a target sound (50 ms duration) followed a central visual cue (200 ms duration) with a randomly chosen delay between 900 and 1,010 ms. The cue was a green arrow, presented on a grey-background screen, pointing either to the left, right, or both sides. The target sound was a monaural harmonic sound (fundamental frequency: 200 Hz, 5 harmonics; 5 ms rise-time, 5 ms fall-time) presented at 15 dB SL (mean ± SD: 43.9 ± 2.2 dBA). In the other 25 %, the same structure was retained, however, a binaural distracting sound (300 ms duration; 70 dB SL; mean ± SD: 56.9 ± 2.2 dBA) was played during the cue-target delay. The distracting sound could equiprobably be presented in three different time periods after the cue offset: in the 150–230 ms range (DIS1), in the 350–430 ms range (DIS2), or in the 550–630 ms range (DIS3).

The cue and target categories were manipulated in the same proportion for trials with and without distracting sound. In 33.3 % of the trials, the cue was pointing left, and the target sound was played in the left ear, and in 33.3 % of the trials, the cue was pointing right, and the target sound was played in the right ear, leading to a total of 66.6 % of *informative* trials. In the last 33.3 % of the trials, the cue was *uninformative*, pointing in both directions, and the target sound was played in the left (16.7 %) or right (16.7 %) ear.

Participants were instructed to perform a detection task by pressing a mouse button as fast as possible when they heard the target sound. Participants were informed that informative cues were 100 % predictive and that a distracting sound could be sometimes played. They were asked to allocate their attention to the cued side in the case of informative cue, to ignore the distractors and to respond as quickly and correctly as possible. Participants had 2,500 ms to answer after target sounds, each trial lasted therefore from 3,600 to 3,710 ms. In the absence of the visual cue, a blue fixation cross was presented at the center of the screen. Subjects were instructed to keep their eyes fixated on the cross and to minimize eye movements and blinks while performing the task. Finally, subjects performed 15 blocks (72 trials each), leading to 810 trials in the NoDIS, 90 in the DIS1, 90 in the DIS2 and 90 in the DIS3 conditions. The whole session lasted around 130 minutes.

5.2 The Competitive Attention Test: First adaptation (CAT 2.0)

This adaptation was utilized to acquire our first simultaneous EEG and MEG recordings from 18 healthy young subjects. We have decided that simultaneous recordings are more informative since EEG served to provide established markers of top-down and bottom-up attentional mechanisms to guide MEG analysis. Moreover, the superior spatial resolution of the MEG signal served to precisely locate the generators of these mechanisms and the interaction between them. For this experiment, several changes were made to CAT1.0 (see Figure 27):

First, in order to render the task more challenging to increase the top-down attentional load, the detection task was replaced by a discrimination task. Participants were instructed to categorize two target sounds as either high- or low-pitched sound, by either pulling or pushing a joystick. The mapping between the targets (low or high) and the responses (pull or push) was counterbalanced across participants, but did not change across the blocks, for each participant. Target sounds were monaural pure tones (duration: 100ms; carrier frequency between 512 and 575 Hz; 5 ms rise-time, 5 ms fall-time) played at 25 dB SL (mean ± SD: 52.4 ± 7.6 dBA).

Second, the delay between the visual cue and the auditory target was fixed at 1000ms, since we compared fixed to jittered cue-target delays and no difference was found. Third, the distribution of the distracting sounds was changed. In the original CAT1.0, distracting sounds were played within discrete time windows. Thus, distracting sounds might have been used as predictive cues of the upcoming target. For this experiment, distracting sounds could be played at any time point in the range of 150–630ms after cue offset. They were played at 35 dB SL (mean ± SD: 47.4 ± 7.6 dBA).

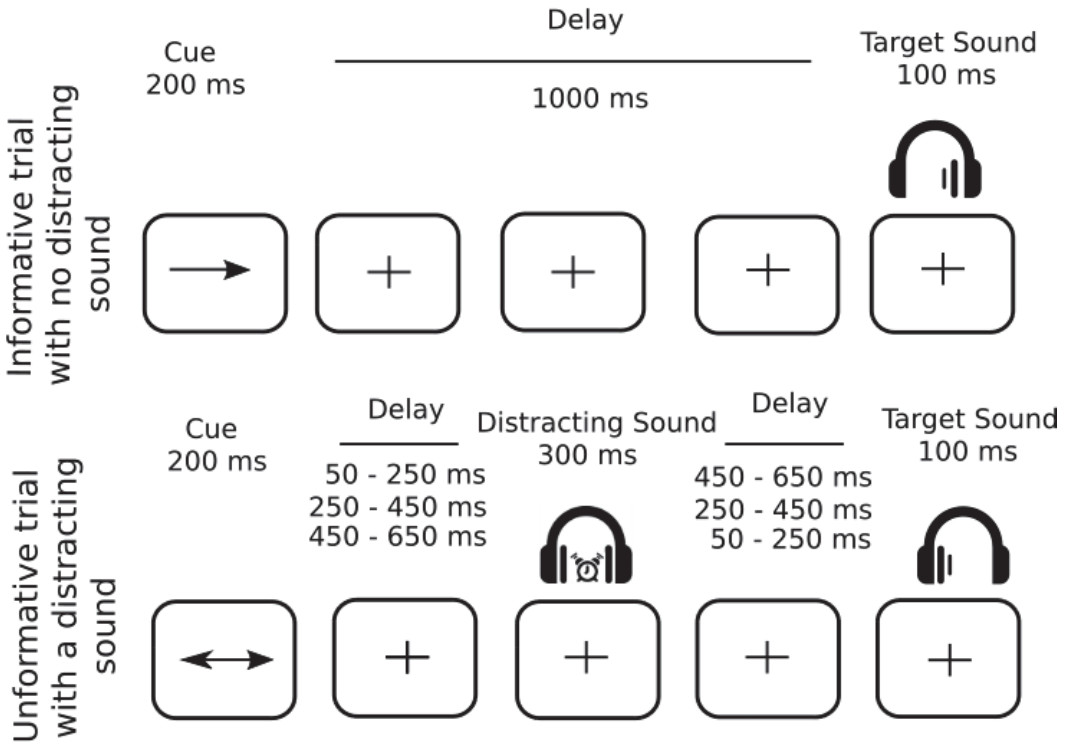


Figure 27. CAT2.0 Design. Top row. Example of an informative trial with no distracting sound: a one-sided visual cue (200 ms duration) indicated in which ear (left or right) the target sound would be played (100 ms duration) after a fixed 1000-ms delay. Bottom row. Example of an uninformative trial with a distracting sound, a two-sided visual cue (200 ms duration) did not provide any indication in which ear (left or right) the target sound will be played. In 25 % of the trials a binaural distracting sound (300 ms duration), such as a clock ring, was played during the delay between cue and target. The distracting sound could equiprobably onset in three different time periods after the cue offset: in the 50–250 ms range, in the 250–450 ms range, or in the 450–650 ms range.

5.3 The Competitive Attention Test: Second Adaptation (CAT 3.0)

This iteration was utilized to acquire simultaneous EEG and MEG recordings from 45 healthy participants (age range: 19-75), and 8 patients with frontal stroke. For this experiment, three main changes were made to CAT2.0. All these changes were made to render the experiment, as a whole, shorter in duration for elderly participants and patients with frontal stroke, while retaining most of the trial proportion in CAT1.0 and CAT2.0 (see Figure 28):

1. Distracting sounds were classified as either DIS1, played from 50 ms to 350 ms after the cue offset or DIS2, played from 350 ms to 650 ms after the cue offset.
2. The proportion of informative to uninformative trials was changed: In 25% of the trials, the cue was pointing left, and the target sound was played in the left ear, and in 25%

of the trials, the cue was pointing right, and the target sound was played in the right ear, leading to a total of 50% of *informative* trials (instead of 67%). In the other 50% (instead of 33%) of the trials, the cue was *uninformative*, pointing in both directions, and the target sound was played in the left (25%) or right (25%) ear.

3. Subjects performed 10 blocks (64 trials each) leading to 480 trials in the NoDIS, 80 in the DIS1 and 80 in the DIS2 conditions. The whole session lasted around 80 minutes.
4. Target sounds were played at 25 dB SL (approximately 63 dB A) and distracting sounds were played at 55 dB SL (approximately 73 dB A).

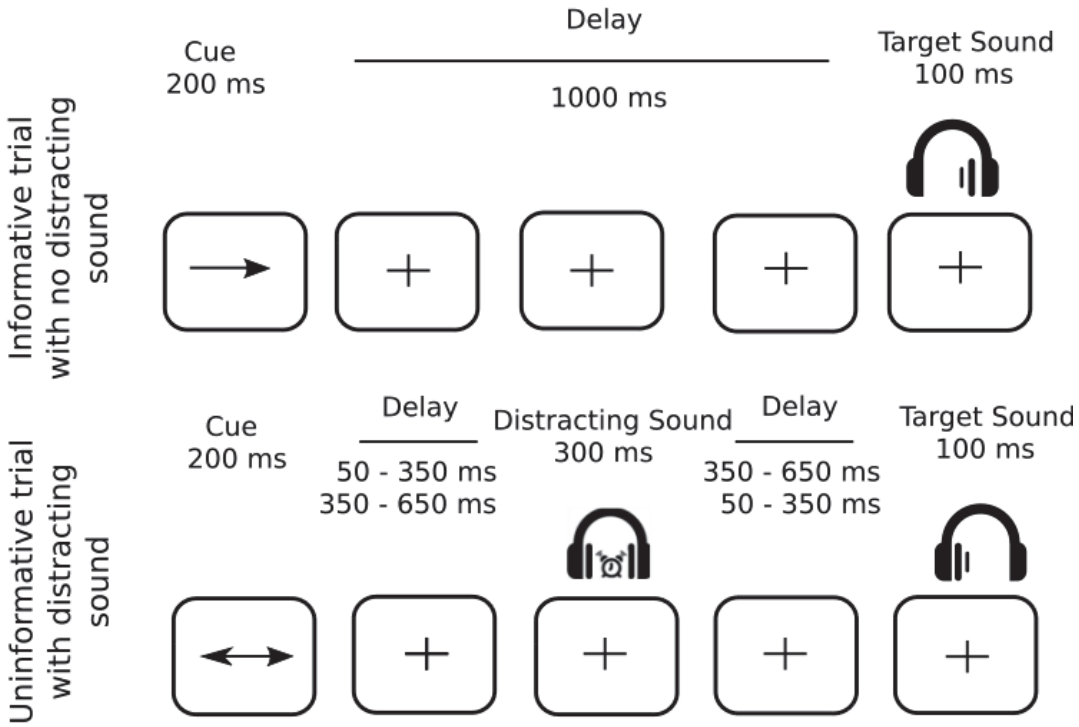


Figure 28. CAT3.0 design. Top row. Example of an informative trial with no distracting sound: a one-sided visual cue (200 ms duration) indicated in which ear (left or right) the target sound would be played (100 ms duration) after a fixed 1000-ms delay. Bottom row. Example of an uninformative trial with a distracting sound, a two-sided visual cue (200 ms duration) did not provide any indication in which ear (left or right) the target sound will be played. In 25 % of the trials a binaural distracting sound (300 ms duration), such as a phone ring, was played during the delay between cue and target. The distracting sound could equiprobably onset in two different time periods after the cue offset: in the 50–350 ms range, or in the 350–650 ms range.

5.4 Discrimination Task

Since participants were required to discriminate two target sounds, we aimed to account for the participants' pitch-discrimination capacities. So, the pitch difference between the two target sounds was defined in a Discrimination Task. The aim of this task was to ensure that, for all participants across all groups, the CAT discrimination task would be neither too easy nor too difficult. Thus, differences in performances in the CAT paradigm between groups would reflect differences in attentional rather than discrimination (sensory) processes.

In this task participants were randomly presented with one of two target sounds: a low-pitched sound (512 Hz) and a high-pitched sound (575 Hz; two semitones higher), equiprobably in each ear (four trials per ear and per pitch). As described above, participants were asked to categorize the target sounds as either high- or low-pitched sound within 3 seconds. If participants failed to respond correctly to more than 85% of the trials, the pitch of the high target sound was augmented, by half a semitone with a maximum difference of 3 semitones between the two new targets.

5.5 Procedure

5.5.1 General Procedure for simultaneous EEG/MEG recordings

The experiments were run at the MEG department of the neuroimaging center in Lyon, the CERMEP (https://www.cermep.fr/). Participants were seated in a sound-attenuated, magnetically shielded recording room, at a 50 cm distance from the screen. The response device was a custom index-operated joystick that participants moved either towards them (when instructed to pull) or away from them (when instructed to push). All stimuli were delivered using Presentation software (Neurobehavioral Systems, Albany, CA, USA). All sounds were presented through air-conducting tubes using Etymotic ER-3A foam earplugs (Etymotic Research, Inc., USA).

First, the auditory threshold was determined for the two target sounds differing by 2 semitones (512 and 575 Hz), for each ear, for each participant using the Bekesy tracking method (Von Békésy and Wever 1960). Second, participants performed the discrimination task. If participants failed to respond correctly to more than 85% of the trials, the pitch of the high target sound was augmented, by half a semitone with a maximum difference of 3 semitones between the two targets (auditory thresholds were then measured with the new targets). Afterwards, participants were trained with a short sequence of the Competitive

Attention Task. Finally, MEG and EEG were recorded. After the MEG/EEG session, participants' subjective reports regarding their strategies were collected.

5.5.2 MEG Recordings

The MEG data were acquired with a 275-sensor axial gradiometer system (CTF Systems Inc., Port Coquitlam, Canada) with continuous sampling at a rate of 600Hz, a 0–150Hz filter bandwidth, and first-order spatial gradient noise cancellation. Moreover, eye-related movements were measured using vertical and horizontal EOG electrodes. Head position relative to the gradiometer array was acquired continuously using coils positioned at three fiducial points; nasion, left and right pre-auricular points. Head position was checked at the beginning of each block to control head movements.

5.5.3 EEG Recordings

The EEG setup varied between CAT2.0 and CAT3.0. For the former, EEG was recorded continuously from 56 scalp electrodes and the ear lobes. In addition, EEG sensor locations were collected and digitized using a Polhemus device (https://polhemus.com/). For the latter, EEG was recorded continuously from only 7 scalp electrodes placed at frontal (Fz, Fc1, Fc2), central (Cz), and parietal (Pz) sites, and at the two mastoids (M1, M2). Electrode placement was chosen in order to capture the well-established event-related markers of attention such as: CNV, taget-P3 and novelty-P3 complex. For both, the reference electrode was placed on the tip of the nose, the ground electrode on the forehead. In addition, one bipolar EOG derivation was recorded from 2 electrodes placed on the supra-orbital ridge of the left eye and infra-orbital ridge of the right eye.

5.5.4 Magnetic Resonance Imaging (MRI) Recordings

After the MEG/EEG recordings, T1-weighted three-dimensional anatomical images were acquired for each participant using a 3T Siemens Magnetom whole-body scanner (Erlangen, Germany). These images were used for reconstruction of individual head shapes to create forward models for the source reconstruction procedures that shall be described later. The processing of these images was carried out using CTF's software (CTF Systems Inc., Port Coquitlam, Canada).

6 MEG Data Analysis

6.1 Preprocessing Pipeline

Here we shall discuss the common preprocessing pipeline that we have utilized for all data analysis in all experiments. It is worth mentioning that in all the experiments we focused mainly on the MEG data and oscillatory activities.

First, based on behavioral data analysis only correct responses that were executed after the onset of the target sound and before the apparition of the following cue were considered for electrophysiological analyses. Data segments contaminated with excessive head movements that exceeded 10 mm from the reference position (measured at the beginning of the session, once the participant was comfortably seated) were excluded. In addition, data segments contaminated with muscular activity or sensor jumps were excluded semi-manually using a threshold of 2200 and 10000 femtoTesla respectively. Independent component analysis was applied on the band-pass filtered (0.1—40Hz) data in order to remove eye-related (blink and saccades) and heart-related artefacts. Subsequently, components were removed from the non-filtered data via the inverse ICA transformation. Data were further notch filtered at 50, 100 and 150Hz and high-pass filtered at either 0.1Hz (CAT2.0) or 0.2Hz (CAT3.0: to remove noticeable slow drifts in the data of several participants). It's worth mentioning that for CAT3.0 data, due to high environmental noises (construction work) during data acquisition, we changed the MEG gradiometers formation from first-order to third-order, offline. The higher-order gradiometer formation is a noise-cancellation technique which permits MEG detectors to be sensitive to the weak signals of the brain, yet impervious to the much stronger sources from the environment (https://goo.gl/92pojU).

6.2 Oscillatory Activity Analysis

For analysis of oscillatory analysis in both alpha and gamma bands, either at the sensor or virtual electrode level, the oscillatory power was calculated using Morlet Wavelet decomposition with a width of four cycles per wavelet (m=7; Tallon-Baudry and Bertrand 1999) at center frequencies of interest (between 5 and 18 Hz for alpha and between 40 and 150 Hz for gamma), in steps of 1 Hz and 10 ms for gamma and 50 ms for alpha.

The advantage of the wavelet method is that it provides better time and frequency resolution than the more classical moving short-term Fourier transform (Bertrand and Tallon-

Baudry 2000). And since the wavelets are applied on each single trial followed by averaging time-frequency power across trials, this method provides the possibility to identify both phase-locked (evoked) and non-phase locked (induced) activity to a certain stimulus (Tallon-Baudry et al. 1999).

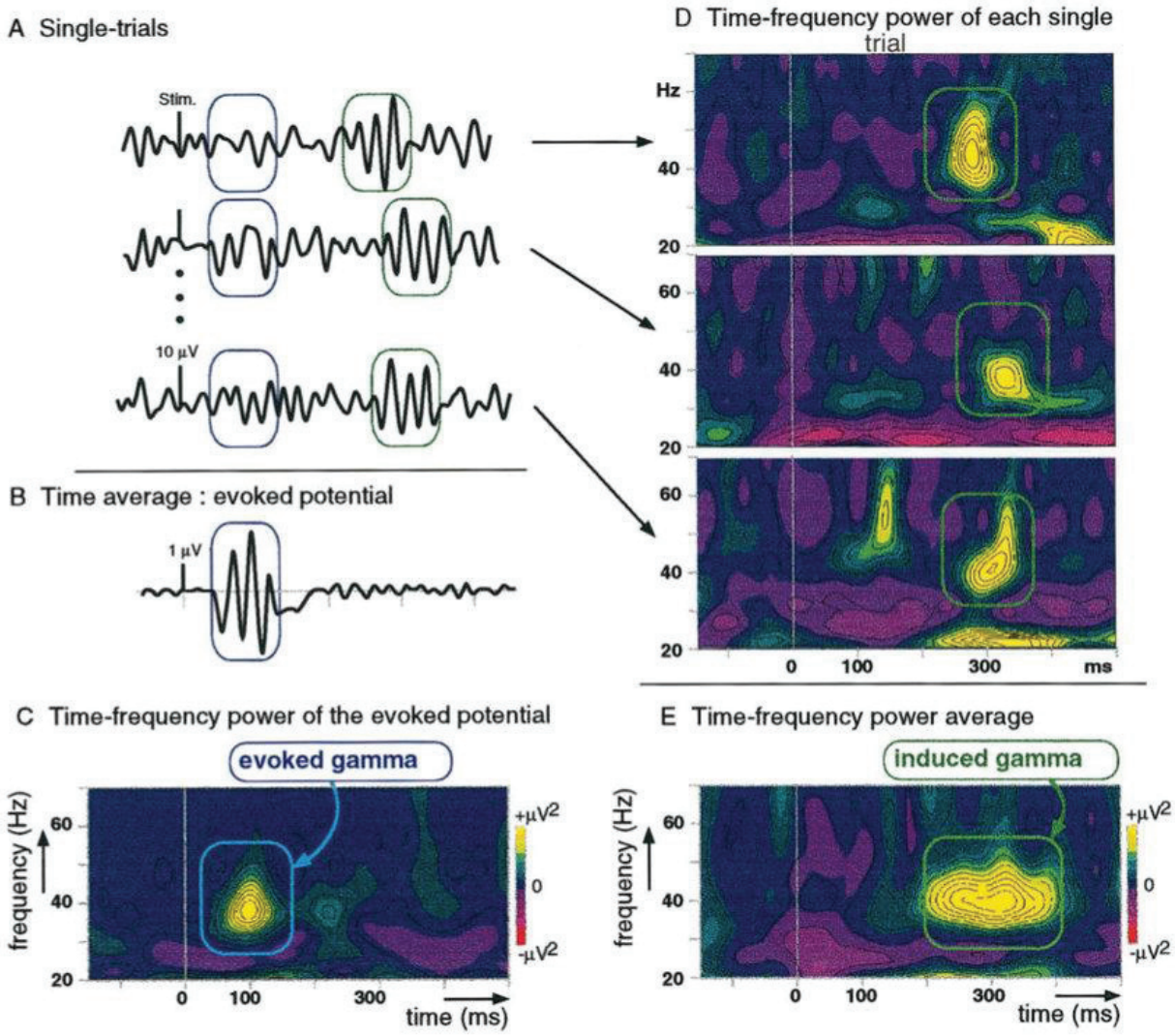


Figure 29. A. Successive simulated EEG trials with an early gamma response phase-locked to stimulus onset full line boxes and a late gamma burst jittering in latency dashed line boxes. B. Averaging in the time domain across trials leads to the conventional evoked potential. C. Time-frequency power representation wavelet transform of the evoked gamma response. The x-axis is time, and the y-axis is frequency. The gray scale codes the variations of power positive or negative with respect to a pre-stimulus baseline. The non-phase-locked activity cancels out. D. Time-frequency power computed for each singe trial. E. Average of time-frequency powers across trials. The induced gamma response is clearly visible. (Adapted from Bertrand and Tallon-Baudry, 2000).

6.3 Source Level Analysis: DICS Beamformer

In order to estimate the brain regions driving activity in time-frequency windows of interest (in alpha or gamma band), we have utilized the frequency–domain adaptive spatial technique of dynamical imaging of coherent sources (DICS; Gross et al., 2001). For each participant:

1. A Cross-spectral density (CSD) matrix was calculated using the multitaper method.
2. An anatomically realistic single-shell headmodel based on the cortical surface was generated from individual head shapes (Nolte, 2003). A grid with 0.5 cm resolution was normalized on an MNI template, and then morphed into the brain volume of each participant.
3. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was subsequently used to estimate the spatial distribution of power for all time-frequency windows of interest.

6.4 Source Level Analysis: Virtual Electrodes

The DICS beamformer provides a snapshot picture of the brain sources of oscillatory activity in a definite time-frequency window i.e. for each voxel, oscillatory power is represented as one value. In order to obtain higher time-frequency resolution, we applied the Virtual Electrode method. For each participant:

1. The source space was subdivided anatomically according to a certain atlas and regions of interest (ROIs) were chosen.
2. For each ROI, in order to reconstruct activity at the source level, we computed the time-frequency signal at the virtual electrode level using the LCMV beamformer. Spatial filters were constructed from the covariance matrix of the averaged single trials at sensor level and the respective leadfield by a linearly constrained minimum variance (LCMV) beamformer (Van Veen et al. 1997). Afterwards, spatial filters were multiplied by the sensor level data in order to obtain the time course activity at each voxel of interest in each ROI. For each ROI, we subtracted the evoked potential (i.e., the signal averaged across all trials) from each trial.
3. Subsequently, time-frequency power was calculated using Morlet Wavelet decomposition as described in section 6.2.

6.5 Statistical Analysis: Cluster Based Permutation Test

For almost all MEG analyses, we have used the nonparametric cluster-based permutation analysis (Maris and Oostenveld 2007). In brief, this test first calculates paired t-tests for each data sample, which are then thresholded at $P < 0.05$. Selected significant samples are clustered in connected sets (clusters) on the basis of temporal, spatial and spectral adjacency. The sum within each cluster (Tsum) is retained, and the procedure is repeated 1000 times on shuffled data in which the condition assignment within each individual is swapped randomly. On each permutation, the maximum Tsum (Tmax) is retained yielding a distribution of 1000 Tmax values. From this distribution, the cluster probability of each empirically observed Tsum can be derived. Clusters are labelled as significant with a P-value ≤ 0.05. Please note, that cluster permutations control for multiple comparisons in time, frequency, sensor space or source space.

6.6 Correlation Analysis

Across the thesis work, we have attempted to correlate behavioral performances (reaction times) to modulations in oscillatory activity (alpha and gamma) in both sensor and source level. Correlation topographies (maps) were created in both sensor and source space domains (Mazaheri et al. 2013). In order to create these topographies, first, we performed a trial-by-trial correlation, using non-parametric Spearman tests, in each participant, between reaction times and each sensor-time frequency point (sensor level) or at each grid point (source level). Then, the correlation coefficients were subsequently converted to z-values using Fisher's r- to z-transformation to obtain a normally distributed variable. The statistical significance of the correlations was assessed at the group level with a one-sample t-test of the correlation z-values at each sensor-time-frequency point (sensor level) or at each grid point (source level), and then subjected to a cluster-level randomization test to correct for multiple comparisons in the sensor-space, time and frequency dimensions (sensor level) or source space (source level). It is important to note that at the source level, single-trial oscillatory activity was reconstructed at each grid point using a Partial Cannonical Correlation (PCC) beamformer, a more computationally efficient alternative to the DICS beamformer.

6.7 Connectivity Analysis

We have also attempted to identify the brain regions that could be functionally connected (in the gamma or alpha band) to the auditory cortices. For that, we have extracted the complex values containing phase information into source space using partial canonical coherence (PCC) beamformer which provides the possibility of extracting both power and phase information on the source level. For each participant:

(1) Cross-spectral density (CSD) matrices were calculated using the multitaper method. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was used to estimate the spatial distribution of power and phase for the time-frequency window of interest.

(2) Phase synchrony (Lachaux et al. 1999) between each voxel in the auditory ROIs and all other voxels was calculated, averaged across voxels of the auditory ROI, and then Fisher Z transformed. Thus, for each extra-auditory brain voxel, a single, phase synchrony value with the entirety of the auditory ROI was obtained.

Part III: Experimental Results

7 Alpha Oscillations and Top-Down Attention

7.1 General Presentation

Within our framework, we have proposed that alpha oscillations play a dual role in top-down attention with their amplitude reflecting local sensory regulation of cortical excitability and information processing (Klimesch et al., 2007; Jensen and Mazaheri, 2010), whereas their phase would reflect long-range inter-areal communication (Palva and Palva, 2007, 2011). In what follows, we have sought to establish that dual role in anticipation of visually-cued auditory target (CAT2.0).

In **study I**, anticipation of the auditory target resulted in a decrease in auditory alpha power around 9Hz (low alpha) and an increase in visual alpha power around 13 Hz (high alpha), with only the latter correlating with reaction times. Moreover, within the right auditory cortex, we demonstrated a larger increase in high alpha power when attending an ipsilateral sound, and a stronger decrease in low alpha power when attending a contralateral sound. In summary, we found facilitatory and suppressive attentional mechanisms with distinct timing in task-relevant and task-irrelevant brain areas, that differentially correlated to behavior and were supported by distinct alpha sub-bands.

In the follow-up **supplementary study I**, we have investigated inter-areal communication by measuring whole brain phase synchrony with the auditory regions of interest (ROIs: defined in **study I**) as a seed. We have demonstrated that alpha phase synchrony significantly increased between the right auditory cortex and the left prefrontal cortex (Frontal Eyes Fields and lPFC) during expectation of an ipsilateral rather than a contralateral target. This provides insight into the role of alpha phase in subtending long-range communication and also sheds some light on the potential role of the lPFC in supporting top-down attentional mechanisms.

Finally, in **supplementary study II**, we have attempted to uncover potential alpha-phase/gamma-amplitude coupling within the auditory ROIs in the time-window of interest previously defined in **study I**. As a first step, we have demonstrated that the amplitude of gamma oscillations was modulated by both the laterality of the anticipated target and the cue information before and after the presentation of the target. However, the question whether gamma oscillations were coupled to the phase of alpha oscillations or not is yet to be investigated in future research.

7.2 Study I: Alpha Activity During Top-Down Attention (CAT 2.0)

Two Sides of the Same Coin: Distinct Sub-Bands in the α Rhythm Reflect Facilitation and Suppression Mechanisms during Auditory Anticipatory Attention

Hesham A. ElShafei,[1] Romain Bouet,[1] Olivier Bertrand,[1] and Aurélie Bidet-Caulet[1]

doi : http://dx.doi.org/10.1523/ENEURO.0141-18.2018

[1] Brain Dynamics and Cognition Team, Lyon Neuroscience Research Center ; CRNL, Institut National de la Santé et de la Recherche Médicale Unité 1028, Centre National de la Recherche Scientifique Unité Mixte de Recherche 5292, Université de Lyon, Lyon, France 69500

rich3/enu-enu/enu-enu/enu00418/enu2683d18z | xppws | S=4 | 7/24/18 | 22:21 | MS: | Ini:

eNeuro

New Research

Cognition and Behavior

Sst1

Two Sides of the Same Coin: Distinct Sub-Bands in the α Rhythm Reflect Facilitation and Suppression Mechanisms during Auditory Anticipatory Attention

AQ: au Hesham A. ElShafei,[1] Romain Bouet,[1] Olivier Bertrand,[1] and Aurélie Bidet-Caulet[1]

DOI:http://dx.doi.org/10.1523/ENEURO.0141-18.2018

[1]Brain Dynamics and Cognition Team, Lyon Neuroscience Research Center; CRNL, Institut National de la Santé et de la Recherche Médicale Unité 1028, Centre National de la Recherche Scientifique Unité Mixte de Recherche 5292,
AQ: 1 Université de Lyon, Lyon, France 69500

Abstract

Anticipatory attention results in enhanced response to task-relevant stimulus, and reduced processing of unattended input, suggesting the deployment of distinct facilitatory and suppressive mechanisms. α Oscillations are a suitable candidate for supporting these mechanisms. We aimed to examine the role of α oscillations, with a special focus on peak frequencies, in facilitatory and suppressive mechanisms during auditory anticipation, within the auditory and visual regions. Magnetoencephalographic (MEG) data were collected from fourteen healthy young human adults (eight female) performing an auditory task in which spatial attention to sounds was manipulated by visual cues, either informative or not of the target side. By incorporating uninformative cues, we could delineate facilitating and suppressive mechanisms. During anticipation of a visually-cued auditory target, we observed a decrease in α power around 9 Hz in the auditory cortices; and an increase around 13 Hz in the visual regions. Only this power increase in high α significantly correlated with behavior. Importantly, within the right auditory cortex, we showed a larger increase in high α power when attending an ipsilateral sound; and a stronger decrease in low α power when attending a contralateral sound. In summary, we found facilitatory and suppressive attentional mechanisms with distinct timing in task-relevant and task-irrelevant brain areas, differentially correlated to behavior and supported by distinct α sub-bands. We provide new insight into the role of the α peak-frequency by showing that anticipatory attention is supported by distinct facilitatory and suppressive mechanisms, mediated in different low and high sub-bands of the α rhythm, respectively.

Key words: α; α sub-bands; attention; audition; magnetoencephalography; oscillations

Significance Statement

We investigated the role of α oscillations, with a special focus on peak frequencies, in facilitatory and suppressive mechanisms during anticipation, using magnetoencephalographic (MEG) data collected during an auditory spatial attention task. We show, during anticipation of a visually-cued auditory target, a decrease in α power around 9 Hz in the auditory cortices, simultaneous to an increase around 13 Hz in in the visual regions, the latter significantly correlated with behavioral performances. Within the right auditory cortex, we show a larger increase in high α when attending an ipsilateral sound; and a stronger decrease in low α when attending a contralateral sound. Therefore, anticipatory attention would be supported by distinct facilitatory and suppressive mechanisms, mediated in different low and high α sub-bands, respectively.

Introduction

We spend a large fraction of our time anticipating stimuli (Requin et al., 1991) and to support this behavior, anticipatory attention promotes the processing of upcoming relevant stimuli, resulting in reduced brain responses to unattended inputs and enhanced processing of relevant information (for review, see Hillyard et al., 1998). These modulations of target processing suggest the deployment of distinct facilitatory and suppressive attentional mechanisms during target expectancy, similarly to the inhibitory and facilitatory mechanisms supporting selective attention (de Fockert and Lavie, 2001; Gazzaley et al., 2005, 2008; Bidet-Caulet et al., 2007, 2010, 2015; Chait et al., 2010; Slagter et al., 2016). However, little is known about the potential facilitatory and suppressive attentional mechanisms activated during anticipation of an upcoming stimulus.

Oscillations in the α band, loosely defined between 8 and 14Hz, have been proposed to play a crucial role in anticipatory attention (for review, see Foxe and Snyder, 2011; Frey et al., 2015). Discovered in 1929 by Hans Berger (Berger, 1929), α oscillations were first considered a marker of cortical idling (Pfurtscheller et al., 1996). However, this idea has been challenged with α oscillations being assigned an active inhibitory role in cognitive processing (Klimesch et al., 2007; Jensen and Mazaheri, 2010). The large literature in the visual modality paints a rather dynamical picture in which, during target expectation, α power decreases in visual areas responsible for processing the attended space while α power increases in (1) visual areas responsible for processing the unattended space with or without distracting stimuli (Kelly et al., 2006; Rihs et al., 2007, 2009), and (2) areas responsible for processing unattended modalities (Foxe et al., 1998; Fu et al., 2001; Gomez-Ramirez et al., 2011; Jiang et al., 2015). Therefore, α oscillations would be a suitable candidate for supporting facilitatory and suppressive mechanisms of anticipatory attention.

Received April 9, 2018; accepted June 21, 2018; First published July 17, 2018.
The authors declare no competing financial interests.
Author contributions: H.A.E. and A.B.-C. designed research; H.A.E. and A.B.-C. performed research; H.A.E., A.B.-C., and R.B. analyzed data; H.A.E., A.B.-C., R.B., and O.B. wrote the paper.
This work was supported by the French National Research Agency (ANR) Grant ANR-14-CE30-0001-01 (to A.B.-C.). This work was performed within the framework of the LABEX CORTEX (ANR-11-LABX-0042) and the LABEX CELYA (ANR-10-LABX-0060) of Université de Lyon, within the program "Investissements d'Avenir" (ANR-11-IDEX-0007) operated by the French ANR.
Acknowledgements: We thank Sebastien Daligault and Claude Delpuech for technical assistance with the acquisition of electrophysiological data.
Correspondence should be addressed to Hesham A. ElShafei, Centre de Recherche en Neurosciences de Lyon, Institut National de la Santé et de la Recherche Médicale Unité 1028, Centre National de la Recherche Scientifique Unité Mixte de Recherche 5292, Université Claude Bernard Lyon 1, Dynamique Cérébrale et Cognition, Centre Hospitalier Le Vinatier, Bâtiment 452, 95 Boulevard Pinel, 69675 Bron Cedex, France, E-mail: hesham.elshafei@inserm.fr.
DOI:http://dx.doi.org/10.1523/ENEURO.0141-18.2018

Interestingly, distinct frequency peaks (sub-bands) in the α band manifest as a function of cortical location and task demand (Haegens et al., 2014). In a similar vein, Mazaheri et al. (2013) compared α activity while participants were cued to either a visual or an auditory target, and found a decrease in α power around 10 Hz in visual regions concomitant to an increase around 15 Hz, in the vicinity of the right auditory cortex. Taken together, these results highlight the importance of considering the frequency peak within the α band.

Contrary to the visual domain, only a handful of studies investigated the impact of anticipatory attention on α modulations in the auditory cortices. A recurrent magnetoencephalographic (MEG) finding is an increased α power, solely in the right auditory cortex, when attention was directed toward the ipsilateral right ear compared to when directed toward the contralateral ear (Müller and Weisz, 2012) or non-spatially oriented (Weisz et al., 2014). These results demonstrate how α oscillations could be involved in the suppressive mechanisms of auditory anticipatory attention (see also Frey et al., 2014; Weise et al., 2016), but do not shed much light on their implication in facilitatory mechanisms.

We aimed to examine the role of α oscillations in attentional facilitatory and suppressive mechanisms during auditory anticipation, within the auditory cortices and also between the visual and auditory regions. For this purpose, we recorded MEG activity during an auditory task in which spatial attention to auditory targets was manipulated by visual cues, either informative or not of the target side. By incorporating spatially uninformative cues, we aimed to delineate facilitating and suppressive mechanisms supporting auditory anticipatory attention (Bidet-Caulet et al., 2010).

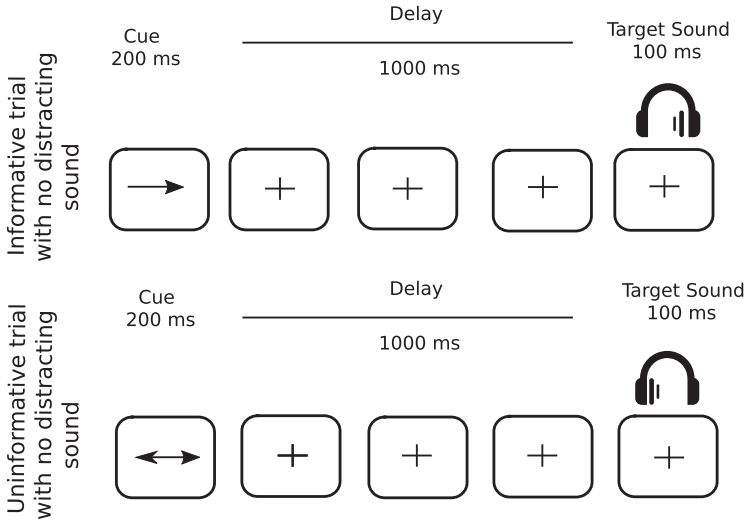
We hypothesized that during a spatial attention task, the balance between facilitatory and suppressive mechanisms of auditory anticipatory attention would be indexed by α activity following two main patterns. (1) A decrease in α power (reflecting inhibition release, i.e., facilitation) in task-relevant auditory areas would be concomitant to an increase in α power (reflecting inhibition/suppression) in task-irrelevant visual cortices. (2) Within the right auditory cortex, we expected a decrease in α power when attention is directed toward the contralateral ear and an increase in α power when attention is directed toward the ipsilateral ear, relative to when attention is not spatially oriented (uninformative cues). Also, if distinct suppressive and facilitating attentional mechanisms are activated during anticipation, they should be differentially correlated to behavioral performances. Finally, to gain further insight into the role of the peak-frequency in the α band (Haegens et al., 2014), we aimed to systematically investigate the effect of the frequency peak with the prediction that facilitatory and suppressive attentional mechanisms would be mediated in different α sub-bands.

Materials and Methods

Participants

Fourteen healthy participants (eight females) took part in this study. The mean age was 25 years $\pm$ 0.85 SEM. All

rich3/enu-enu/enu-enu/enu00418/enu2683d18z | xppws | S=4 | 7/24/18 | 22:21 | MS: | Ini:



AQ: 2 **Figure 1.** Protocol. Top row, In informative trials (67% of all trials), a one-sided visual cue (200-ms duration) indicated in which ear (left or right) the target sound will be played (100-ms duration) after a fixed 1000-ms delay. Bottom row, In uninformative trials (33% of all trials), a two-sided visual cue (200-ms duration) did not provide any indication in which ear (left or right) the target sound will be played. In 25% of all trials (not depicted in figure), a binaural distracting sound (300-ms duration), such as a phone ring, was played during the delay between cue and target.

participants were right handed, and reported normal hearing, and normal or corrected-to-normal vision. All participants were free from any neurologic or psychiatric disorders. The study was approved by the local ethical committee, and subjects gave written informed consent, according to the Declaration of Helsinki, and they were paid for their participation.

Stimuli and tasks

Competitive attention task (CAT)

In 75% of the trials, a target sound (100-ms duration) followed a central visual cue (200-ms duration) with a
F1 fixed delay of 1000 ms (Fig. 1). The cue was a green arrow, presented on a gray-background screen, pointing either to the left, right, or both sides. Target sounds were monaural pure tones (carrier frequency between 512 and 575 Hz; 5-ms rise time, 5-ms fall time). In the other 25%, the same structure was retained, however, a binaural distracting sound (300-ms duration) was played during the cue-target delay (50- to 650-ms range). However, for the purpose of this study, only distractor-free trials were analyzed. The cue and target categories were manipulated in the same proportion for trials with and without distracting sound. In 33.3% of the trials, the cue was pointing left and the target sound was played in the left ear, and in 33.3% of the trials, the cue was pointing right and the target sound was played in the right ear, leading to a total of 66.6% of informative trials. In the last 33.3% of the trials, the cue was uninformative, pointing in both directions, and the target sound was played in the left (16.7%) or right (16.7%) ear.

Participants were instructed to categorize two target sounds as either high- or low-pitched sound, by either pulling or pushing a joystick. The mapping between the targets (low or high) and the responses (pull or push) was counterbalanced across participants, but did not change across the blocks, for each participant. to account for the participants' pitch-discrimination capacities, the pitch difference between the two target sounds was defined in a discrimination task (see below). Participants were informed that informative cues were 100% predictive and that a distracting sound could be sometimes played. They were asked to allocate their attention to the cued side in the case of informative cue, to ignore the distractors and to respond as quickly and correctly as possible. Participants had a 3.4-s (3400-ms) response window. In the absence of the visual cue, a blue fixation cross was presented at the center of the screen. Subjects were instructed to keep their eyes fixated on the cross and to minimize eye movements and blinks while performing the task.

Discrimination task

Participants were randomly presented with one of two target sounds: a low-pitched sound (512 Hz) and a high-pitched sound (575 Hz; two semitones higher), equiprobably in each ear (four trials per ear and per pitch). As described above, participants were asked to categorize the target sounds as either high- or low-pitched sound within 3 s.

Procedure

Participants were seated in a sound-attenuated, magnetically shielded recording room, at a 50-cm distance from the screen. The response device was an index-operated joystick that participants moved either toward them (when instructed to pull) or away from them (when instructed to push). All stimuli were delivered using Presentation software (Neurobehavioral Systems, RRID: SCR_002521). All sounds were presented through air-conducting tubes using Etymotic ER-3A foam earplugs (Etymotic Research, Inc.).

First, the auditory threshold was determined for the two target sounds differing by two semitones (512 and 575 Hz), in each ear, for each participant using the Bekesy

tracking method (Von Békésy and Wever, 1960). The target sounds were then presented at 15-dB sensation level while the distracting sounds were played at 35-dB sensation level. Second, participants performed the discrimination task. If participants failed to respond correctly to >85% of the trials, the pitch of the high target sound was augmented, by half a semitone with a maximum difference of three semitones between the two targets (auditory thresholds were then measured with the new targets). Afterward, participants were trained with a short sequence of the CAT. Finally, MEG and EEG were recorded while subjects performed 15 blocks (72 trials each). Each trial lasted from 4.6–4.8 s, leading to a block duration of ~5 min and a MEG/EEG session of ~1 h 35 min (breaks included). After the MEG/EEG session, participants' subjective reports regarding their strategies were collected.

Behavioral data analysis

For behavioral data analysis, a response was considered correct, if it matched the response mapped to the target sound and was executed before the apparition of the following cue. The influence of the factor cue (three levels: left, right and uninformative) on the percentage of correct responses was tested using a linear mixed-effects models [lme4 package (Bates et al., 2014) for R Team, 2014; RRID:SCR_015654].

For *post hoc* analysis, we used the Lsmean package (Lsmean version 2.20-23; Searle et al., 1980) where p values were considered as significant at $p < 0.05$ and adjusted for the number of comparisons performed (Tukey method). Incorrect trials were excluded from further analysis, leaving on average (216 ± 6.92 SEM) trials per cue condition per participant. The influence of the cue on the median of reaction times (RTs) of the correct trials were tested using the same tests.

Magnetoencephalography

Recordings

Simultaneous EEG and MEG data were recorded, although the EEG data will not be presented here. The MEG data were acquired with a 275-sensor axial gradiometer system (CTF Systems Inc.) with continuous sampling at a rate of 600 Hz, a 0- to 150-Hz filter bandwidth, and first-order spatial gradient noise cancellation. Moreover, eye-related movements were measured using vertical and horizontal EOG electrodes.

Head position relative to the gradiometer array was acquired continuously using coils positioned at three fiducial points; nasion, left and right pre-auricular points. Head position was checked at the beginning of each block to control head movements.

In addition to the MEG/EEG recordings, T1-weighted three-dimensional anatomic images were acquired for each participant using a 3T Siemens Magnetom whole-body scanner. These images were used for reconstruction of individual head shapes to create forward models for the source reconstruction procedures. The processing of these images was conducted using CTF's software (CTF Systems Inc.).

Outline of the electrophysiological data analyses

The analyses reported here focused on modulations of oscillatory activity in the α band during top-down anticipatory attention, i.e., during the cue-target delay in trials with no distractor and a correct response. MEG data were pre-processed in the sensor space using the software package for electrophysiological analysis (ELAN Pack; Aguera et al., 2011). Further analyses were performed using Fieldtrip (www.fieldtriptoolbox.org; Oostenveld et al., 2011, RRID:SCR_004849), an open source toolbox for MATLAB (RRID:SCR_001622), custom-written functions and R (www.r-project.org; RRID:SCR_001905).

First, significant modulations of oscillatory activity in the α band after cue onset (cue-related activity) were assessed by contrasting post-cue activity against pre-cue activity in the sensor level time-frequency domain (see below, Sensor-level analysis).

Second, based on the sensor level results, two post-cue and one pre-cue time windows in two distinct frequency bands were chosen for source analyses (see below, Source-level analysis). Based on the results of post-/pre-cue contrast in the source domain, auditory and visual regions of interest (ROIs) were selected for further virtual electrode analysis, i.e., time-resolved estimation of source activity (see below, Defining ROIs and virtual electrodes). From these activities, we then specified the time courses, power spectrum, and the α peak frequency for each virtual electrode (see below, Reconstruction of source activity) and assessed the attentional modulations of the cue-related α activity (see below, Attentional modulation of α activity).

Third, correlation between RTs and cue-target activity was investigated in the sensor (see below, Correlation between α activity and behavioral data: sensor level) and source (see below, Correlation between α activity and behavioral data: source level) domains.

Data pre-processing

Head movements

As participants had an EEG cap on, head movements were relatively more difficult to control, in comparison to standard MEG procedures, where the participant's head is relatively stabilized to the MEG dewar via an inflatable cushion. Thus, in reference to the first block, head positions in the following blocks exceeded the pre-determined threshold of ±1 cm. This would have compelled us to exclude a huge portion of the trials if all 15 blocks were concatenated together. Therefore, for each subject, data were organized in three groups of five blocks so that, within each group, differences in head positions, recorded at the beginning of each block, did not exceed a threshold of ±1 cm.

It is noteworthy that for data pre-processing and sensor level analysis (described below) trials from the three groups were concatenated. However, for source level and virtual electrode analyses (described below), each group was processed separately, and outputs were eventually averaged.

Pre-processing

Only correct trials were considered for electrophysiological analyses. Data segments contaminated with mus-

cular activity or sensor jumps were excluded semi-manually using a threshold of 2200 and 10,000 femtoTesla, respectively. Independent component analysis was applied on the bandpass filtered (0.1–40 Hz) data to remove eye-related (blink and saccades) and heart-related (ECG) artefacts. Subsequently, components (four on average) were removed from the non-filtered data via the inverse ICA transformation. Data were further notch filtered at 50, 100, and 150 Hz and high-pass filtered at 0.1 Hz.

Cue- and target-related activity

Sensor-level analysis

To investigate the dynamics of α power modulations after the visual cue, the oscillatory power of trials from the three cue conditions all together was calculated using Morlet Wavelet decomposition with a width of four cycles per wavelet (m = 7; Tallon-baudry and Bertrand, 1999) at center frequencies between 5 and 18 Hz, in steps of 1 Hz and 50 ms. Activity of interest (defined between 0 and 2 s post-cue and 7–15 Hz) was contrasted against mean baseline activity (−0.6 to −0.2 s pre-cue) using a non-parametric cluster-based permutation analysis (Maris and Oostenveld, 2007). In brief, this test first calculates paired *t* tests for each sensor at each time-frequency point, which are then thresholded at $p < 0.05$. The sum within each cluster (Tsum) is retained, and the procedure is repeated 1000 times on shuffled data in which the condition assignment within each individual swapped randomly. On each permutation, the maximum Tsum (Tmax) is retained yielding a distribution of 1000 Tmax values. From this distribution, the cluster probability of each empirically observed Tsum can be derived. Clusters are labeled as significant with $p \leq 0.05$. Please note, that for this test, cluster permutations control for multiple comparisons in time, frequency and sensor space dimensions.

Source-level analysis

To elucidate the possible brain regions underlying the sensor-level α modulations, we have defined two post-cue (0.2–0.6, 0.6–1.0) and one pre-cue (−0.6 to −0.2) time-windows in two different frequency bands (9 and 13 ± 2 Hz). These time-frequency windows have been chosen based on the results from the statistical contrast in the sensor level.

To estimate the brain regions driving activity in these time-frequency windows, we have used the frequency–domain adaptive spatial technique of dynamical imaging of coherent sources (DICS; Gross et al., 2001). Data, from all conditions, within each group of blocks were concatenated, and cross-spectral density (CSD) matrix (−0.7 to 2 s, relative to cue onset) were calculated using the multitaper method with a target frequency of 11 (±4) Hz.

For each participant, an anatomically realistic single-shell headmodel based on the cortical surface was generated from individual head shapes (Nolte, 2003). A grid with 0.5-cm resolution was normalized on a MNI template, and then morphed into the brain volume of each participant. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was used to estimate the spatial distribution of power for all time-frequency windows of interest per group of blocks. For each participant, these power distributions were averaged across the three groups of blocks. Afterward, Each post-cue window was contrasted against a corresponding baseline pre-cue window using a nonparametric cluster-based permutation analysis (Maris and Oostenveld, 2007). For this test, cluster permutations control for multiple comparisons in the source space dimension.

Defining ROIs and virtual electrodes

The aforementioned source-level analysis provides a snapshot picture of underlying cortical activity. To go a step further, we defined virtual electrodes within ROIs, for the purpose of resolving the time course of activity at the source level. The source space was subdivided into 116 anatomically defined ROIs according to the macroscopic anatomic parcellation of the MNI template using the automated anatomic labeling (AAL) map (Tzourio-Mazoyer et al., 2002). We limited our analysis to four auditory regions; left and right Heschl gyri (HG) and superior temporal gyri (STG) and two occipital regions (left and right middle/superior gyri). For each auditory region; virtual electrodes were defined as the average of five neighboring voxels exhibiting the strongest α power modulations, i.e., highest *t* values in the source-level baseline contrast in the 0.6 to 1s (relative to cue onset) and 7- to 11-Hz time-frequency window. Same procedure was used for the occipital regions; however, voxels were chosen based on the highest *t* values in the source-level baseline contrast in the 0.6- to 1-s (relative to cue onset) and 11- to 15-Hz time-frequency window.

Reconstruction of source activity

To get a time-resolved estimation of source activity, we computed the time-frequency signal at the virtual electrode (defined above) level using the LCMV beamformer. Spatial filters were constructed from the covariance matrix of the averaged single trials at sensor level (−0.7 to 2 s, relative to cue onset, 1–20 Hz, λ 15%) and the respective leadfield by a linearly constrained minimum variance (LCMV) beamformer (Van Veen et al., 1997). Afterward, spatial filters were multiplied by the sensor level data to obtain the time course activity at each voxel of interest. Activity was averaged across the five voxels defined for each ROI (see section above) and for each hemisphere. Moreover, activity was averaged across the two auditory ROIs (HG and STG). Thus, limiting our analysis to four ROIs (one auditory and one occipital in each hemisphere).

For each ROI, we subtracted the evoked potential (i.e., the signal averaged across all trials) from each trial. Subsequently, time-frequency power was calculated in the same manner as in the sensor level analysis using Morlet Wavelet decomposition.

To visualize the different profiles observed on both sensor and source levels, α power (computed using Morlet Wavelets) was averaged between 7 and 11 Hz, and between 11 and 15 Hz, for auditory and visual regions, separately, to extract the time course of α activity in these two α sub-bands.

In addition, α power (computed using Morlet Wavelets) was averaged between 0.6 and 1s for each ROI, to extract the power spectrum in each subject. Afterward, individual α peak frequency (iAPF) was defined separately for auditory and visual regions, in each subject. For auditory virtual electrodes, the peak was defined as the frequency with the maximum α power decrease relative to the baseline (-0.6 to -0.2 s pre-cue onset) between 5 and 15 Hz. For visual virtual electrodes, the peak was defined as the frequency with the maximum α power increase relative to the baseline. The median APFs across subjects and hemispheres were 9 and 13 Hz in the auditory and visual virtual electrodes, respectively.

Attentional modulation of α activity

A linear mixed-effects model (lme) was fit to predict modulation of α activity uniquely in auditory virtual electrodes between 600 and 1000 ms (relative to cue onset) with the following factors as fixed effect: (1) cue laterality according to the auditory cortices (three levels: ipsilateral, contralateral, and uninformative); (2) hemisphere (two levels: left and right); and (3) frequency (two levels: 9 and 13 Hz). A random effect was included for each participant and thus allowing us to model variability between participants. The chosen frequencies were the median APFs calculated in the previous analysis (see above, Reconstruction of source activity). Similar to the previous step, for *post hoc* analysis, we used the Lsmean package.

Correlation between α activity and behavioral data: sensor level

As a final step, and to assess the relationship between the cue-related changes in α power, in the sensor space, and RTs, correlation topographies were created (Mazaheri et al., 2013). First, we performed a trial-by-trial correlation, using non-parametric Spearman tests, in each participant, between RTs and post-cue α power at each time frequency point (between 6 and 16 Hz, by steps of 1 Hz, and between 0 and 1200 ms post-cue onset, by steps of 50 ms) for each sensor, to create topographies of the correlation (Mazaheri et al., 2013). The correlation coefficients were subsequently converted to *z* values using Fisher's r- to z-transformation to obtain a normally distributed variable. The statistical significance of the correlations was assessed at the group level with a one-sample *t* test of the correlation *z* values at each sensor and each time-frequency point, and then subjected to a cluster-level randomization test to correct for multiple comparisons in the sensor space, time, and frequency dimensions.

Correlation between α activity and behavioral data: source level

To assess the relationship between cue related changes in α power and RTs in source-space, single trial α activity was reconstructed at each grid point using a partial cannonical correlation (PCC) beamformer, a more computationally efficient alternative to the DICS beamformer. Afterward, we performed a trial-by-trial correlation, using non-parametric Spearman tests, in each participant, between RTs and post-cue α power (between 10 and 16 Hz, and between 900 and 1200 ms, according to the sensor level results) at each grid point (Mazaheri et al., 2013). The correlation coefficients were subsequently converted to *z* values using Fisher's r- to z-transformation to obtain a normally distributed variable. The statistical significance of the correlations was assessed at the group level with a one-sample *t* test of the correlation *z* values at each grid point and then subjected to a cluster-level randomization test to correct for multiple comparisons in the source space dimension.

Power analysis

To demonstrate the statistical robustness of our tests (see above, Behavioral data analysis and Attentional modulation of α activity), we have applied sensitivity power analyses using the G*Power software (Faul et al., 2007, 2009), using a power of 0.8, an α error of 0.05, and correlation of 0.5 among repeated-measures; for all the analysis based on linear mixed-effects models (as an approximation), we ran the sensitivity power analysis for a repeated-measures ANOVA. Results are detailed in relevant sections.

Results

Behavioral analysis

The percentage of correct responses (on average: 96.05 $\pm$ 0.73 SEM) was not significantly modulated by the cue category. For the median RTs, as shown in Figure 2, F2
we found a significant main cue effect ($F_{(2,26)} = 31.5$, $p < 0.01$, $\eta^2 = 0.7$). The reported effect size (f; Cohen, 1988) AQ: 3
of this test is 1.52 superior to the required effect size of 0.35 as calculated by the G*Power software.

Post hoc tests indicated that participants were faster when the cue was informative (either right or left) in comparison to the uninformative cue ($p < 0.01$). No significant differences were found between the left and right cue conditions.

Cue- and target-related α activity: sensor level analysis

On contrasting post-cue activity to baseline activity, two profiles centered on two distinct frequencies (9 and 13 Hz; low and high α) were distinguished. In the low α frequencies, a widespread decrease lasted between cue onset and 600 ms (post-cue-onset; early period). Later on, this activity was spatially focused to left temporo-parietal sensors just before the target onset (late period). Simultaneously, in the high α frequencies, the early period displayed an occipitally focalized decrease followed by an increase that spreads to right temporal sensors in the late period (Fig. 3). F3

Cue- and target-related α activity: source level analysis

Sources of these activities were estimated and contrasted to the baseline window. In the early period (200–600 ms), a general decrease of the low-α can be observed in several occipital, temporal and central brain regions, bilaterally (Table 1). However, in the same time period, at T1
higher α frequency, this decrease was restricted to regions dedicated to visual processing in the occipital and temporal lobes (Table 1). In the late period, the low-α

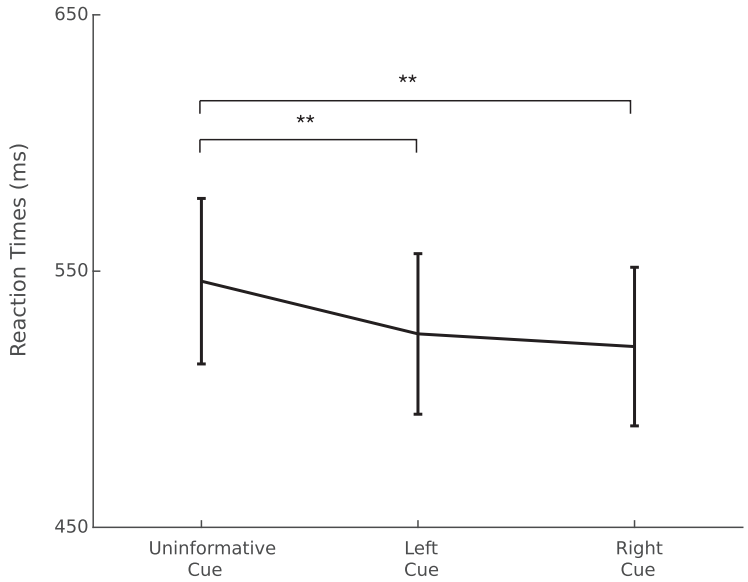


Figure 2. Mean of median RT (ms) per condition; $**p < 0.01$. Error bars represent SEM.

decrease became more restricted to the auditory regions in the temporal cortices, e.g., bilateral HG and STG, and to motor areas (Table 1). However, at higher frequencies, an α increase was maximal in occipital, parietal and temporal regions dedicated to visual processing, and in parietal regions (Table 1).

ROI analysis: α time course and peak frequency

At the virtual electrode level, we were able to confirm that the time-frequency profiles of both auditory and visual ROIs are consistent with the profiles that have been demonstrated at the sensor level (Fig. 4*A*). We could also confirm, at the virtual electrode level, the frequency differences that have been observed at the sensor level. Indeed, the median α frequency peak across subject was 9 Hz in auditory cortices and 13 Hz in visual cortices (Fig. 4*B*). Moreover, as can be observed in Figure 4*C*, these α peak frequencies were well circumscribed within the 7- to 15-Hz α band.

ROI analysis: attentional modulations of α activity

In order investigate the modulation of α activity in auditory virtual electrodes, a lme model was used with three factors: (1) cue laterality according to the auditory cortices (three levels: ipsilateral, contralateral and uninformative); (2) hemisphere (two levels: left and right); and (3) frequency (two levels: 9 and 13 Hz).

The lme model yielded several significant main effects and interactions (listed in Table 2 with interaction of interest in bold font). The highest-order significant interaction of interest is the three-level interaction between cue laterality, hemisphere, and frequency ($F_{(2,26)} = 3.07$, $p = 0.04$, $\eta^2 = 0.17$). The reported effect size (f) of this test is 0.65 superior to the required effect size of 0.28 as calculated by the G*Power software.

To elucidate this interaction, we performed *post hoc* lme models testing the influence of the cue laterality (three levels: ipsilateral, contralateral, and uninformative) and hemisphere (two levels: left and right), for each frequency (9 and 13 Hz), since we aimed to shed more light onto the role of peak frequencies on α modulations (Fig. 5)

At 9 Hz (low α), only the two-level interaction between cue laterality and hemisphere ($F_{(2,26)} = 5.2$, $p = 0.005$, $\eta^2 = 0.17$) reached significance. The reported effect size (f) of this test is 0.45 while the required effect size as calculated by the G*Power software was 0.23; 2 by 2 *post hoc* testing revealed that in the right hemisphere (auditory cortex), α power was significantly lower in the contralateral cue condition, in comparison to the ipsilateral and uninformative cue condition ($p = 0.004$ and $p = 0.01$, respectively). No significant effects were found in the left hemisphere (Fig. 5). In summary, a facilitatory effect on the low α power was found in the right auditory cortex for the contralateral cue.

At 13 Hz (high α), only the two-level interaction between cue laterality and hemisphere ($F_{(2,26)} = 4.95$, $p = 0.007$, $\eta^2 = 0.1$) reached significance. The reported effect size (f) of this test is 0.33 while the required effect size as calculated by the G*Power software was 0.28; 2 by 2 *post hoc* testing revealed that in the right hemisphere (auditory cortex), α power was significantly higher in the ipsilateral cue condition, in comparison to the uninformative cue condition ($p = 0.007$), but not to the contralateral cue condition ($p = 0.16$). No significant effects were found in the left hemisphere (Fig. 5).

In summary, a suppressive effect on the high α power was found in the right auditory cortex for the ipsilateral cue.

Correlation between α activity and behavioral data

At the sensor level, pre-target activity between 0.9 and 1.2 s (relative to cue onset) in the 10- to 15-Hz frequency band at a cluster centered around right occipital and parietal sensors was found to negatively correlate with RTs ($p = 0.001$). In other words, the higher individual α power in that cluster, the faster the participant. At the

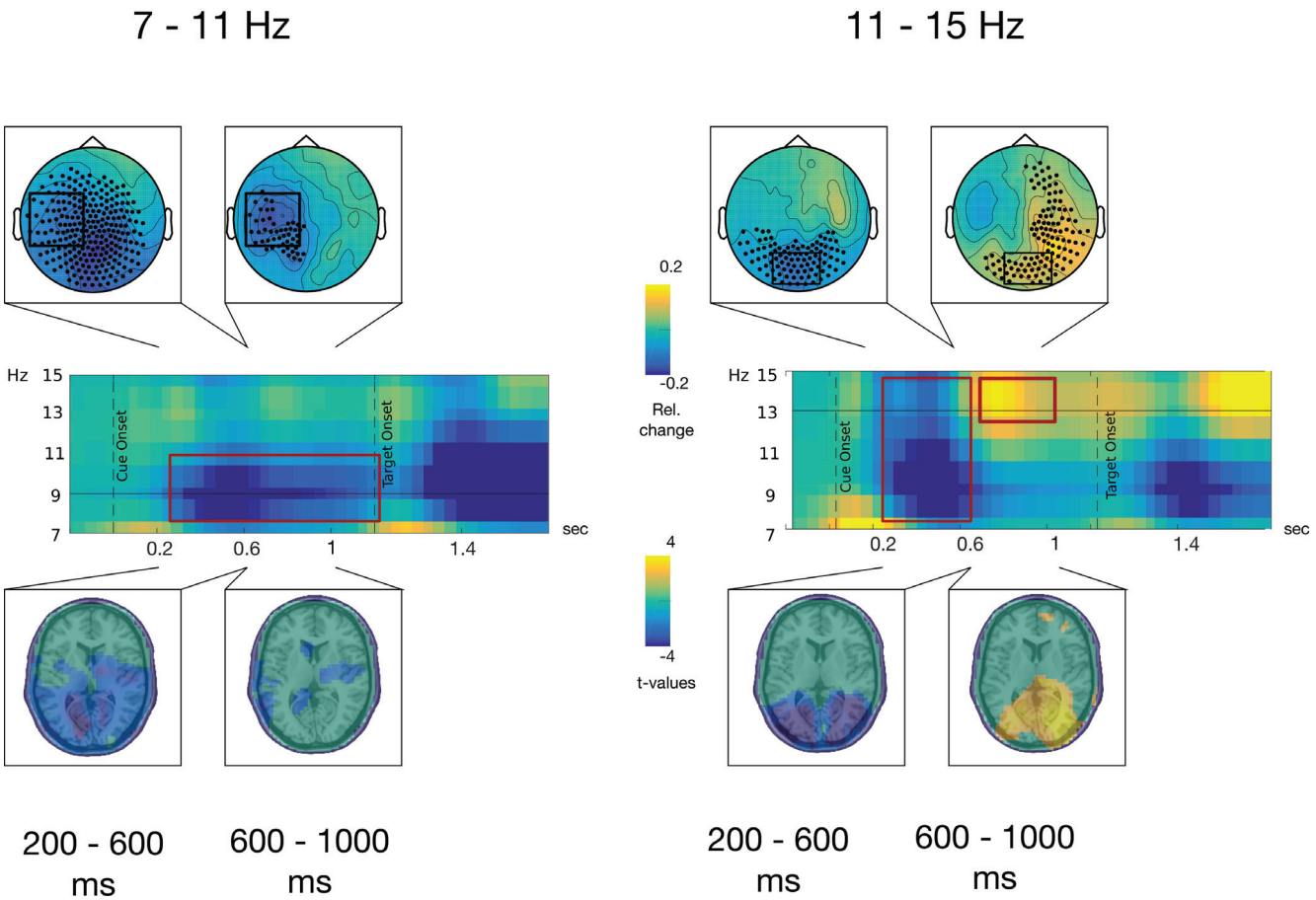


Figure 3. Comparison between low (7–11 Hz; left panel) and high (11–15 Hz; right panel) α activity. First row, Topographical maps of baseline corrected (−600 to −200 ms pre-cue onset) α power averaged in the respective frequency bands during two latency windows: (1) 200–600 ms and (2) 600–1000 ms, relative to cue onset. Sensors highlighted with black dots present α activities statistically significant from the baseline using cluster-based permutation tests and sensors highlighted by black boxes were used to represent the time-frequency activity in the second row. Second row, Time-frequency representations of α power baseline corrected (−600 to −200 ms pre-cue onset) averaged across sensors highlighted by the black boxes over the topographical maps on the first row. Third row, Distributions of t values, masked at $p < 0.05$, from cluster-based permutation tests contrasting time-frequency windows of interest against baseline activity at the source level.

source level, α activity between 0.9 and 1.2 s (relative to cue onset) and 10–16 Hz, mainly in the left and right superior occipital gyri, the left middle occipital gyrus, the right calcarine, and the right postcentral gyrus, was found to negatively correlate with RTs ($p = 0.01$; Fig. 6).

Discussion

In this study, we have demonstrated that (1) anticipating a visually-cued auditory target differentially modulates α power in the auditory and visual cortices; (2) these modulations occur within different α sub-bands; (3) modulations in the right auditory cortex (facilitation and suppression) also occur within different α sub-bands; and (4) RTs to the auditory target correlate with the α power increase in the visual cortices.

Behavioral measure of top-down anticipatory attention

Participants identified the target pitch faster in trials with an informative cue, in agreement with several previous studies (Golob et al., 2002; Bidet-Caulet et al., 2015). This effect is more likely to be related to differences in anticipatory attention since the informative cue provided additional information solely about the location of the target and not about its category neither its mapped response, thus motor preparation was equivalent across all conditions.

Distinct profiles of α activity in visual and auditory regions

In line with our hypothesis, anticipating an auditory target modulated α power differently in the auditory and visual cortices, following different patterns. In the auditory cortex, after the visual cue onset, low-frequency α (~9 Hz) power continuously decreased until target onset. Simultaneously, in the visual cortices, a transient decrease in low and high-frequency (~13 Hz) α power between 200 and 600 ms post-cue onset was followed by a power increase, uniquely in high α, before target onset.

According to recent hypotheses, α oscillations reflect regulation of cortical excitability (Klimesch et al., 2007; Jensen and Mazaheri, 2010; Foxe and Snyder, 2011). This

Table 1. Brain regions displaying significant α activity modulations in the low (7–11 Hz) or high (11–15 Hz) α frequency bands in two time windows on baseline contrast in the source level

7–11 Hz	Early time window (200–600 ms) Left and right ↓: Heschl gyrus Inferior, middle, and STG calcarine Cuneus Inferior, middle, and superior occipital gyri Inferior parietal gyrus Postcentral gyrus Precentral gyrus Precuneus Supp. motor area	Late time window (600–1000 ms) Left and right ↓: Heschl gyrus Inferior, middle, and STG Inferior parietal gyrus Postcentral gyrus Precentral gyrus Supp. motor area
11–15 Hz	Early time window (200–600 ms) Left and right ↓: Calcarine Cuneus Inferior and middle occipital gyri Inferior and middle temporal gyri	Late time window (600–1000 ms) Left and right ↑: Calcarine Cuneus Precuneus Inferior and middle occipital gyri Inferior and middle temporal gyri Inferior and superior parietal gyri

Up-arrows indicate α synchronization (relative increase in power) while down-arrows indicate α desynchronization (relative decrease in power).

gauge would be supported by α power increases in task-irrelevant regions and by α power decreases in task relevant regions. In line with previous findings in the visual (Sauseng et al., 2005; Thut, 2006), somatosensory (Haegens et al., 2012), auditory (Müller and Weisz, 2012; Weisz et al., 2014), and audiovisual (Mazaheri et al., 2013; Frey et al., 2014; Van Diepen and Mazaheri, 2017) domains, we have found that anticipating an auditory target resulted in (1) a decrease in α power, possibly leading to increased excitability, in task-relevant auditory cortical regions, simultaneous to (2) an increase in α power, probably reducing excitability, in task-irrelevant visual regions.

Top-down modulation of α activity in the auditory cortex

A scant literature (Gomez-Ramirez et al., 2011; Weisz et al., 2011, 2014; Müller and Weisz, 2012; Frey et al., 2014; Weise et al., 2016), mostly using MEG, exists on α generators in the auditory cortices, probably due to the limitations of EEG technique to capture their activity (Frey et al., 2014). In the present study, using MEG, we could show not only that α activity, in the auditory cortices, is modulated according to the visual cue information, but also that these modulations occur within different α sub-bands.

In the auditory cortices, to optimize the processing of an upcoming monaural sound, two phenomena might be expected: (1) an inhibition (increase in α activity) in the auditory cortex ipsilateral to the attended side, and (2) a pre-activation (or released inhibition, i.e., decrease in α power) in the contralateral auditory cortex. The question is: which of these two modulations (down- or upregulation) would drive anticipatory attention? By incorporating an uninformative cue condition, we could delineate these facilitatory and suppressive mechanisms.

We observed α power modulations according to the visual cue information, in the right auditory cortex, only. At lower α frequencies (~9 Hz), we found a decrease in α power (relative to the baseline), in the three cue conditions (contralateral, ipsilateral and uninformative). Importantly, this decrease was most prominent when a contralateral sound was expected rather than an ipsilateral or a spatially non-cued sound. On the other hand, at higher α frequencies (~13 Hz), an increase in α power (relative to the baseline) was observed in all conditions. Interestingly, this increase was more prominent when an ipsilateral, rather than a spatially non-cued target was expected.

The present results corroborate previous findings (Müller and Weisz, 2012; Weisz et al., 2014) showing that the right auditory cortex plays a special role in auditory spatial attention. We extend these findings by demonstrating that the excitability of the right auditory cortex can be both (1) downregulated for processing an ipsilateral right-ear sound and (2) upregulated for processing a contralateral left-ear sound. Importantly, to our knowledge, the present study is the first one to demonstrate that these modulations occur at different α frequencies, suggesting that the dynamic equilibrium between suppressive and facilitatory mechanisms of auditory anticipatory attention would be supported by different high and low α sub-bands, respectively.

Finally, α activity in the left auditory cortex was not modulated by top-down attention. This asymmetry could be interpreted in the light of the right hemispheric specialization in pitch processing (Milner, 1962; Zatorre and Belin, 2001; Zatorre et al., 2002; Lattner et al., 2005; Hyde et al., 2008). Since participants performed a pitch categorization task, the right auditory cortex would be more relevant for target sound processing and thus more influenced by top-down attention. The asymmetry of α activity modulations could also be interpreted in the light of the right hemispheric dominance in spatial attention that has been illustrated for the auditory (Zatorre and Penhune, 2001; Spierer et al., 2009) and visual (Nobre et al., 1997; Corbetta and Shulman, 2002) modalities. This dominance would reflect a functional asymmetry in auditory processing, wherein the left auditory cortex preferentially processes sounds within the contralateral egocentric space, whereas the right auditory cortex processes the entire acoustic space (Spierer et al., 2011).

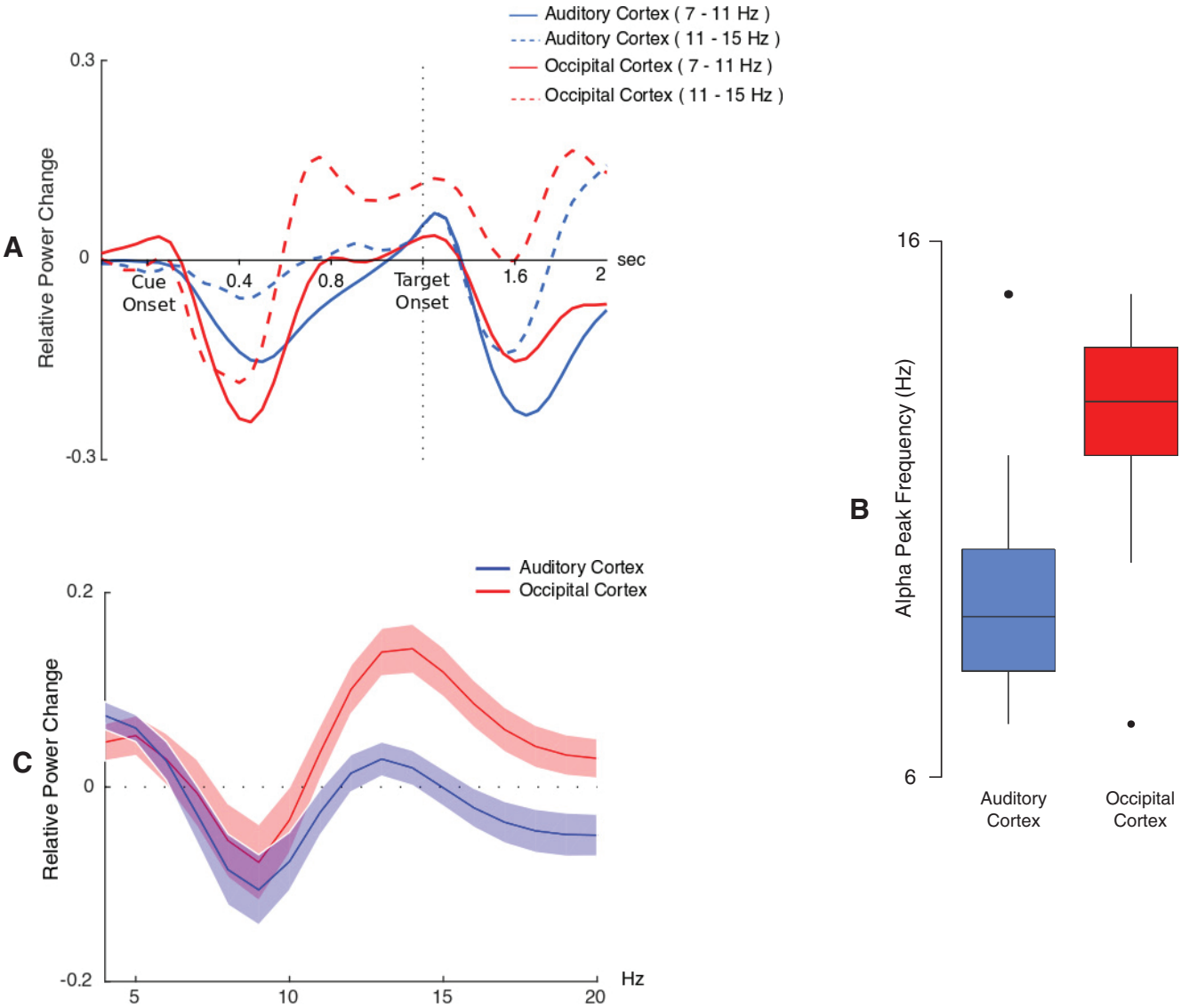


Figure 4. Source level activity. ***A***, Time course of α (relative to baseline) between 7–11 and 11–15 Hz, for occipital and auditory virtual electrodes averaged across both hemispheres. Note that subtracting the evoked response from single trials before time-frequency transformation only partially removed the evoked response to the target in the α bands. ***B***, Boxplot of Individual α peak frequency in visual and auditory regions. ***C***, Relative power spectrum averaged between 600 and 1000 ms post-cue in visual and auditory regions.

Correlation between α activity and behavioral performances

We found that the higher α power in the occipital cortices, the faster participants correctly discriminated the upcoming target sound. In other words, the stronger inhibition of task-irrelevant regions, the faster the subjects. This result is in line with previous findings that behavioral performances correlate with the increase in α power (Haegens et al., 2012) and reinforces the hypothesis that α oscillations exert an inhibitory role (Jensen and Mazaheri, 2010; Klimesch, 2012). Importantly, this correlation between an increase in α power in irrelevant brain regions and behavior was only found significant in the higher α frequencies (10–15 Hz), bringing further evidence for a specificity of the high α sub-band in suppressive attentional mechanisms.

Contradictory to the present findings, a positive correlation between α power in the auditory cortices and RTs in a sound discrimination task was found in a previous study (Mazaheri et al., 2013). However, differences between the

Table 2. Significant results of the LME model testing the modulation of α activity by cue laterality, hemisphere, and frequency

Factor	*p* value	*f* statistic
Hemisphere	0.02	5.3
Frequency	<0.001	141
Cue laterality by hemisphere	0.01	4.0
Cue laterality by hemisphere by frequency	**0.04**	**3.1**

The interaction of interest is highlighted in bold.

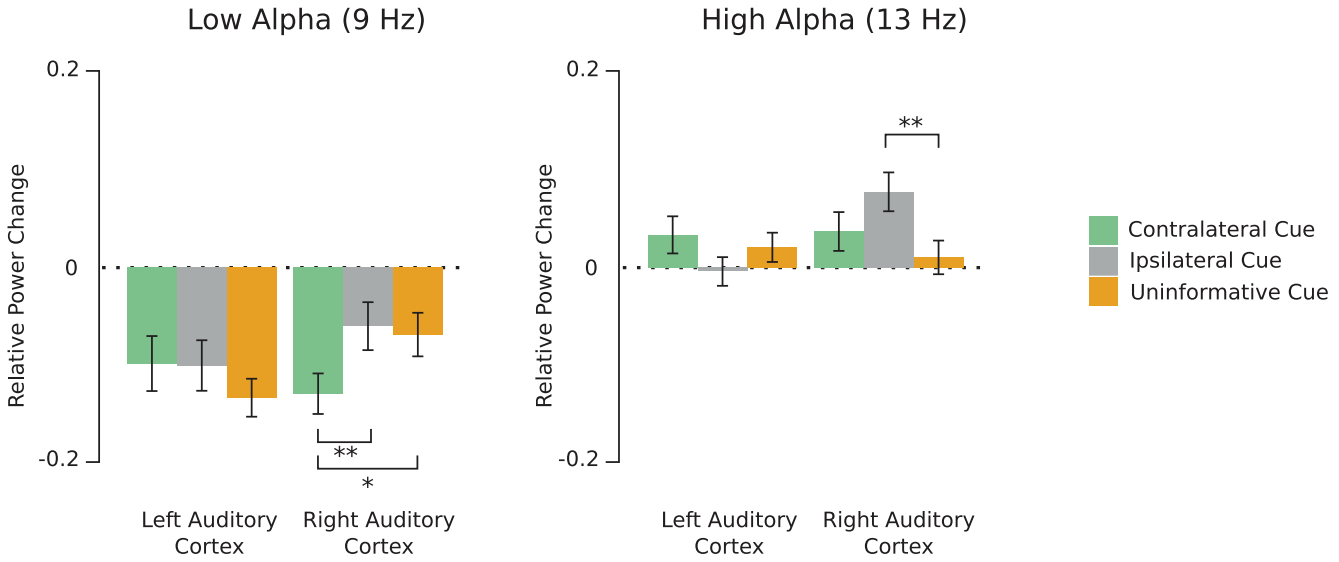


Figure 5. α Power (relative to baseline) averaged between 600 and 1000 ms (post-cue onset) at 9 Hz (left panel) and 13 Hz (right panel) for the three cue conditions; $*p < 0.05$, $**p < 0.01$. Error bars represent SEM.

two studies might explain this discrepancy. First, in their study, spatial attention was not modulated, i.e., the auditory target was always binaural. Second, participants discriminated three auditory target frequencies that were further apart in pitch and much easier to discriminate in comparison to our paradigm (250, 1000, and 4000 Hz vs 512 and 575 Hz). We posit that in the case of an easy task the excitability of relevant areas can be up and down regulated and correlate with task performance; whereas in the case of a difficult task, the excitability of relevant areas would be maximal and only the inhibition of signal dispersion to irrelevant areas could fluctuate and correlate with performance.

The role of different α frequency sub-bands

The present study highlights specificities of low and high α sub-bands: (1) the peak frequency of the α increase in visual regions was found to be higher (~13 Hz) in comparison to that of the α decrease in auditory regions (~9 Hz); (2) the α increase in visual regions was found to be significantly correlated to behavior in the high α frequencies, only; (3) in the right auditory cortex, a larger decrease in α power during contralateral sound expectation was found in the low α, whereas a stronger increase in α power during ipsilateral sound anticipation was found in the high α. The existence of different sub-bands of the α rhythm is not a new concept (Klimesch et al., 1993, 1999; Sauseng et al., 2005; Groppe et al., 2013), but their functional role is still unclear. Recently, α generators have been observed in each of the cortical laminae (Haegens et al., 2015) in primary sensory cortices. Interestingly, the α activity seems to peak at different frequencies according to the layers, providing neuronal underpinnings to different α sub-bands. In the present study, the differences observed across frequencies can be interpreted differently by considering the α peak frequency as a "trait" or "state" variable (Haegens et al., 2014), providing information into their functional role, as discussed in the following.

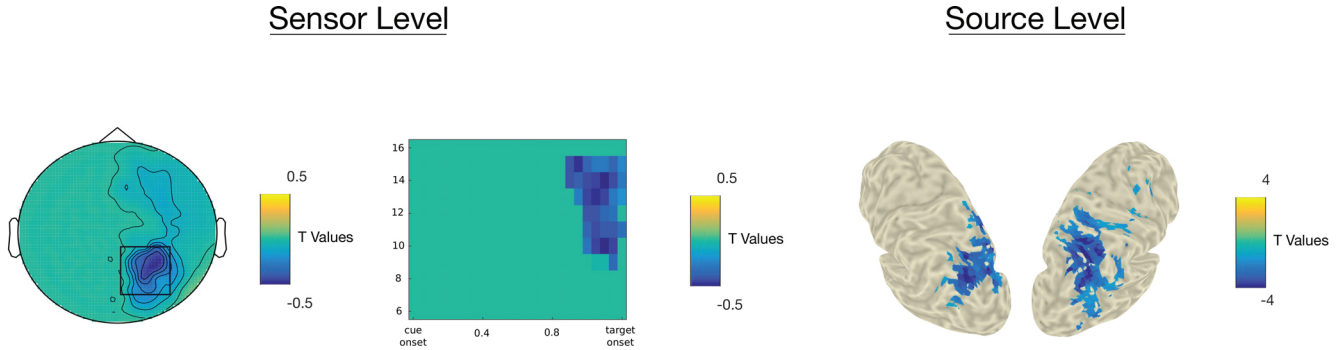


Figure 6. ***A***, Topography of *t* values, masked at $p < 0.05$, from cluster-based permutation testing of the significance of the correlation between α activity (900–1200 ms, 10–15 Hz) and RT at the sensor level. ***B***, Time-frequency distribution of *t* values, masked at $p < 0.05$, averaged across sensors highlighted by the black box on the topography in ***A***. ***C***, *t* values source distributions, masked at $p < 0.05$, from cluster-based permutation testing of the significance of the correlation between α activity (900–1200 ms, 10–16 Hz) and RT. Please note, that negative *t* values signify negative correlation between RTs and α activity.

The present results of different dominant frequencies in the visual and auditory regions are in line with evidence from previous studies demonstrating that α peak frequency varies as a function of cortical location (Kawasaki et al., 2010; Haegens et al., 2014). α Peak frequency could be considered as a trait or a "characteristic" variable that changes across individuals (Klimesch, 1999; Başar, 2012) and cortical regions, as found during resting state, in parietal and occipital regions (Haegens et al., 2014). In this light, the differences in α peak frequency reported here might be related to anatomic and physiologic disparities between the visual and auditory cortices. However, one should note that no difference in α peak frequencies was found between the macaque auditory, visual and somatosensory primary areas (Haegens et al., 2015).

Nonetheless, the present findings also show an increase in high α power, when attending an ipsilateral sound, in the right auditory cortex. This is in agreement with the results of Mazaheri et al. (2013) pointing to an α activity increase in the vicinity of the auditory cortices to be centered around higher α frequencies. Therefore, α peak frequency could also be considered as a state variable that would index performance fluctuations, cognitive demands and probably the functional task-relevance of a certain cortical region (Klimesch, 1999; Başar, 2012; Haegens et al., 2014). The present results show that suppressive attentional mechanism in the visual non-relevant regions are indexed by an increase in high α power which is correlated to behavior. Moreover, within the right auditory cortex, suppression (downregulation) of brain activity when attending an ipsilateral sound is reflected in the high α sub-band; whereas brain processing facilitation of the contralateral expected sound is indexed in the low α sub-band. Taken together, the present results highly suggest that different high and low α sub-bands would support suppressive and facilitatory mechanisms of anticipatory attention, respectively.

Conclusion

The current study replicates and extends previous findings of the presence of α generators in the auditory cortices and of the right hemispheric dominance of auditory spatial attentional modulations.

Importantly, the present work provides evidence of distinct facilitatory and suppressive mechanisms supporting anticipatory attention. These two attentional mechanisms have distinct timing in task-relevant and task-irrelevant brain areas, are differentially correlated to behavior, and are supported by different sub-bands of the α rhythm.

Therefore, the present findings provide new insight into the role of the peak-frequency in the α band by showing that anticipatory attention is a dynamic process supported by a balance between facilitatory and suppressive mechanisms, which would be mediated in different low and high sub-bands of the α rhythm, respectively.

References

Aguera PE, Jerbi K, Caclin A, Bertrand O (2011) ELAN: a software package for analysis and visualization of MEG, EEG, and LFP signals. Comput Intell Neurosci 2011:158970. CrossRef

Başar E (2012) A review of alpha activity in integrative brain function: fundamental physiology, sensory coding, cognition and pathology. Int J Psychophysiol 86:1–24. CrossRef Medline

Bates D, Mächler M, Bolker B, Walker S (2014) Fitting linear mixed-effects models using lme4. arXiv Prepr arXiv14065823.

Berger H (1929) Über das elektrenkephalogramm des menschen. Eur Arch Psychiatry Clin Neurosci 87:527–570. CrossRef

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. J Neurosci 27:9252–9261. CrossRef

Bidet-Caulet A, Mikyska C, Knight RT (2010) Load effects in auditory selective attention: evidence for distinct facilitation and inhibition mechanisms. Neuroimage 50:277–284. CrossRef

Bidet-Caulet A, Buchanan KG, Viswanath H, Black J, Scabini D, Bonnet-Brilhault F, Knight RT (2015) Impaired facilitatory mechanisms of auditory attention after damage of the lateral prefrontal cortex. Cereb Cortex 25:4126–4134. CrossRef Medline

Chait M, de Cheveigné A, Poeppel D, Simon JZ (2010) Neural dynamics of attending and ignoring in human auditory cortex. Neuropsychologia 48:3262–3271. CrossRef Medline

Cohen J (1988) Statistical power analysis for the behavioral sciences. 2nd.

Corbetta M, Shulman GL (2002) Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci 3. CrossRef

de Fockert JW, Lavie N (2001) The role of working memory in visual selective attention. Sci 291:1803–1806. CrossRef Medline

Faul F, Erdfelder E, Lang AG, Buchner A (2007) G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 39:175–191. CrossRef

Faul F, Erdfelder E, Buchner A, Lang AG (2009) Statistical power analyses using G* Power 3.1: tests for correlation and regression analyses. Behav Res Methods 41:1149–1160. CrossRef

Foxe JJ, Snyder AC (2011) The role of alpha-band brain oscillations as a sensory suppression mechanism during selective attention. Front Psychol 2:154. CrossRef

Foxe JJ, Simpson GV, Ahlfors SP (1998) Parieto-occipital ~10 Hz activity reflects anticipatory state of visual attention mechanisms. Neuroreport 9:3929–3933. CrossRef

Frey JN, Mainy N, Lachaux J-P, Muller N, Bertrand O, Weisz N (2014) Selective modulation of auditory cortical alpha activity in an audiovisual spatial attention task. J Neurosci 3:6634–6639.

Frey JN, Ruhnau P, Weisz N (2015) Not so different after all: the same oscillatory processes support different types of attention. Brain Res 1626:183–197. CrossRef

Fu KMG, Foxe JJ, Murray MM, Higgins BA, Javitt DC, Schroeder CE (2001) Attention-dependent suppression of distracter visual input can be cross-modally cued as indexed by anticipatory parieto-occipital alpha-band oscillations. Cogn Brain Res 12:145–152. CrossRef

Gazzaley A, Cooney JW, McEvoy K, Knight RT, D'Esposito M (2005) Top-down enhancement and suppression of the magnitude and speed of neural activity. J Cogn Neurosci 17:507–517. CrossRef Medline

Gazzaley A, Clapp W, Kelley J, McEvoy K, Knight RT, D'Esposito M (2008) Age-related top-down suppression deficit in the early stages of cortical visual memory processing. Proc Natl Acad Sci USA 105:13122–13126. CrossRef

Golob EJ, Pratt H, Starr A (2002) Preparatory slow potentials and event-related potentials in an auditory cued attention task. Clin Neurophysiol 113:1544–1557. Medline

Gomez-Ramirez M, Kelly SP, Molholm S, Sehatpour P, Schwartz TH, Foxe JJ (2011) Oscillatory sensory selection mechanisms during intersensory attention to rhythmic auditory and visual inputs: a

human electrocorticographic investigation. J Neurosci 31:18556–18567. CrossRef Medline

Groppe DM, Bickel S, Keller CJ, Jain SK, Hwang ST, Harden C, Mehta AD (2013) Dominant frequencies of resting human brain activity as measured by the electrocorticogram. Neuroimage 79:223–233. CrossRef Medline

Gross J, Kujala J, Hamalainen M, Timmermann L, Schnitzler A, Salmelin R (2001) Dynamic imaging of coherent sources: studying neural interactions in the human brain. Proc Natl Acad Sci USA 98:694–699. CrossRef Medline

Haegens S, Luther L, Jensen O (2012) Somatosensory anticipatory alpha activity increases to suppress distracting input. J Cogn Neurosci 24:677–685. CrossRef Medline

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

Haegens S, Barczak A, Musacchia G, Lipton ML, Mehta AD, Lakatos P, Schroeder CE (2015) Laminar profile and physiology of the α rhythm in primary visual, auditory, and somatosensory regions of neocortex. J Neurosci 35:14341–14352. CrossRef Medline

Hillyard SA, Vogel EK, Luck SJ (1998) Sensory gain control (amplification) as a mechanism of selective attention: electrophysiological and neuroimaging evidence. Philos Trans R Soc London B Biol Sci 353:1257–1270. CrossRef Medline

Hyde KL, Peretz I, Zatorre RJ (2008) Evidence for the role of the right auditory cortex in fine pitch resolution. Neuropsychologia 46:632–639. CrossRef Medline

Jensen O, Mazaheri A (2010) Shaping functional architecture by oscillatory alpha activity: gating by inhibition. Front Hum Neurosci 4:186. CrossRef

Jiang H, Bahramisharif A, van Gerven MAJ, Jensen O (2015) Measuring directionality between neuronal oscillations of different frequencies. Neuroimage 118:359–367. CrossRef

Kawasaki M, Kitajo K, Yamaguchi Y (2010) Dynamic links between theta executive functions and alpha storage buffers in auditory and visual working memory. Eur J Neurosci 31:1683–1689. CrossRef Medline

Kelly SP, Lalor EC, Reilly RB, Foxe JJ (2006) Increases in alpha oscillatory power reflect an active retinotopic mechanism for distracter suppression during sustained visuospatial attention. J Neurophysiol 95:3844–3851. CrossRef

Klimesch W (1999) EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res Brain Res Rev 29:169–195. Medline

Klimesch W (2012) Alpha-band oscillations, attention, and controlled access to stored information. Cell 16:606–617. CrossRef

Klimesch W, Schimke H, Pfurtscheller G (1993) Alpha frequency, cognitive load and memory performance. Brain Topogr 5:241–251. Medline

Klimesch W, Sauseng P, Hanslmayr S (2007) EEG alpha oscillations: the inhibition–timing hypothesis. Brain Res Rev 53:63–88. CrossRef

Lattner S, Meyer ME, Friederici AD (2005) Voice perception: sex, pitch, and the right hemisphere. Hum Brain Mapp 24:11–20. CrossRef Medline

Maris E, Oostenveld R (2007) Nonparametric statistical testing of EEG- and MEG-data. J Neurosci Methods 164:177–190. CrossRef Medline

Mazaheri A, van Schouwenburg MR, Dimitrijevic A, Denys D, Cools R, Jensen O (2013) Region-specific modulations in oscillatory alpha activity serve to facilitate processing in the visual and auditory modalities. Neuroimage 87:356–362. CrossRef

Milner B (1962) Laterality effects in audition. In: Interhemispheric relations and cerebral dominance. Baltimore, MD: Johns Hopkins University Press.

Müller N, Weisz N (2012) Lateralized auditory cortical alpha band activity and interregional connectivity pattern reflect anticipation of target sounds. Cereb Cortex 22:1604–1613. CrossRef Medline

Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RS, Frith CD (1997) Functional localization of the system for visuospatial attention using positron emission tomography. Brain J Neurol 120:515–533. CrossRef

Nolte G (2003) The magnetic lead field theorem in the quasi-static approximation and its use for magnetoencephalography forward calculation in realistic volume conductors. Phys Med Biol 48:3637. Medline

Oostenveld R, Fries P, Maris E, Schoffelen JM (2011) FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. Comput Intell Neurosci 2011:156869. CrossRef

Pfurtscheller G, Stancák A Jr, Neuper C (1996) Event-related synchronization (ERS) in the alpha band—an electrophysiological correlate of cortical idling: a review. Int J Psychophysiol 24:39–46. Medline

Requin J, Brener J, Ring C (1991) Preparation for action. In: Handbook of cognitive psychophysiology: central and autonomic nervous system approaches. New York: Wiley & Sons.

Rihs TA, Michel CM, Thut G (2007) Mechanisms of selective inhibition in visual spatial attention are indexed by alpha-band EEG synchronization. Eur J Neurosci 25:603–610. CrossRef Medline

Rihs TA, Michel CM, Thut G (2009) A bias for posterior alpha-band power suppression versus enhancement during shifting versus maintenance of spatial attention. Neuroimage 44:190–199. CrossRef

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. Eur J Neurosci 22:2917–2926. CrossRef Medline

Searle SR, Speed FM, Milliken GA (1980) Population marginal means in the linear model: an alternative to least squares means. Am Stat 34:216–221. CrossRef

Slagter HA, Prinssen S, Reteig LC, Mazaheri A (2016) Facilitation and inhibition in attention: functional dissociation of pre-stimulus alpha activity, P1, and N1 components. Neuroimage 125:25–35. CrossRef

Spierer L, Bellmann-Thiran A, Maeder P, Murray MM, Clarke S (2009) Hemispheric competence for auditory spatial representation. Brain 132:1953–1966. CrossRef Medline

Spierer L, De Lucia M, Bernasconi F, Grivel J, Bourquin NMP, Clarke S, Murray MM (2011) Learning-induced plasticity in human audition: objects, time, and space. Hear Res 271:88–102. CrossRef Medline

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

R Team (2014) R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing.

Thut G (2006) alpha-Band electroencephalographic activity over occipital cortex indexes visuospatial attention bias and predicts visual target detection. J Neurosci 26:9494–9502. CrossRef

Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002) Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 15:273–289. CrossRef Medline

van Diepen RM, Mazaheri A (2017) Cross-sensory modulation of alpha oscillatory activity: suppression, idling, and default resource allocation. Eur J Neurosci 45:1431–1438. CrossRef Medline

Van Veen BD, van Drongelen W, Yuchtman M, Suzuki A (1997) Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. Biomed Eng IEEE Trans 44:867–880. CrossRef Medline

Von Békésy G, Wever EG (1960) Experiments in hearing. New York: McGraw-Hill.

Weise A, Hartmann T, Schröger E, Weisz N, Ruhnau P (2016) Cross-modal distractors modulate oscillatory alpha power: the neural basis of impaired task performance. Psychophysiology 53:1651–1659. CrossRef Medline

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

Weisz N, Muller N, Jatzev S, Bertrand O (2014) Oscillatory alpha modulations in right auditory regions reflect the validity of acoustic cues in an auditory spatial attention task. Cereb Cortex 24:2579–2590. CrossRef

Zatorre RJ, Belin P (2001) Spectral and temporal processing in human auditory cortex. Cereb Cortex 11:946–953. Medline

Zatorre RJ, Penhune VB (2001) Spatial localization after excision of human auditory cortex. J Neurosci 21:6321–6328. Medline

Zatorre RJ, Belin P, Penhune VB (2002) Structure and function of auditory cortex: music and speech. Trends Cogn Sci 6:37–46. Medline

7.3 Supplementary Study I: Alpha Connectivity during Top-Down Attention (CAT2.0)

7.3.1 Introduction

In the introductory section, we have reviewed evidence that communication between nodes of the dorsal fronto-parietal top-down attention network could be established via oscillatory activity in the alpha band (Capotosto et al. 2009). However, in the auditory domain, evidence of such connectivity (between the auditory cortices and regions of the dorsal network) have been contradictory. For example, in their 2012 study, Muller and Weisz demonstrated an increased functional connectivity between the right auditory cortex and the frontal eyes fields for attended ipsilateral (to the auditory cortex) auditory targets in comparison to attended contralateral target, i.e. enhanced dorsal connectivity with the task-irrelevant auditory cortex. On the contrary, in two later studies, while attending to a monaural target, in comparison to the ipsilateral (to the auditory target) auditory cortex, stronger connectivity has been observed between the contralateral auditory cortex and the left intraparietal sulcus (Huang et al. 2014) or the right intraparietal lobule (Weisz et al. 2014), i.e. enhanced dorsal connectivity with the task-relevant auditory cortex.

In our framework, long-range communication in the dorsal network of top-down attention is supported by phase synchrony in the alpha band. Thus, we have aimed to investigate the functional connectivity between the auditory ROIs, already defined in the previous study, and the rest of the brain regions during the anticipation of a visually cued auditory target and how this connectivity would be modulated by the cue information.

Several measures have been proposed to compute functional connectivity (review in Bastos and Schoffelen 2016). Two major candidates for these analyses were coherence (Rosenberg et al. 1989) and Phase Synchrony (Lachaux et al. 1999). However, the fact that the calculation of the former takes into account the amplitude of the signal, we have opted for the latter in order to assure that our results are driven by pure phase-to-phase synchrony.

7.3.2 Materials and Methods

We have extracted the complex values of the Fourier transform containing phase information and transferred these complex values into source space using partial canonical coherence (PCC) beamformer, a computationally efficient alternative to the DICS that provides the possibility of extracting both power and phase information on the source level. For each participant:

(1) Data, from all conditions were concatenated, and cross-spectral density (CSD) matrix (-0.8 to 2 s, relative to cue onset) were calculated using the multitaper method with a target frequency of **10** (±5) Hz. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was used to estimate the spatial distribution of power and phase for the time-frequency window of interest (0.6-1 s post-cue onset, 7-15 Hz). Please note that since we had no a priori hypotheses on the role of previously highlighted alpha sub-bands, we have opted to analyze a frequency window that englobes both bands i.e. 7—15Hz.

(2) For each auditory ROI, phase synchrony between each voxel within the ROI and all other voxels was calculated. For each voxel outside of the auditory ROIs, the obtained values were averaged across auditory voxels leading to a single value of phase synchrony between each non-auditory voxel and each auditory ROI. These values were then FisherZ transformed.

Finally, for each ROI, post-non-informative cue alpha phase synchrony (relative to baseline) was subtracted from contralateral and ipsilateral cue conditions, separately. Then ipsilateral activity was contrasted against the contralateral activity using non-parametric cluster-based permutation analysis (Maris and Oostenveld 2007). Please note, that for this test, cluster-based permutations control for multiple comparisons in the source space dimension.

7.3.3 Results

Only for the right auditory ROI, a significant cluster ($p < 0.01$) extended notably to the vicinity of left dorsolateral prefrontal cortex, the left frontal eye fields and the left pre-central gyrus. For all these regions, phase synchrony in the ipsilateral (right) cue was higher than that in the contralateral (left) cue condition (see Figure 1A). Please note that similar analyses have been undertaken in theta (2-6Hz), beta (20-30Hz) and gamma (60-100Hz) bands with neither significant emergence of such connectivity nor modulations by the cue information.

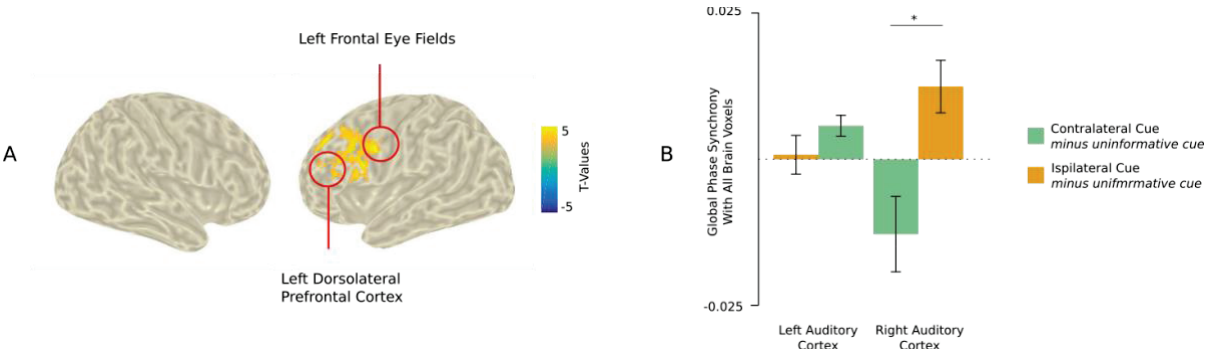


Figure 1. Distributions of T-values, masked at p<0.05, from Cluster Based Permutation tests contrasting contralateral and ipsilateral post-cue phase synchrony with the Right auditory ROI (7-15Hz and 0.6-1 post-cue).

7.3.4 Discussion

In this study, we have analyzed phase synchrony between the auditory cortices and the rest of the brain in the time-frequency window (0.6-1 s post-cue onset, 7-15 Hz) where we have previously highlighted significant modulation of alpha activity by the information of the visual cue. We have demonstrated that attending to a right auditory target increased synchrony between the right ipsilateral auditory cortex and regions in the vicinity of the left Frontal eye fields (FEF) and the left dorsolateral prefrontal cortex (dlPFC). This result corroborates (1) the established role of the FEF as a source of top-down signals responsible for controlling alpha activity in the task (ir)relevant sensory cortices (Capotosto et al. 2009) and (2) the role of the lPFC in modulating the neural processing of (ir)relevant stimuli (Johnson et al. 2007; Miller, Vytlacil, et al. 2011; Zanto et al. 2011).

Nevertheless, our finding contradicts previous studies (Huang et al. 2014; Weisz et al. 2014), where the opposite pattern has been found i.e. increased synchrony between nodes of the dorsal top-down network and the auditory cortex contralateral to the attended target.

However, differences between these three studies might explain this discrepancy. We consider the discrimination task (512 vs 575 Hz) in our paradigm to be more demanding than both the detection (Weisz et al., 2014) and the discrimination (800 vs 1500Hz: Huang et al., 2014) tasks used in previous studies. In our discrimination task (study I), we have demonstrated that, globally, only alpha synchronization in visual task-irrelevant regions correlated with better performances. In a similar vein, we posit that due to the difficulty of the task, in anticipation of an auditory target, the excitability of relevant (contralateral) auditory cortex would be maximal and only the inhibition of signal dispersion to the "relatively" irrelevant (ipsilateral) auditory cortex could fluctuate and would necessitate more top-down inhibitory control signals. This also reinforces the hypothesis that alpha oscillations mainly exert an inhibitory role on underlying cortical excitability (Jensen and Mazaheri 2010; Klimesch 2012).

Finally, we have previously interpreted the auditory laterality asymmetry (lack of synchrony effects in the left auditory cortex) in the light of (1) the right hemispheric specialization in pitch processing (Milner 1962; Zatorre and Belin 2001; Zatorre et al. 2002; Lattner et al. 2005; Hyde et al. 2008), and (2) the right hemispheric dominance in spatial attention that has been illustrated for the auditory (Zatorre and Penhune 2001; Spierer et al. 2009) and visual (Nobre et al. 1997; Corbetta and Shulman 2002) modalities. Furthermore, only contralateral frontal regions (FEF and dlPFC) showed higher phase synchrony with the right auditory cortex. This pattern is in line with recent work mainly in the visual modality using both fMRI (Szczepanski et al. 2010; Vossel et al. 2012) and combined TMS/MEG (Marshall, O'Shea, et al. 2015) recordings. These studies have demonstrated that attention signals in fronto-parietal regions, e.g. FEF, were spatially specific i.e. stronger when attention was directed to the contralateral than to the ipsilateral visual field.

Taken together, these results demonstrate how alpha phase synchrony would support inter-areal communication during (top-down) anticipation of an auditory target in manner that shows high specificity in the laterality of both auditory and frontal regions to the anticipated target.

7.4 Supplementary Study II: Gamma Activity during Top-Down Attention (CAT2.0)

7.4.1 Introduction

In the previous two studies, we have demonstrated how both amplitude and phase of alpha oscillations would support modulations and long-range communication in the dorsal top-down network of attention, respectively. In the introductory section, we have highlighted that while anticipatory alpha activity decreases contralaterally and increases ipsilaterally to the attended side, stimulus-induced gamma power is boosted contralaterally and attenuated ipsilaterally (Marshall, O'Shea, et al. 2015) in both the visual (Fries et al. 2001, 2008, Fries 2005, 2009; Taylor et al. 2005; Womelsdorf and Fries 2007; Siegel et al. 2008; Popov et al. 2017) and auditory (Debener et al. 2003; Bidet-Caulet et al. 2007; Schadow et al. 2009) modalities. In addition, we have reviewed evidence that amplitude of gamma oscillations is often coupled to the phase of ongoing alpha oscillations (review in Bonnefond et al. 2017).

In our framework, we have hypothesized that the amplitude of gamma oscillations would be coupled to the phase of alpha oscillations and subsequently would reflect modulations of top-down attention before and after target presentation. Originally, we have planned to compute phase-amplitude coupling in the auditory ROIs but prior to that, we have aimed to investigate whether (1) anticipation of an auditory target would impact gamma activity (power) in the auditory cortices before and after the presentation of an auditory target and (2) whether, similarly to alpha activity, gamma activity (power) before the auditory target would correlate with behavioral performances.

7.4.2 Material and Methods

7.4.2.1 Definition of Cue and Target Related Gamma Band

Gamma band activity before and after the target was investigated at the source level within auditory ROIs (defined in study I). The bandwidth of this gamma band was defined between 60 and 100 Hz, based upon results of **study II** (see chapter 8.2) whereas the time windows of interest before (pre-) and after (post-) the presentation of the auditory target were defined as follows:

- For the pre-target window, we based our choice upon results from **study I** i.e. 600 to 1000ms (post-cue onset).
- For the post-target window, we have averaged oscillatory activity from both auditory ROIs and between 60 and 100Hz. Afterwards activity of interest (defined between 1

and 2s post-cue) was contrasted against mean baseline activity (-0.4 to -0.2s pre-cue) in steps of 10ms using a non-parametric cluster-based permutation analysis (Maris and Oostenveld 2007). For this test, cluster permutations control for multiple comparisons only in the time dimension.

7.4.2.2 Gamma Activity Modulation

In order to investigate gamma modulation before target presentation, a linear mixed-effects model (lme) was fit to predict modulation of gamma activity in auditory ROIs between 600 and 1000ms (relative to cue onset) and between 60 and 100Hz with the following factors as fixed effects: (1) cue laterality according to the auditory cortices (3 levels: ipsilateral, contralateral and uninformative), and (2) hemisphere (2 levels: left and right). A random effect was included for each participant, allowing us to model variability between participants.

Moreover, in order to investigate gamma modulation after target presentation, a similar mixed-effects model (lme) was fit to predict modulation of gamma activity in auditory ROIs in the same frequency band but between 1300 and 1450ms (relative to cue onset). For this test the fixed effects were: (1) target laterality according to the auditory cortices (2 levels: ipsilateral, contralateral), and (2) hemisphere (2 levels: left and right), and (3) cue information (2 levels: informative and uninformative).

For post-hoc analysis (of both tests) we used the Lsmean package (Lsmean version 2.20-23; Searle et al., 1980) where p-values were considered as significant at $p<0.05$ and adjusted for the number of comparisons performed (Tukey method).

7.4.2.3 Gamma Activity and Behavioral Performances

In order to evaluate the relationship between cue related changes in gamma power and reaction times in source-space, single trial gamma activity was reconstructed at each grid point using a Partial Cannonical Correlation (PCC) beamformer, a more computationally efficient alternative to the DICS beamformer. Afterwards, we performed a trial-by-trial correlation, using non-parametric Spearman tests, in each participant, between reaction times and post-cue gamma power (between 60 and 100Hz, and between 600 and 1000 ms, according to the sensor level results) at each grid point (Mazaheri et al. 2013). The correlation coefficients were subsequently converted to z-values using Fisher's r- to z-transformation to obtain a normally distributed variable. The statistical significance of the correlations was

assessed at the group level with a one-sample t-test of the correlation z-values at each grid point and then subjected to a cluster-level randomization test to correct for multiple comparisons in the source space dimension.

7.4.3 Results

7.4.3.1 Definition of Cue and Target Related Gamma Band

Upon contrasting post-cue gamma activity to baseline activity in both auditory ROIs, we have identified a significant cluster (p = 0.022) extending between 1300 and 1450 ms (post-cue onset). This has been defined as the post-target gamma time-window of interest (see Figure 1).

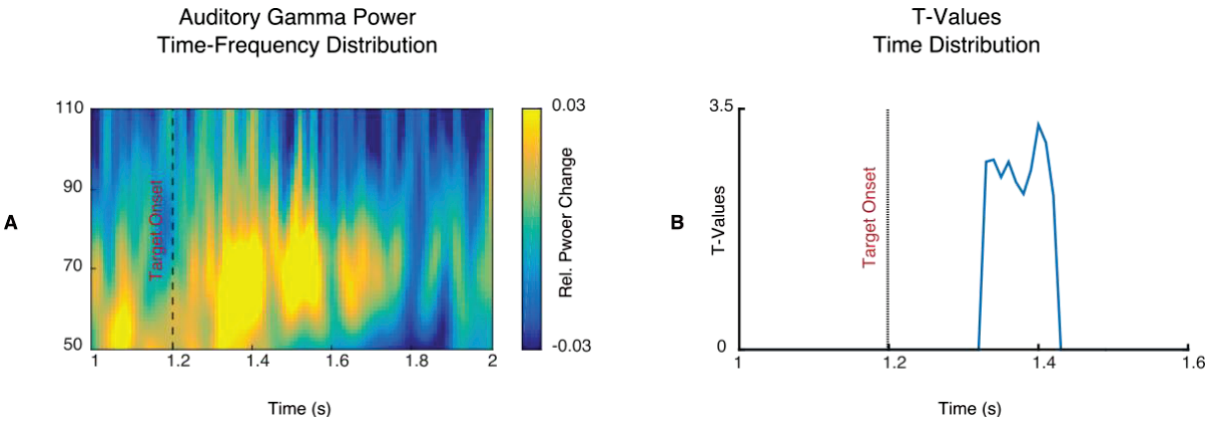


Figure 1. (A) Gamma power, relative to baseline (400-200 pre-cue onset), averaged across both auditory virtual ROIs. (B) Time distribution of t-values, masked at p<0.05, from Cluster Based Permutation tests contrasting post-target gamma activity against baseline activity at the virtual electrode level.

7.4.3.2 Gamma Activity Modulation

In the pre-target window, only an effect of cue laterality ($F(1, 13) = 22.5$, $p < 0.01$, $\eta^2 = 0.002$) reached significance. 2 by 2 post-hoc testing revealed that in auditory cortices, gamma power was significantly higher in the contralateral cue condition, in comparison to the ipsilateral and uninformative cue condition ($p < 0.001$).

In the post-target window, we found an effect of target laterality ($F(2, 13) = 10.27$, $p < 0.01$, $\eta^2 = 0.17$). Gamma power was significantly higher in response to contralateral than to ipsilateral targets in both hemispheres. Moreover, we found an effect of cue information (F(2, 13) = 8,6,

$p < 0.01$, $\eta^2 = 0.09$). Regardless of the hemisphere and target side, gamma power was significantly higher when the cue was informative rather than uninformative of the target ear presentation.

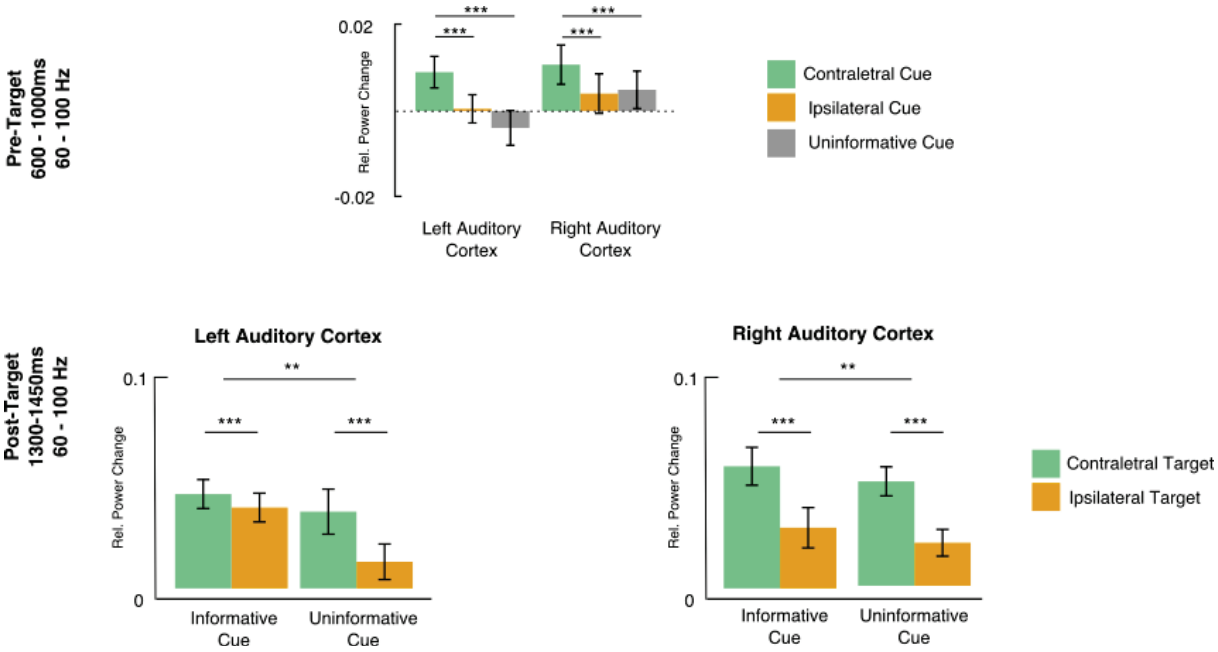


*Figure 2. Upper panel: Pre-target gamma power (relative to baseline) averaged between 600 and 1000ms (post-cue onset) and 60-100Hz for the three cue conditions, in each hemisphere. Lower panel: Post-target gamma power (relative to baseline) averaged between 1300 and 1400ms (post-cue onset) and 60-100Hz according to cue information and target presentation conditions, in each hemisphere. *P < 0.05, **P < 0.01, ***P < 0.001. Error bars represent SEM.*

7.4.3.3 Gamma Activity and Behavioral Performances

Gamma activity between 600 and 1000ms (relative to cue onset) and 60-100Hz, mainly in the right auditory cortex and the right temporoparietal junction, was found to negatively correlate with reaction times ($p = 0.03$). The larger the gamma activity, the shorter the reaction times. Other regions included, the right middle temporal and occipital gyri, the fusiform, the calcarine, and the inferior partial gyrus (see Figure 3).

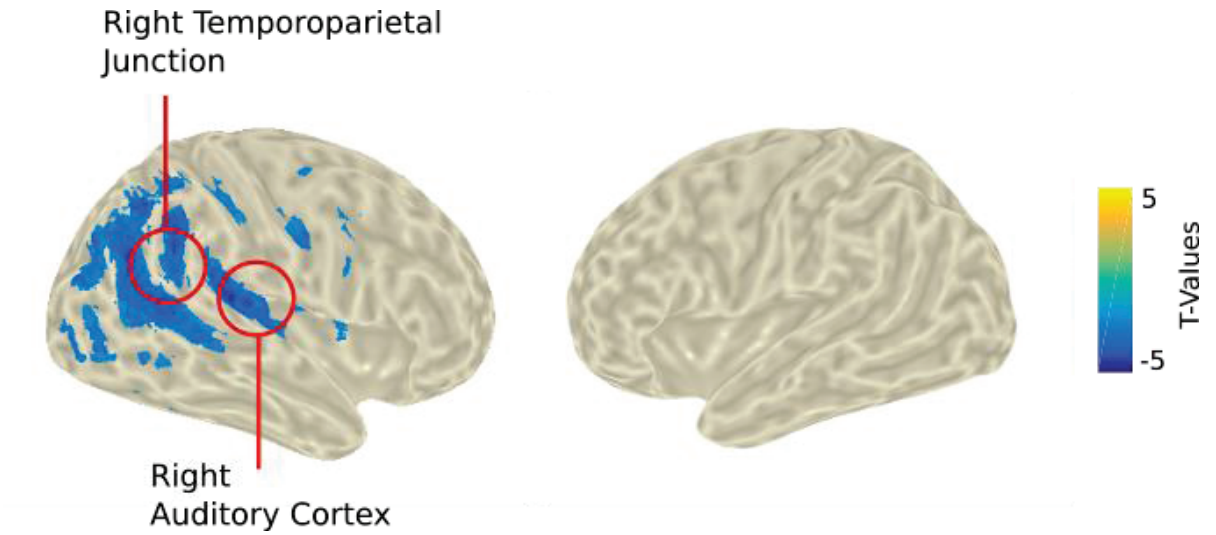


Figure 3. T-value source distributions, masked at p<0.05, from Cluster Based Permutation testing the significance of the correlation between gamma activity (600-1000ms, 60-100Hz) and reaction time. Please note, that negative t-values signify negative correlation between reaction times and gamma activity.

7.4.4 Discussion

In this study we have demonstrated that induced gamma activity in the auditory cortices before the presentation of an auditory target was differentially modulated by the type of the visual cue, i.e. in both auditory cortices, gamma power was higher when attending to a contralateral auditory target, in comparison to both the ipsilateral and uninformative conditions. In addition, we have demonstrated that in both auditory cortices, higher gamma power in response to contralateral rather than to ipsilateral targets, and that the presentation of an auditory target preceded by an informative cue induced an increase in gamma activity in comparison to when preceded by an uninformative cue. Finally, before the presentation of the auditory target, gamma power in the right auditory cortex and the right temporoparietal junction (TPJ) correlated negatively with reaction times i.e. the higher the gamma power was, the faster the participants were.

These findings corroborate the growing literature that ties gamma activity to local neuronal processing (Fries 2005, 2009) where, first, lateralized gamma activity after target presentation would reflect the preferential contralateral processing in the auditory cortices, in relation to the anatomical organization of the auditory system. Second, increased gamma responses to targets when preceded by an informative (rather than an uninformative) cue would reflect the effect of top-down attention on target processing. Third, the increase of gamma activity during expectation of a contralateral (rather than an ipsilateral) target would reflect cortical pre-activation of the relevant areas in order to better process the upcoming target.

Finally, the correlation between reaction times and gamma activity in the right auditory cortex is consistent with the right hemispheric specialization in pitch processing (Milner 1962; Zatorre and Belin 2001; Zatorre et al. 2002; Lattner et al. 2005; Hyde et al. 2008). Since participants performed a pitch categorization task, the right auditory cortex would be more relevant for target sound processing. In addition, it has been proposed that the right TPJ plays a role in mediating endogenous attention shifts of auditory spatial attention (Salmi et al. 2009) where it would operate as a filter for incoming stimuli (Larson and Lee 2013b, 2014). Taken together, this affirms the role of gamma oscillations in promoting the activation of task-relevant processes across the brain and not only in sensory (auditory) cortices.

8 Gamma Oscillations and Bottom-Up Attention

8.1 General Presentation

Within our framework, we have proposed that the power of gamma oscillations would support the activation of the ventral bottom-up attention network. We have also proposed that the lateral prefrontal cortex (lPFC) would play a role in (1) subtending bottom-up gamma synchrony, and (2) the interaction between bottom-up and top-down mechanisms indexed by gamma power modulations and/or fluctuations in the alpha-gamma coupling.

In **study II**, in response to an unexpected salient distracting sound (CAT 3.0), we have observed an increase in gamma power in the left and right auditory cortices, the bilateral temporo-parietal junctions, and the right ventrolateral frontal cortex. This activation pattern highly corresponds to previous results from functional magnetic resonance imaging (fMRI) studies of both visual (see Corbetta and Shulman 2002; Corbetta et al. 2008 for review) and auditory (e.g. Salmi et al. 2009; Alho et al. 2014; Salo et al. 2017; Long and Kuhl 2018) bottom-up attention. In addition, we have demonstrated, using gamma oscillatory activity for the first time, how deployment of top-down attention can modulate distracting sound processing. However, contrary to our initial hypothesis, the locus of this interaction was in in the dorso- and ventromedial prefrontal cortices and the anterior cingulate cortex, i.e. the hub of the inhibitory control system (Salmi et al. 2009; Løvstad, Funderud, Meling, et al. 2012; Ossandon et al. 2012; Erika-Florence et al. 2014). Importantly, we have demonstrated that during the presentation of a distracting sound, gamma activity is synchronous between the auditory cortices and several distant brain regions, notably the lPFC. This hints to an important role of the lPFC in supporting bottom-up attention while its role in the interaction between top-down and bottom-up mechanisms (possibly through phase-amplitude coupling) remains to be established.

In **supplementary study III**, we have demonstrated that even after the presentation of a distracting sound, a similar pattern of auditory alpha power as in the absence of a distracting sound (see **Study I**) was re-established.

8.2 Study II: Distractor-related Gamma Activity (CAT3.0)

What's in Your Gamma? Activation of The Ventral Fronto-Parietal Network in Response to A Distracting Sound.

Hesham A. ElShafei[1], Lesly Fornoni, Rémy Masson, Olivier Bertrand & Aurélie Bidet-Caulet[1].

In preparation.

[1] Brain Dynamics and Cognition Team, Lyon Neuroscience Research Center; CRNL, INSERM U1028, CNRS UMR5292, University of Lyon 1, Université de Lyon, Lyon, France

Abstract

Auditory attention operates through top-down (TD) and bottom-up (BU) mechanisms that are supported by dorsal and ventral brain networks, respectively, with the main overlap in the lateral prefrontal cortex (lPFC). A good TD/BU balance is essential, yet it is rarely investigated. Oscillatory activity is a novel method to probe the attentional dynamics with evidence that gamma activity (>30Hz) could signal BU processing and thus would be a good candidate to support the activation of the ventral BU network. MEG data were collected from 21 young adults performing the Competitive Attention Task which enables simultaneous investigation of BU and TD attentional mechanisms. Distracting sounds elicited an increase in gamma activity in regions of the BU ventral network. TD attention modulated these gamma responses in regions of the inhibitory cognitive control system: the medial prefrontal and anterior cingulate cortices. Finally, distracting-sound-induced gamma activity was synchronous between the auditory cortices and several distant brain regions, notably the lPFC. We provide novel insight into (1) the role of gamma activity in supporting the activation of the BU ventral network and its modulation by TD attention, and (2) the role of the prefrontal cortex in subtending BU attentional mechanisms and their balance with TD mechanisms.

Keywords: auditory attention; attentional capture; gamma oscillations; phase synchrony; prefrontal cortex

1 Introduction

In an environment that contains far more information than we can process at a time, we rely on our attention to prioritize the processing of only a fragment of these incoming stimuli (Desimone and Duncan 1995). Attention can be oriented endogenously (top-down), in anticipation of an upcoming stimulus for example, or it can be captured exogenously (bottom-up) by a salient irrelevant stimulus such as a telephone ringing (Posner and Petersen 1990; Petersen and Posner 2012). A dynamic balance between top-down (TD) and bottom-up (BU) mechanisms of attention is essential to be task-efficient while being aware, yet not fully distracted, of our surroundings.

Two major neural networks support TD (endogenous) and BU (exogenous) mechanisms of attention: a dorsal frontoparietal network comprising the posterior frontal and intraparietal cortices; and a ventral frontoparietal network, largely lateralized to the right hemisphere, comprising the temporo-parietal junction (TPJ) and the ventral prefrontal cortex (vPFC); with the two networks overlapping mainly in the lateral prefrontal cortex (lPFC) (Kim et al. 1999; Miller and Cohen 2001; Corbetta and Shulman 2002; Fox et al. 2006; He et al. 2007; Corbetta et al. 2008; Asplund et al. 2010).

A promising way of addressing the dynamics of TD and BU attentional systems is to explore brain rhythms. On one hand, TD anticipatory attention is indexed by (de)synchronisation of oscillatory activity in the alpha band (review in Klimesch et al. 2007; Jensen and Mazaheri 2010; Frey et al. 2014; e.g. ElShafei et al. 2018). On the other hand, BU attentional capture is signalled by an increased activity in the gamma band in the primate brain (Buschman and Miller, 2007).

Activation in the gamma band (>30 Hz) has been associated to attention, with enhanced gamma activity in the visual (e.g. Fries et al. 2001) or auditory (e.g. Ray et al. 2008) cortices, in response to attended visual or auditory stimuli, respectively. Gamma activity has also been observed in regions other than sensory regions (e.g. dorsolateral prefrontal cortex, intraparietal sulcus and temporo-parietal junction) in several working memory (Michels et al. 2010; Albouy et al. 2013), and visual (Akimoto et al. 2013, 2014) or auditory (Lee et al. 2007; Ahveninen et al. 2013) oddball tasks. Thus, gamma activity seems to promote the activation of relevant processes across the brain and not only in sensory cortices. Finally, it has been demonstrated that attention increases the coupling between frontal and relevant sensory

regions via gamma synchrony (Buschman and Miller 2007; Gregoriou et al. 2009; Baldauf and Desimone 2014). Therefore, gamma activity would be a good candidate to support activation of the ventral network of attention. However, to our knowledge, no study has investigated the role of gamma activity in the balance between BU and TD mechanisms of attention in the human brain.

Distraction by unexpected sounds has been mostly investigated using variations of the reaction-time based oddball paradigm. In this paradigm, the response time to a target stimulus is compared in the presence (vs. absence) of a rare deviation (oddball) within a sequence of irrelevant stimuli that could be in the same (Schröger 1996) or a different (Escera et al. 1998) modality than the attended target. However, the adequacy of such paradigm to provide a reliable measure of attentional capture has been recently criticized (review in Parmentier and Andrés 2010; Bidet-Caulet et al. 2014; Dalton and Hughes 2014; Masson and Bidet-Caulet 2018).

In 2014, Bidet-Caulet and colleagues proposed a novel paradigm, the Competitive Attention Task (CAT), an adaptation of the Posner cueing paradigm using visual cues and monaural auditory targets. In this task, TD anticipatory attention is measured by comparing trials with informative cues to trials with uninformative cues. BU attentional capture is triggered by a binaural distracting sound played during the delay between the cue and the target in only 25 % of the trials. Distraction is assessed as the impact of distracting sounds on task performance and the balance between TD and BU mechanisms can be measured by comparing responses to distracting sounds following informative vs. uninformative cues.

We have recorded MEG activity from young healthy adults performing the CAT to test the following hypotheses. (1) BU attentional capture by an isolated unexpected stimulus would be indexed by gamma activity in the ventral attentional network including the TPJ and VPFC. (2) The lPFC would support the balance between BU and TD attention by demonstrating modulations of gamma activity to distracting sounds by cue information, since the lPFC is part of both the ventral and dorsal networks of attention. Finally, we sought to investigate the connectivity, subtended by gamma activity, between the auditory cortices and other brain regions during the presentation of a distracting sound, with a prediction that the mains hubs of this connectivity would lie within the lPFC.

2 Material & METHODS

2.1 Participants

Twenty-one healthy participants (9 females) took part in this study. The mean age was 24.7 years ± 0.62 Standard Error of Mean (SEM). All participants were right handed, and reported normal hearing, and normal or corrected-to-normal vision. All participants were free from any neurological or psychiatric disorders. The study was approved by the local ethical committee, and subjects gave written informed consent, according to the Declaration of Helsinki, and they were paid for their participation.

2.2 Stimuli and tasks

2.2.1 Competitive Attention Task (CAT)

In 75 % of the trials, a target sound (100 ms duration) followed a central visual cue (200 ms duration) with a fixed delay of 1000 ms (see Figure 1). The cue was a green arrow, presented on a grey-background screen, pointing either to the left, right, or both sides. Target sounds were monaural pure tones (carrier frequency between 512 and 575 Hz; 5 ms rise-time, 5 ms fall-time). In the other 25 %, the same structure was retained, however, a binaural distracting sound (300 ms duration) was played during the cue-target delay (50-650 ms range after cue offset). Trials with a distracting sound played from 50 ms to 350 ms after the cue offset were classified as DIS1, those with a distracting sound played from 350 ms to 650 ms after the cue offset were classified as DIS2, those with no distracting sound were classified as NoDIS. A total of 40 different ringing sounds were used as distracting sounds (clock-alarm, door-bell, phone ring, etc.) for each participant.

The cue and target categories were manipulated in the same proportion for trials with and without distracting sound. In 25% of the trials, the cue was pointing left, and the target sound was played in the left ear, and in 25% of the trials, the cue was pointing right, and the target sound was played in the right ear, leading to a total of 50% of *informative* trials. In the other 50% of the trials, the cue was *uninformative*, pointing in both directions, and the target sound was played in the left (25%) or right (25%) ear. To compare brain responses to acoustically matched sounds, the same distracting sounds were played in each combination of cue category (informative, uninformative) and distractor condition (DIS1 or DIS2). Each distracting sound was thus played 4 times during the whole experiment, but no more than

once during each single block to limit habituation. Participants were instructed to categorize two target sounds as either high- or low-pitched sound, by either pulling or pushing a joystick.

The target type (high or low) was manipulated in the same proportion in all conditions. The mapping between the targets (low or high) and the responses (pull or push) was counterbalanced across participants but did not change across the blocks for each participant. In order to account for the participants' pitch-discrimination capacities, the pitch difference between the two target sounds was defined in a Discrimination Task (see section 2.2.2). Participants were informed that informative cues were 100 % predictive and that a distracting sound could be sometimes played. They were asked to allocate their attention to the cued side in the case of informative cue, to ignore the distractors and to respond as quickly and correctly as possible. Participants had a 3.4 second (3400 ms) response window. In the absence of the visual cue, a blue fixation cross was presented at the center of the screen. Subjects were instructed to keep their eyes fixated on the cross.

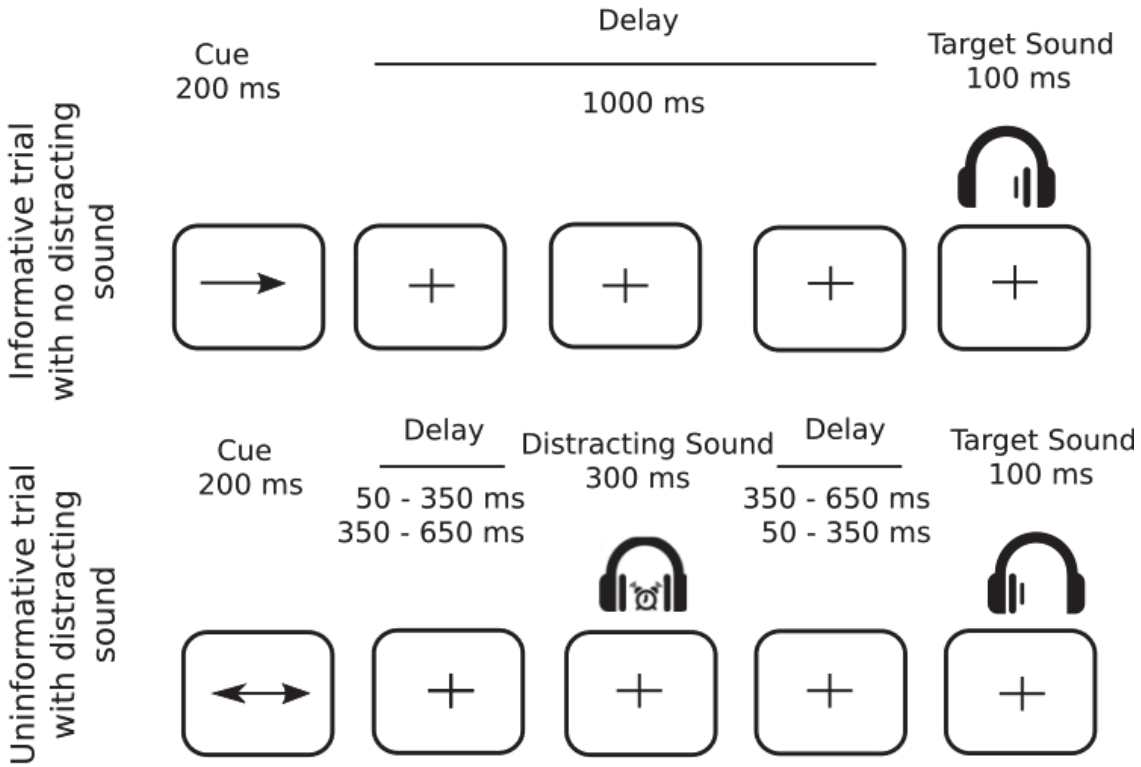


Figure 1. Protocol. Top row. Example of an informative trial with no distracting sound: a one-sided visual cue (200 ms duration) indicated in which ear (left or right) the target sound would be played (100 ms duration) after a fixed 1000-ms delay. Bottom row. Example of an uninformative trial with a distracting sound: a two-sided visual cue (200 ms duration) did not provide any indication in which ear (left or right) the target sound will be played. In 25 % of the trials, a binaural distracting sound (300 ms duration), such as a clock ring, was played during the delay between cue and target. The distracting sound could equiprobably onset in two different time periods after the cue offset: in the 50–350 ms range, or in the 350–650 ms range.

2.2.2 Discrimination Task

Participants were randomly presented with one of two target sounds: a low-pitched sound (512 Hz) and a high-pitched sound (575 Hz; two semitones higher), equiprobably in each ear (four trials per ear and per pitch). As described above, participants were asked to categorize the target sounds as either high- or low-pitched sound within 3 seconds.

2.2.3 Procedure

Participants were seated in a sound-attenuated, magnetically shielded recording room, at a 50 cm distance from the screen. The response device was an index-operated joystick that

participants moved either towards them (when instructed to pull) or away from them (when instructed to push). All stimuli were delivered using Presentation software (Neurobehavioral Systems, Albany, CA, USA). All sounds were presented through air-conducting tubes using Etymotic ER-3A foam earplugs (Etymotic Research, Inc., USA).

First, the auditory threshold was determined for the two target sounds differing by 2 semitones (512 and 575 Hz), for each ear, for each participant using the Bekesy tracking method (Von Békésy and Wever 1960). The target sounds were then monaurally presented at 25 dB sensation level (between 37.5 and 52.1 dB A across subjects) while the distracting sounds were binaurally played at 55 dB sensation level (between 47.5 and 62.1 dB A across subjects), above the target sound thresholds. Second, participants performed the discrimination task. Afterwards, participants were trained with a short sequence of the Competitive Attention Task. Finally, MEG and EEG were recorded while subjects performed 10 blocks (64 trials each) leading to 240 trials in the NoDIS and 80 in the DIS conditions, for informative and uninformative cues, separately. The whole recording session lasted around 80 minutes. After the MEG/EEG session, participants' subjective reports regarding their strategies were collected.

2.3 Behavioral Data Analysis

For behavioral data analysis, a button press before target onset was considered as a false alarm (FA). A trial with no button-press after target onset and before the next cue onset was considered as a miss trial. A trial with no FA and with a button-press after target onset was counted as correct if the pressed button matched the response mapped to the target sound, and as incorrect if otherwise. Reaction-times (RTs) to targets were analysed in the correct trials only.

The influence of (1) cue condition (2 levels: informative and uninformative) and (2) distractor condition (3 levels: NoDis, DIS1 and DIS2) on median reaction times (RTs) of correct responses and on percentage of incorrect responses was tested using a linear mixed-effects models using the lme4 package (Bates et al. 2014) for R (Team 2014). For post-hoc analysis we used the Lsmean package (Searle et al. 1980) where p-values were considered as significant at $p<0.05$ and adjusted for the number of comparisons performed (Tukey method).

2.4 Brain Recordings

Simultaneous EEG and MEG data were recorded, although the EEG data will not be presented here. The MEG data were acquired with a 275-sensor axial gradiometer system (CTF Systems Inc., Port Coquitlam, Canada) with continuous sampling at a rate of 600Hz, a 0–150Hz filter bandwidth, and first-order spatial gradient noise cancellation. Moreover, eye-related movements were measured using vertical and horizontal EOG electrodes. Head position relative to the gradiometer array was acquired continuously using coils positioned at three fiducial points; nasion, left and right pre-auricular points. Head position was checked at the beginning of each block to control head movements.

In addition to the MEG/EEG recordings, T1-weighted three-dimensional anatomical images were acquired for each participant using a 3T Siemens Magnetom whole-body scanner (Erlangen, Germany). These images were used for reconstruction of individual head shapes to create forward models for the source reconstruction procedures. The processing of these images was carried out using CTF's software (CTF Systems Inc., Port Coquitlam, Canada).

2.5 Data Pre-processing

Only correct trials were considered for electrophysiological analyses. Data segments for which the head position differed for more than 10 mm from the median position during the 10 blocks were excluded. In addition, data segments contaminated with muscular activity or sensor jumps were excluded semi-manually using a threshold of 2200 and 10000 femtoTesla respectively. For all participants, more than 75 % of trials remained after rejection for further analyses.

Independent component analysis was applied on the band-pass filtered (0.1-40Hz) data in order to remove eye-related (blink and saccades) and heart-related artefacts. Subsequently, components (four on average) were removed from the non-filtered data via the inverse ICA transformation. Data were further notch filtered at 50, 100 and 150Hz and high-pass filtered at 0.2Hz.

2.6 Distractor-locked Gamma Activity

2.6.1 Gamma Band (Sensor level): Definition

The goal of this step was to define the time-frequency range of gamma activity of interest. First, for each distractor onset time-range, surrogate distractors were created in the NoDIS trials with similar distribution over time than the real distractors. Afterwards, the time-frequency power, of distractor (and of surrogate distractor) trials was calculated using Morlet Wavelet decomposition with a width of four cycles per wavelet (m=7; Tallon-Baudry and Bertrand 1999) at center frequencies between 40 and 150 Hz, in steps of 1 Hz and 10 ms. Activity between 0 and 0.35s post-distractor onset and 50-110Hz was contrasted between distractor and surrogate trials using a nonparametric cluster-based permutation analysis (Maris and Oostenveld 2007). This contrast extracts distractor-related activity clear of cue-related activity (see Figure 2).

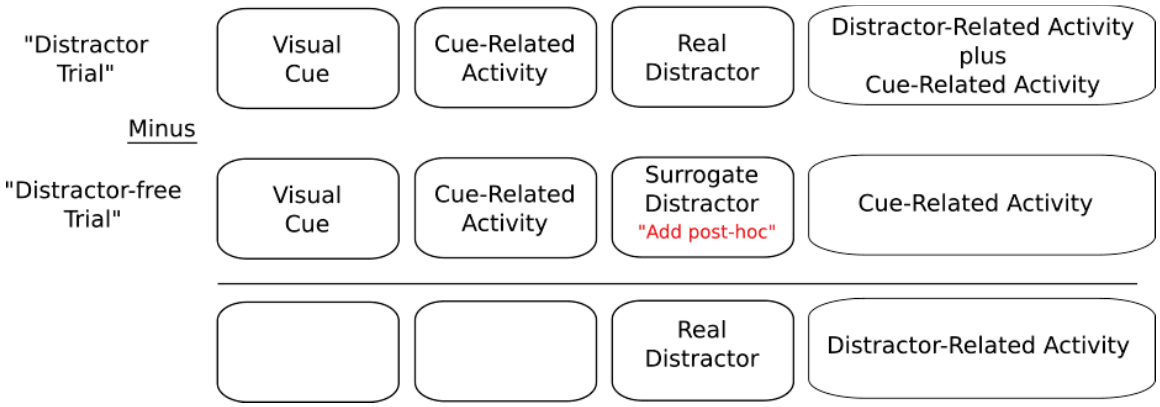


Figure 2. Schematic depiction for baseline correction of trials with a distracting sound.

2.6.2 Gamma Band (Source level): Computation

The goal of this step was to estimate the brain regions driving gamma activity in response to distracting sounds in the time-frequency window of interest (0.1-0.3 s post-distractor onset, 60 to 100Hz) defined from the sensor-level analysis (part 2.6.1). We utilized the frequency–domain adaptive spatial technique of dynamical imaging of coherent sources (DICS; Gross et al., 2001). Data from both surrogate and real distractors were concatenated, and cross-spectral density (CSD) matrix (-0.2 to 0.6 s, relative to real/surrogate distractor onset) were calculated using the multitaper method with a target frequency of 80 (±30) Hz. For each participant, an anatomically realistic single-shell headmodel based on the cortical surface was

generated from individual head shapes (Nolte, 2003). A grid with 0.5 cm resolution was normalized on an MNI template, and then morphed into the brain volume of each participant. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was used to estimate the spatial distribution of power for time-frequency window of interest (0.1-0.3 s post-distractor onset, 60 to 100Hz).

2.6.3 Gamma Band (Source Level): Analysis

For each participant, we estimated source-level activity (0.1-0.3 s post-distractor onset, 60 to 100Hz) for each cue category (informative and uninformative) and for both cue categories concatenated. We performed two analyses:

(1) In order to characterize the brain areas activated in the gamma band during the distracting sound presentation, distractor-locked gamma activity was contrasted to surrogate distractor-locked gamma activity

(2) In order to investigate the interaction between distractor response and cue information, surrogate-corrected gamma activity in the informative cue condition was contrasted to surrogate-corrected gamma activity in the uninformative cue condition.

Both tests have been carried out using non-parametric cluster-based permutation analysis (Maris and Oostenveld 2007). Please note, that for these tests, cluster permutations control for multiple comparisons in the source space dimension.

2.6.4 Gamma Band (Source Level): Connectivity Analysis

The aim of this analysis was to identify the brain regions that could be functionally connected in the gamma band to the auditory cortices during the presentation of the distracting sound. We have extracted the complex values containing phase information into source space using partial canonical coherence (PCC) beamformer, a computationally efficient alternative to the DICS that provides the possibility of extracting both power and phase information on the source level. For each participant:

(1) Similarly, to the DICS beamformer, data from both surrogate and real distractors were concatenated, and cross-spectral density (CSD) matrix (-0.2 to 0.6 s, relative to real/surrogate distractor onset) were calculated using the multitaper method with a target frequency of 80 (±30) Hz. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was used to estimate the spatial

distribution of power and phase for the time-frequency window of interest (0.1-0.3s post-distractor onset, 60 to 100Hz).

(2) One auditory region of interest (ROI) was defined by including, in both hemispheres, the Broadmann areas 22, 41 and 42, according to the Talairach Tournoux atlas (Talairach and Tournoux 1988; Lancaster et al. 1997).

(3) Phase synchrony (Lachaux et al. 1999) between each voxel in the auditory ROIs and all other voxels was calculated, averaged across voxels of the auditory ROI, and then Fisher Z transformed. Thus, for each extra-auditory brain voxel, a single phase synchrony value with the entirety of the auditory ROI was obtained.

Finally, distractor-locked gamma phase synchrony was contrasted to surrogate distractor-locked gamma phase synchrony using non-parametric cluster-based permutation analysis (Maris and Oostenveld 2007). Please note, that for this test, cluster permutations control for multiple comparisons in the source space dimension.

3 Results

3.1 Behavioral Analysis

Participants correctly performed the discrimination task in 96.04 ± 0.29 SEM % of the trials. The remaining trials were either incorrect trials (3.95 ± 0.29 SEM %), missed trials (0.27 ± 0.06 %) or trials with FAs (0.02 ± 0.01 %).

3.1.1.1 Median Reaction Times

We found a significant main effect of cue category ($F(1, 20) = 4.9$, $p = 0.02$, $\eta^2 = 0.36$) on median reaction times in correct trials. Participants were faster when the cue was informative in comparison to the uninformative cue. In addition, we found a significant main effect of the distractor condition ($F(2, 42) = 34.2$, $p < 0.01$, $\eta^2 = 0.49$). Post-hoc tests indicated that, in comparison to the NoDIS condition, participants were faster in the early DIS1 condition ($p < 0.001$) but slower in the late DIS2 condition ($p < 0.001$). Participants were also faster in the early DIS1 than in the late DIS2 condition ($p < 0.001$). No interaction effect was found significant.

3.1.1.2 Percentage of Incorrect Responses

Only a main effect of the distractor condition ($F(2, 42) = 3.8$, $p = 0.02$, $\eta^2 = 0.17$) was found significant on the percentage of incorrect responses. Post-hoc tests indicated that participants, committed more errors in the late DIS2 condition in comparison to the NoDIS ($p = 0.02$) and early DIS1 ($p = 0.07$) conditions.

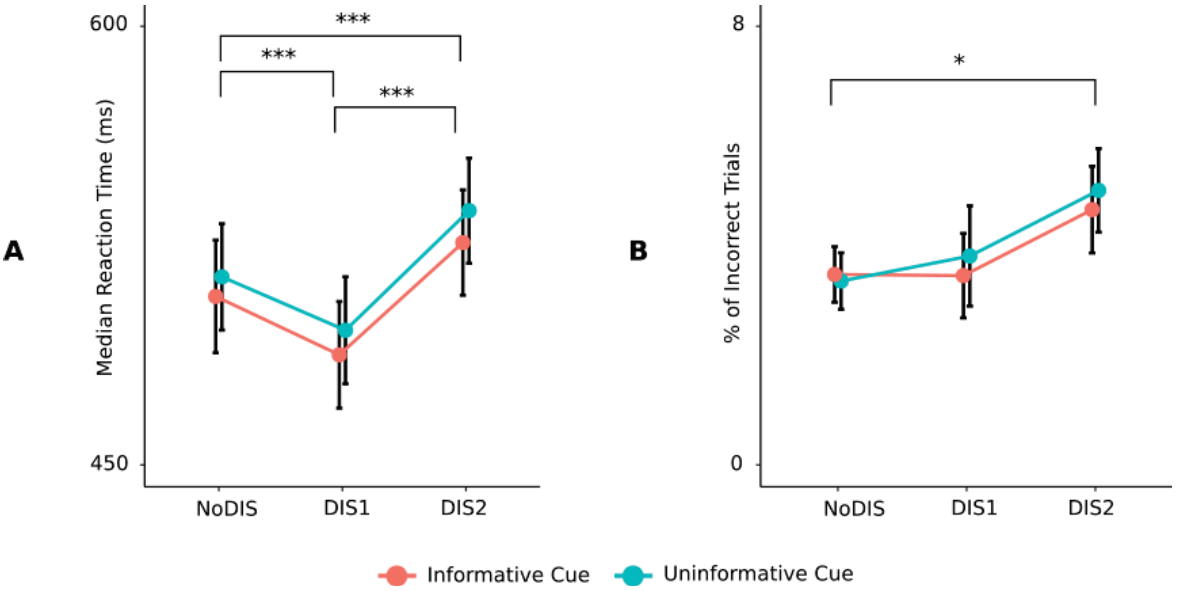


Figure 3. A. Median Reaction Times (RTs) according to cue and distractor conditions. **B.** Percentage of Incorrect Responses according to cue and distractor conditions. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Error bars represent SEM.

3.2 Gamma Activity Analysis

3.2.1 Gamma Sensor Level Activation

Real-distractor high-frequency activity was contrasted to that of surrogate-distractor using non-parametric cluster-based permutation testing. As shown in Figure 4, this contrast revealed one significant positive cluster (p = 0.002) indicating an increase in gamma activity centered spatially around left and right temporal sensors (Fig 4A), temporally between 0.1 and 0.3s post-distractor onset (Fig 4B & C), and frequency-wise, between 60 and 100 Hz (Fig 4B & D).

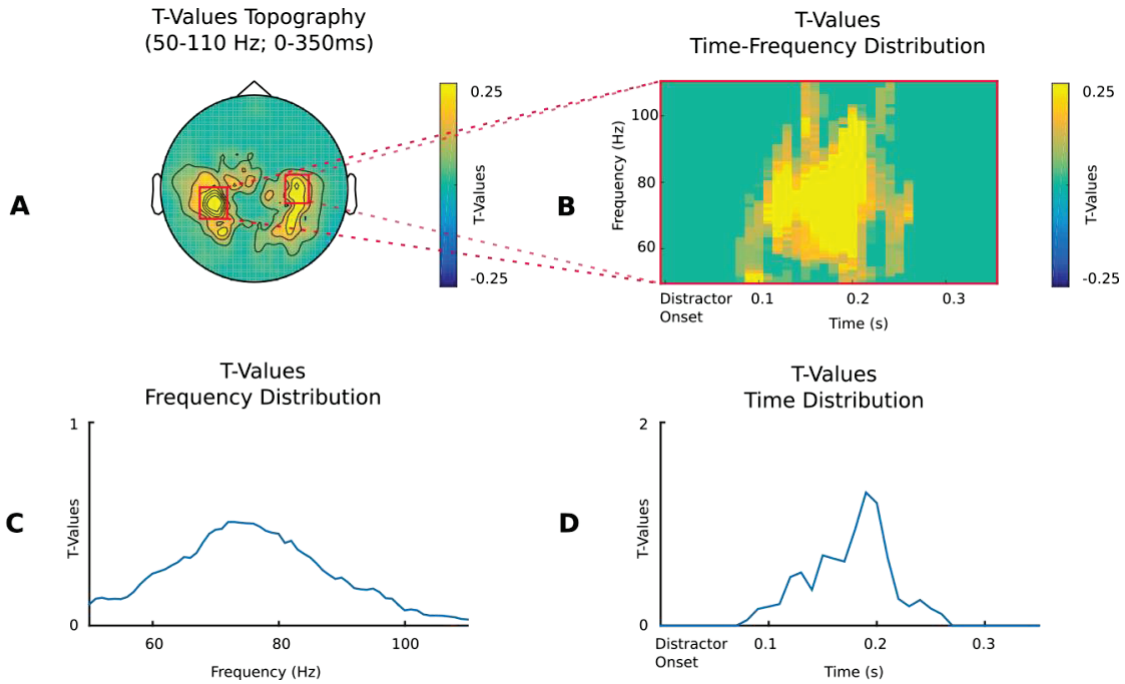


Figure 4. Gamma activity to distractor at the sensor level. A. Topographical maps averaged between 50-110 Hz and 0-0.35 seconds post-distractor onset, of the t-values, masked at $p < 0.05$ of the contrast between distractor and surrogate distractor gamma activity. **B.** Time-frequency representations of the t-values (of the aforementioned test) of the sensors highlighted by red boxes in A. **C.** Frequency distribution of t-values of the aforementioned sensors averaged across the time dimension. **D.** Time distribution of t-values of the aforementioned sensors averaged across the frequency dimension.

3.2.2 Gamma Source Level Activation

The aim of this test was to highlight the regions driving gamma activity observed at the sensor level. Based upon the sensor level results, we have computed DICS beamformer sources for each participant between 60-100Hz and 0.1-0.3s post-distractor. Real-distractor gamma activity was contrasted to that of surrogate distractors using non-parametric cluster-based permutation testing. A significant positive cluster ($p < 0.01$) indicating an increase in gamma activity notably in (1) the left and right auditory cortices, (2) the left and right tempo-parietal junctions, and (3) the right ventrolateral prefrontal cortex (vlPFC). Other regions included the calcarine, the anterior, middle and posterior cingulate gyri, the inferior temporal gyri and the Precuneus.

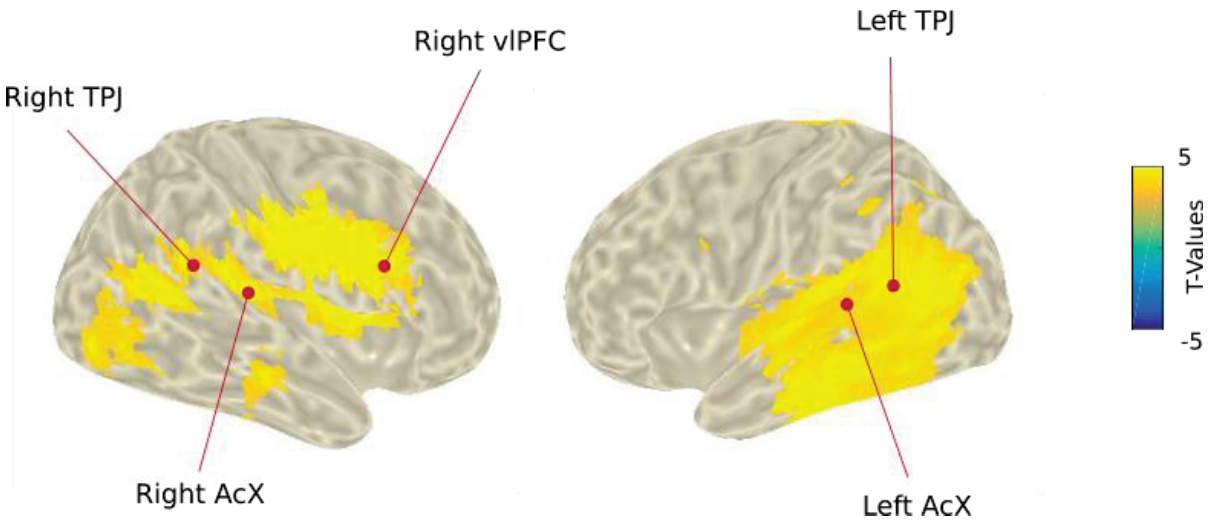


Figure 5. Gamma activity to distractor at the source level. Distributions of T-values, masked at *p<0.05*, from Cluster Based Permutation tests contrasting real and surrogate distractor gamma activity (60-100Hz and 0.1-0.3 post-distractor) at the source level. AcX: Auditory Cortex. TPJ: temporo-parietal junction. vlPFC: ventrolateral prefrontal cortex.

3.2.3 Gamma Source Level Cue Effect Comparison

To investigate the effect of top-down attention on bottom-up processing, we analysed the effect of cue information on the gamma response to distracting sounds. For each participant, real distractor source-level data (60-100 Hz, 0.1-0.3s) were baseline corrected by subtracting surrogate-distractor activity. Corrected distractor gamma activity was contrasted between the two cue categories (informative vs. uninformative) using non-parametric cluster-based permutation testing. A significant cluster (p = 0.014) extended notably to (1) the left dorsomedial and ventromedial prefrontal cortices, and (2) the left anterior cingulate gyrus. Other regions included the left pre- and post- central gyri, the left supplementary motor area, the left superior parietal lobule. All these regions displayed a significantly higher activation when the distracting sound was preceded by an informative cue rather than an uninformative cue.

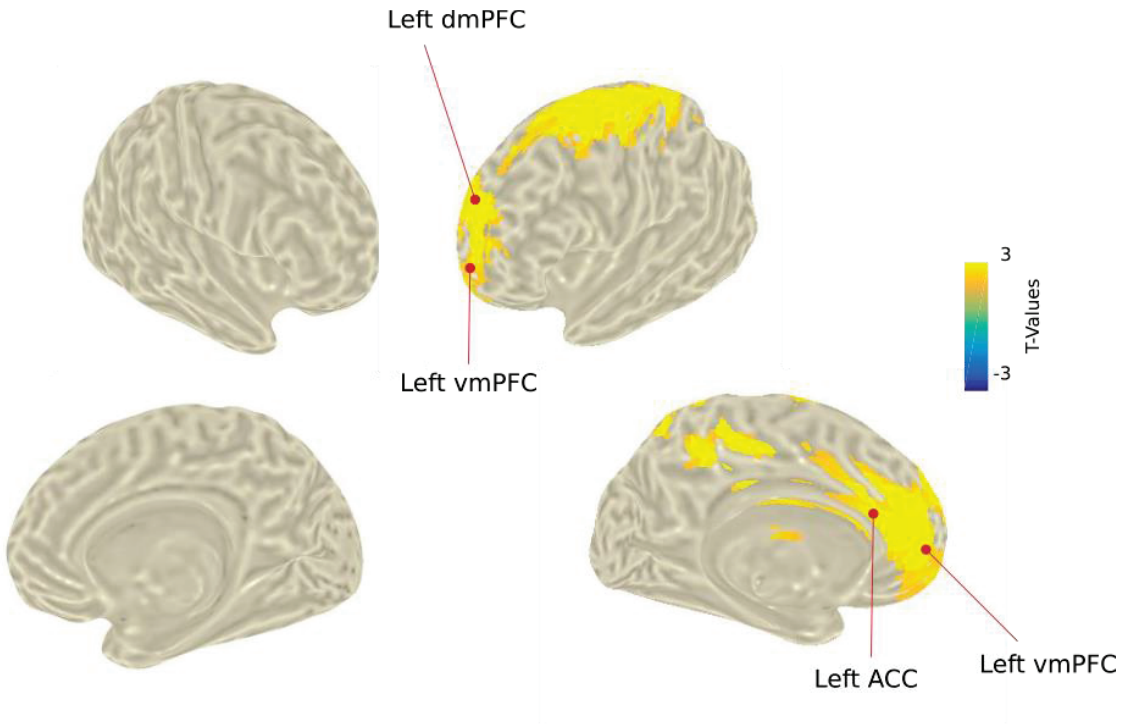


Figure 5. Top-down modulation of gamma activity to distractor at the source level. Distributions of T-values, masked at *p<0.05*, from Cluster Based Permutation tests contrasting surrogate-corrected distractor gamma activity (60-100Hz and 0.1-0.3 post-distractor) within informative and uninformative cue conditions. dmPFC: dorsomedial prefrontal cortex. vmPFC: ventromedial prefrontal cortex. ACC: anterior cingulate cortex.

3.2.4 Gamma Source Level Connectivity Analysis

Real-distractor phase synchrony (both auditory ROIs averaged being the reference) in the gamma band (60-100 Hz, 0.1-0.3s) was contrasted to that of surrogate distractors using non-parametric cluster-based permutation testing. A significant cluster ($p < 0.01$) indicated an increase in gamma synchrony notably in the ventrolateral and the dorsolateral prefrontal cortex in both hemispheres. Other regions included the pre- and post- central gyri, the supplementary motor areas, the frontal eye fields and the paracentral lobule, in the left hemisphere.

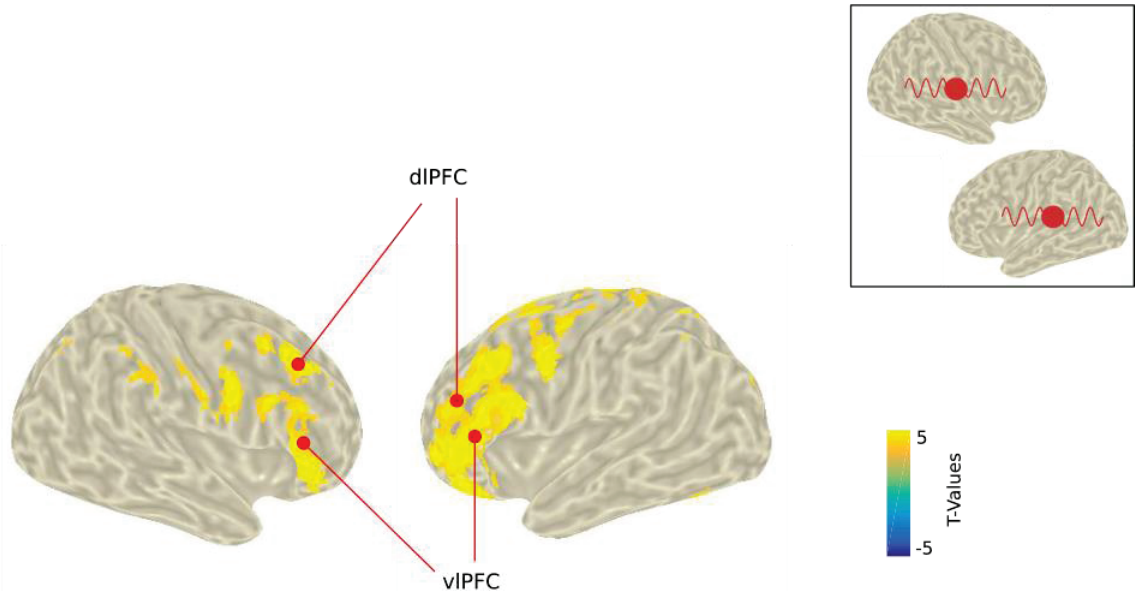


Figure 6. Gamma connectivity to distractor at the source level. Distributions of T-values, masked at *p<0.05*, from Cluster Based Permutation tests contrasting real and surrogate distractor gamma phase synchrony (60-100Hz and 0.1-0.3 post-distractor) at the source level between the auditory ROI and all other cortical regions. dlPFC: dorsolateral prefrontal cortex. vlFPC: ventrolateral prefrontal cortex.

4 Discussion

In the present study, we have demonstrated that in response to a salient unexpected distracting sound, the auditory cortices and the temporo-parietal junctions in both hemispheres, and the right ventrolateral PFC were activated in the gamma band. In addition, modulation by top-down attention of gamma activity to distracting sound was found in the left dorsomedial and ventromedial prefrontal cortices. Finally, we have evidenced synchrony in the gamma band between regions in the dorsolateral and ventrolateral prefrontal cortices and the auditory cortices during distracting sound processing.

4.1 Behavioral measures of TD and BU attentional mechanisms

Behaviorally, participants discriminated the target pitch faster in trials with an informative cue in comparison to trials with an uninformative cue. This effect is in agreement with several previous studies (Golob et al. 2002; Bidet-Caulet et al. 2014; ElShafei et al. 2018). It is most likely related to differences in TD anticipatory attention since the informative cue provided additional information solely about the location of the target and not about its category neither its mapped response, leading to equivalent motor preparation across conditions.

In trials with distracting sounds, participants responded faster to the following target in trials with early distracting sounds rather than with late distracting sounds. This pattern can be explained in light of the phenomena triggered by a distracting sound (Bidet-Caulet et al., 2014; Masson and Bidet-Caulet, 2018): (1) a persistent increase in arousal resulting in RT reduction (behavioral benefit) and (2) a strong transient attentional capture (exogenous orienting) leading to RT augmentation (behavioral cost); with the behavioral net effect of distracting sound varying according to the time interval between the distracting and the target sounds. Importantly, we also found that participants were less accurate to discriminate the auditory targets when preceded by late distracting sounds in comparison to the no distractor condition. This result provides further evidence of a detrimental behavioral effect of distracting sounds which orient attention away from the task at hand.

Therefore, these behavioral results demonstrate that, in the CAT paradigm, TD attention is enhanced in trials with informative cue, and that a strong transient bottom-up attentional capture is triggered by distracting sounds.

4.2 Activation of the Ventral Bottom-Up Attentional Network in the Gamma band

In line with our hypothesis, in response to an unexpected salient distracting sound, we have observed an increase in gamma activity in the left and right auditory cortices, the bilateral temporo-parietal junctions, and the right ventrolateral frontal cortex. This present result is highly consistent with the proposal by Corbetta and Shulman (2002 and 2008), based on functional magnetic resonance imaging (fMRI) studies of visual attention, that the ventral attention system, involved in bottom-up attention, includes the temporo-parietal junction and the ventral frontal cortex. This present finding is also in agreement with fMRI (e.g. Salmi et al. 2009; Alho et al. 2014; Salo et al. 2017) and MEG/EEG (e.g. Ahveninen et al. 2013) studies in the auditory modality. In addition, the right lateralization of the frontal activation is consistent with findings of a ventral network predominantly localized to the right hemisphere in the visual modality (Corbetta and Shulman 2002; review in Corbetta et al. 2008). Also, the bilateral activation of the TPJ is in line with a meta-analysis showing stronger activation of the left TPJ to auditory than to visual irrelevant oddball stimuli (review in Kim 2014).

Importantly, we found that the gamma activation in the ventral network in response to distracting sounds lasted from 100 to 300ms after distracting sound onset. This result confirms that BU attentional capture is a rapid and transient phenomenon, in agreement with a behavioral cost observed only for late distracting sounds offsetting between 50 and 350 ms before target onset. Such activation in high frequency gamma oscillations is also consistent with the fast nature of the attentional capture phenomenon. Finally, it is worth noting that the activation of the ventral attentional network was found in response to entirely task-irrelevant distracting sounds, contrary to earlier studies which suggested that task-relevance rather than saliency is critical to the engagement of the ventral network (Serences et al. 2005; Indovina and Macaluso 2007; Corbetta et al. 2008). The short duration of the ventral network activation might have precluded its observation using techniques with low temporal resolution (fMRI) in these studies.

4.3 The PFC and the balance between TD and BU attentional mechanisms

We did not find any significant effect of cue information on gamma activity within the regions of the ventral attentional network, suggesting no direct influence of top-down attention on this bottom-up attention network. However, in several regions of the left prefrontal cortex,

notably (and contrary to our original hypothesis) in the dorso- and ventro-medial prefrontal cortices and the anterior cingulate cortex (ACC), gamma activity was more pronounced in response to distracting sounds preceded by an informative cue rather than an uninformative cue.

These medial frontal regions have been hypothesized to play a role in the inhibition of irrelevant stimuli with an increase in the activation of these regions during presentation of irrelevant salient stimuli (e.g. Rule et al. 2002; Salmi et al. 2009). In the non-human primate auditory system, such role is supported by cortico-cortical connections between these regions (the medial PFC and the ACC) and inhibitory neurons in auditory association regions in order to suppress irrelevant signals (Matsumoto and Tanaka 2004; Barbas et al. 2005, 2012; Medalla et al. 2007). Importantly, electrical stimulation of the ACC has been shown to reduce auditory evoked activity in non-human primate superior temporal cortices (Müller-Preuss et al. 1980; Müller-Preuss and Ploog 1981), providing direct evidence of an inhibitory role of these medial frontal regions. Therefore, in the present study, the larger gamma activation of the medial PFC regions and the ACC, during distracting sounds preceded by an informative cue, could reflect a strong and fast inhibitory signal to regions involved in the processing of task-irrelevant information. This stronger inhibition could result from an increased top-down attention load with informative cues, in line with shorter reaction times, compared to trials with uninformative cues.

The medial prefrontal localization of such regions contradicts our original hypothesis that more lateral prefrontal regions would play a prominent role in orchestrating the interplay between TD and BU attentional mechanisms, as suggested by previous studies using fMRI in human subjects (Fox et al. 2006; Corbetta et al. 2008; Alho et al. 2014; Katsuki and Constantinidis 2014; Vossel et al. 2014). However, we believe that such role for the lPFC cannot be ruled out. As evidenced in the non-human primate brain, the ACC has excitatory and inhibitory connections to the anterior and posterior parts of the lPFC, respectively (Medalla and Barbas 2010), with the former momentarily suspending current tasks and the latter facilitating attentional switch to a novel task (review in Barbas et al. 2012). In the context of the present paradigm, (1) a stronger ACC to lPFC signal could facilitate switching from the TD task to the BU distracting sound processing, and vice versa, and (2) the opposite effects on the anterior and posterior parts of the lPFC combined to the insufficient spatial resolution of MEG could preclude the observation of significant gamma activation in the lPFC.

To the best of our knowledge, this is the first study, to utilize gamma activity to highlight the potential role of the prefrontal cortex in subtending the balance between top-down and bottom-up attentional mechanisms. Both the medial PFC and the ACC were more activated during bottom-up processing of distracting sound under increased TD attentional load. They could orchestrate the interplay between top-down and bottom-up attention by (1) exercising a TD inhibitory attentional control via direct projection to the auditory cortices, and (2) by controlling task-switching between TD and BU brain operations via projections to the lateral PFC. Therefore, the brain regions supporting the interaction between TD and BU attention would not be part of the ventral nor of the dorsal attentional networks. This is in line with earlier studies suggesting that dorsal and ventral networks would not directly interact but would be linked through other regions of the prefrontal cortex (e.g. Fox et al. 2006).

4.4 Functional Connectivity During Distractor Processing

Finally, we have demonstrated that during the presentation of a distracting sound, gamma activity was synchronous between the auditory cortices and several distant brain regions, notably the dorso- and ventro-lateral prefrontal cortices. As discussed above, the lateral prefrontal cortex is a recurrent candidate for the interaction between dorsal and ventral networks of attention in both the visual (Buschman and Miller 2007; Corbetta et al. 2008; Katsuki and Constantinidis 2014) and the auditory (Salmi et al. 2009; Alho et al. 2014) domains.

Specifically, the lPFC seems to play an important role in bottom-up attentional mechanisms. fMRI studies suggest that the lPFC is involved in attentional capture in both auditory (Watkins et al. 2007) and visual (Han and Marois 2014) modalities with its activation being associated with the inhibition of distraction responses (Dolcos et al. 2007; Suzuki and Gottlieb 2013) and with reduced activity in the lPFC being linked to impaired distraction processing (Gaebler et al. 2015). In addition, it has been demonstrated that activity in the lPFC (specifically the dorsolateral prefrontal cortex) correlates with distractor suppression (Suzuki and Gottlieb 2013; Yan et al. 2016), and that lPFC stimulation decreases susceptibility to attentional capture (Cosman et al. 2015). Thus, the lateral PFC could be attributed a role in cognitive inhibitory control.

We have discussed above how gamma power modulations in the ACC and the medial PFC would reflect top-down attentional control. We posit that the lateral PFC, through gamma phase modulations, could also play a complementary role in the propagation of this top-down

signal. We suggest that gamma connectivity between the lateral PFC and the auditory cortices (investigated here) and the medial PFC and ACC (to be investigated in future research) reflects the propagation of the inhibitory (control) top-down signal aimed to filter out task irrelevant distracting sounds in anticipation of the upcoming relevant target sound. This interpretation is in line with the Communication-Through-Coherence (CTC) hypothesis which proposes that anatomical connections are dynamically rendered effective or ineffective through the presence or absence of rhythmic synchronization, particularly in the gamma band (Fries 2005).

Moreover, this suggested link between the lateral and medial subdivisions of the prefrontal cortex is in line with previous studies highlighting high interconnectivity between the lateral and medial PFC (Miller and Cohen 2001; Cole et al. 2013). In their study, Cole and colleagues (2013) demonstrated that the lateral PFC along with the posterior parietal cortex, constitute a highly flexible connectivity hub that could be involved in implementing task demands by biasing information flow across multiple large-scale functional networks. Thus, the lateral PFC could act as an inhibitory (control) signal relay hub between nodes of the ventral bottom-up network (e.g. the auditory cortex) and the medial PFC and ACC.

Finally, to our surprise, we found no synchrony in the gamma band between the auditory cortices and other nodes of the ventral attentional network, such as the temporo-parietal junction or the ventrolateral frontal cortex. An interpretation is that the non-synchronized gamma activation of the ventral network nodes (i.e. TPJ, ventrolateral frontal cortex and auditory cortex) would reflect only the involuntary processing of the distracting sound in separate brain regions; while the lPFC synchrony with each of these nodes would contribute to the suppression of such involuntary processing.

5 Conclusion

Using the high temporal and spatial resolution of magnetoencephalography, we demonstrate for the first time, in the human brain, how gamma oscillations would support activation and communication within the ventral BU attentional network and its interaction with TD attention. This corroborates the proposed role for gamma oscillations as a promoter of rapid transfer of information through the cortical hierarchy (Sedley and Cunningham 2013). Moreover, we suggest that this finding fits in a wider framework proposing that activity in different attentional networks would be supported by different frequency bands. More precisely, slow oscillations (namely alpha) would support more top-down attentional mechanisms, while faster oscillations (namely gamma) would support more bottom-up attentional mechanisms (Buschman and Miller 2007). Importantly, we have provided evidence that the medial prefrontal cortex would support the balance between top-down and bottom-up mechanisms of attention, while the lateral prefrontal cortex would potentially regulate the processing of distracting sounds.

6 References

Ahveninen J, Huang S, Belliveau JW, Chang W-T, Hämäläinen M. 2013. Dynamic oscillatory processes governing cued orienting and allocation of auditory attention. Psychologist. 26:194–198.

Akimoto Y, Kanno A, Kambara T, Nozawa T, Sugiura M, Okumura E, Kawashima R. 2013. Spatiotemporal Dynamics of High-Gamma Activities during a 3-Stimulus Visual Oddball Task. PLoS One. 8:1–12.

Akimoto Y, Nozawa T, Kanno A, Ihara M, Goto T, Ogawa T, Kambara T, Sugiura M, Okumura E, Kawashima R. 2014. High-gamma activity in an attention network predicts individual differences in elderly adults' behavioral performance. Neuroimage. 100:290–300.

Albouy P, Mattout J, Bouet R, Maby E, Sanchez G, Aguera PE, Daligault S, Delpuech C, Bertrand O, Caclin A, Tillmann B. 2013. Impaired pitch perception and memory in congenital amusia: The deficit starts in the auditory cortex. Brain. 136:1639–1661.

Alho K, Salmi J, Koistinen S, Salonen O, Rinne T. 2014. Top-down controlled and bottom-up triggered orienting of auditory attention to pitch activate overlapping brain networks. Brain Res. 1626:1–10.

Asplund CL, Todd JJ, Snyder AP, Marois R. 2010. A central role for the lateral prefrontal cortex in goal-directed and stimulus-driven attention. Nat Neurosci. 13:507–512.

Baldauf D, Desimone R. 2014. Neural Mechanisms of object-based attention. Science (80-). 344:420–424.

Barbas H, Bunce JG, Medalla M. 2012. Prefrontal pathways that control attention. Princ Front lobe Funct. 31–48.

Barbas H, Medalla M, Alade O, Suski J, Zikopoulos B, Lera P. 2005. Relationship of prefrontal connections to inhibitory systems in superior temporal areas in the rhesus monkey. Cereb Cortex. 15:1356–1370.

Bastos AM, Vezoli J, Bosman CA, Schoffelen J-MM, Oostenveld R, Dowdall JR, DeWeerd P, Kennedy H, Fries P, De Weerd P, Kennedy H, Fries P. 2015. Visual areas exert feedforward and feedback influences through distinct frequency channels. Neuron. 85:390–401.

Bates D, Mächler M, Bolker B, Walker S. 2014. Fitting linear mixed-effects models using lme4. arXiv Prepr arXiv14065823.

Bidet-Caulet A, Bottemanne L, Fonteneau C, Giard M-H, Bertrand O. 2014. Brain Dynamics of Distractibility: Interaction Between Top-Down and Bottom-Up Mechanisms of Auditory Attention. Brain Topogr. 28:423–436.

Buschman TJ, Miller EK. 2007. Top-Down Versus Bottom-Up Control of Attention in the Prefrontal and Posterior Parietal Cortices. Science (80-). 8–11.

Cole MW, Reynolds JR, Power JD, Repovs G, Anticevic A, Braver TS. 2013. Multi-task connectivity reveals flexible hubs for adaptive task control. Nat Neurosci. 16:1348–1355.

Corbetta M, Patel G, Shulman G. 2008. The reorineting system of the human brain: From environment to theory of mind. Neuron. 58:306–324.

Corbetta M, Shulman GL. 2002. Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci. 3:201.

Cosman JD, Atreya P V, Woodman GF. 2015. Transient reduction of visual distraction following electrical stimulation of the prefrontal cortex. Cognition. 73–76.

Dalton P, Hughes RW. 2014. Auditory attentional capture: Implicit and explicit approaches. Psychol Res. 78:313–320.

Desimone R, Duncan J. 1995. Neural mechanisms of selective visual attention. Annu Rev

Neurosci. 18:193–222.
Dolcos F, Miller B, Kragel P, Jha A, McCarthy G. 2007. Regional brain differences in the effect of distraction during the delay interval of a working memory task. Brain Res. 1152:171–181.
ElShafei HA, Bouet R, Bertrand O, Bidet-Caulet A. 2018. Two Sides of the Same Coin: Distinct Sub-Bands in the Alpha Rhythm Reflect Facilitation and Suppression Mechanisms during Auditory Anticipatory Attention. Eneuro. ENEURO.0141-18.2018.
Escera C, Alho K, Winkler I, Näätänen R. 1998. Neural mechanisms of involuntary attention to acoustic novelty and change. J Cogn Neurosci. 10:590–604.
Fox MD, Corbetta M, Snyder AZ, Vincent JL, Raichle ME. 2006. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proc Natl Acad Sci. 103:9381–9386.
Frey JN, Mainy N, Lachaux J-P, Muller N, Bertrand O, Weisz N. 2014. Selective Modulation of Auditory Cortical Alpha Activity in an Audiovisual Spatial Attention Task. J Neurosci. 34:6634–6639.
Fries P. 2005. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends Cogn Sci. 9:474–480.
Fries P, Reynolds JH, Rorie AE, Desimone R. 2001. Modulation of oscillatory neuronal synchronization by selective visual attention. Science (80-). 291:1560–1563.
Gaebler AJ, Mathiak K, Koten JW, König AA, Koush Y, Weyer D, Depner C, Matentzoglu S, Edgar JC, Willmes K, Zvyagintsev M. 2015. Auditory mismatch impairments are characterized by core neural dysfunctions in schizophrenia. Brain. 138:1410–1423.
Golob EJ, Pratt H, Starr A. 2002. Preparatory slow potentials and event-related potentials in an auditory cued attention task. Clin Neurophysiol. 113:1544–1557.
Gregoriou GG, Gotts SJ, Zhou H, Desimone R. 2009. High-Frequency, long-range coupling between prefrontal and visual cortex during attention. Science (80-). 324:1207–1210.
Gross J, Kujala J, Hämäläinen M, Timmermann L, Schnitzler A, Salmelin R. 2001. Dynamic imaging of coherent sources: studying neural interactions in the human brain. Proc Natl Acad Sci. 98:694–699.
Han SW, Marois R. 2014. Functional Fractionation of the Stimulus-Driven Attention Network. J Neurosci. 34:6958–6969.
He BJ, Snyder AZ, Vincent JL, Epstein A, Shulman GL, Corbetta M. 2007. Breakdown of Functional Connectivity in Frontoparietal Networks Underlies Behavioral Deficits in Spatial Neglect. Neuron. 53:905–918.
Indovina I, Macaluso E. 2007. Dissociation of stimulus relevance and saliency factors during shifts of visuospatial attention. Cereb Cortex. 17:1701–1711.
Jensen O, Mazaheri A. 2010. Shaping Functional Architecture by Oscillatory Alpha Activity: Gating by Inhibition. Front Hum Neurosci. 4:1–8.
Katsuki F, Constantinidis C. 2014. Bottom-up and top-down attention: Different processes and overlapping neural systems. Neuroscientist. 20:509–521.
Kim H. 2014. Involvement of the dorsal and ventral attention networks in oddball stimulus processing: A meta-analysis. Hum Brain Mapp. 35:2265–2284.
Kim YH, Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Mesulam MM. 1999. The large-scale neural network for spatial attention displays multifunctional overlap but differential asymmetry. Neuroimage. 9:269–277.
Klimesch W, Sauseng P, Hanslmayr S. 2007. EEG alpha oscillations: The inhibition–timing hypothesis. Brain Res Rev. 53:63–88.

Lachaux JP, Rodriguez E, Martinerie J, Varela FJ. 1999. Measuring phase synchrony in brain signals. Hum Brain Mapp. 8:194–208.

Lancaster JL, Rainey LH, Summerlin JL, Freitas CS, Fox PT, Evans AC, Toga AW, Mazziotta JC. 1997. Automated labeling of the human brain: a preliminary report on the development and evaluation of a forward-transform method. Hum Brain Mapp. 5:238.

Lee B, Park KS, Kang D-H, Kang KW, Kim YY, Kwon JS. 2007. Generators of the gamma-band activities in response to rare and novel stimuli during the auditory oddball paradigm. Neurosci Lett. 413:210–215.

Maris E, Oostenveld R. 2007. Nonparametric statistical testing of EEG- and MEG-data. J Neurosci Methods. 164:177–190.

Masson R, Bidet-Caulet A. 2018. Fronto-central P3a to distracting sounds: an index of their arousing properties. bioRxiv. 333419.

Matsumoto K, Tanaka K. 2004. The role of the medial prefrontal cortex in achieving goals. Curr Opin Neurobiol. 14:178–185.

Medalla M, Barbas H. 2010. Anterior cingulate synapses in prefrontal areas 10 and 46 suggest differential influence in cognitive control. J Neurosci. 30:16068–16081.

Medalla M, Lera P, Feinberg M, Barbas H. 2007. Specificity in Inhibitory Systems Associated with Prefrontal Pathways to Temporal Cortex in Primates. Cereb Cortex. 17:i136–i150.

Michels L, Bucher K, Lüchinger R, Klaver P, Martin E, Jeanmonod D, Brandeis D. 2010. Simultaneous EEG-fMRI during a working memory task: Modulations in low and high frequency bands. PLoS One. 5.

Miller E, Cohen J. 2001. An integrative theory of prefrontal cortex function. Annu Rev Neurosci. 167–202.

Müller-Preuss P, Newman JD, Jürgens U. 1980. Anatomical and physiological evidence for a relationship between the “cingular” vocalization area and the auditory cortex in the squirrel monkey. Brain Res. 202:307–315.

Müller-Preuss P, Ploog D. 1981. Inhibition of auditory cortical neurons during phonation. Brain Res. 215:61–76.

Nolte G. 2003. The magnetic lead field theorem in the quasi-static approximation and its use for magnetoencephalography forward calculation in realistic volume conductors. Phys Med Biol. 48:3637.

Parmentier FBR, Andrés P. 2010. The Involuntary Capture of Attention by Sound. Exp Psychol. 57:68–76.

Petersen S., Posner M. 2012. The attention system of the human brain: 20 years after. Annu Rev Neurosci. 21:73–89.

Posner MI, Petersen S. 1990. The attention system of the human brain. Annu Rev Neurosci. 13:25–42.

Ray S, Niebur E, Hsiao SS, Sinai A, Crone NE. 2008. High-frequency gamma activity (80-150 Hz) is increased in human cortex during selective attention. Clin Neurophysiol. 119:116–133.

Richter CG, Thompson WH, Bosman CA, Fries P. 2017. Top-Down Beta Enhances Bottom-Up Gamma. J Neurosci. 37:6698–6711.

Rule RR, Shimamura AP, Knight RT. 2002. Orbitofrontal cortex and dynamic filtering of emotional stimuli. Cogn Affect Behav Neurosci. 2:264–270.

Salmi J, Rinne T, Koistinen S, Salonen O, Alho K. 2009. Brain networks of bottom-up triggered and top-down controlled shifting of auditory attention. Brain Res. 1286:155–164.

Salo E, Salmela V, Salmi J, Numminen J, Alho K. 2017. Brain activity associated with selective attention, divided attention and distraction. Brain Res. 1664:25–36.

Schröger E. 1996. A Neural Mechanism for Involuntary Attention Shifts to Changes in Auditory Stimulation. J Cogn Neurosci. 8:527–539.

Searle SR, Speed FM, Milliken GA. 1980. Population marginal means in the linear model: an alternative to least squares means. Am Stat. 34:216–221.

Sedley W, Cunningham MO. 2013. Do cortical gamma oscillations promote or suppress perception? An under-asked question with an over-assumed answer. Front Hum Neurosci. 7:595.

Serences JT, Shomstein S, Leber AB, Golay X, Egeth HE, Yantis S. 2005. Coordination of Voluntary and Stimulus-Driven Attentional Control in Human Cortex. Psychol Sci. 16:114.

Suzuki M, Gottlieb J. 2013. Distinct neural mechanisms of distractor suppression in the frontal and parietal lobe. Nat Neurosci. 16:98–104.

Talairach J, Tournoux P. 1988. Co-planar stereotaxic atlas of the human brain: 3-dimensional proportional system: an approach to cerebral imaging.

Tallon-Baudry, Bertrand. 1999. Oscillatory gamma activity in humans and its role in object representation. Trends Cogn Sci. 3:151–162.

Team RC. 2014. R: A Language and Environment for Statistical Computing. Vienna: R Foundation for Statistical Computing. Available online at: h ttp. www R-project org.

Von Békésy G, Wever EG. 1960. Experiments in hearing. McGraw-Hill New York.

Vossel S, Geng JJ, Fink GR. 2014. Dorsal and ventral attention systems: Distinct neural circuits but collaborative roles. Neuroscientist. 20:150–159.

Watkins S, Dalton P, Lavie N, Rees G. 2007. Brain Mechanisms Mediating Auditory Attentional Capture in Humans. Cereb Cortex.

Yan Y, Wei R, Zhang Q, Jin Z, Li L. 2016. Differential roles of the dorsal prefrontal and posterior parietal cortices in visual search: A TMS study. Sci Rep. 6:1–9.

8.3 Supplementary Study III: Early Distractor-Related Alpha Activity (CAT3.0)

8.3.1 Introduction

In the previous study, we investigated gamma responses to distracting sounds. We were also interested in exploring alpha responses to the same sounds, specifically, to investigate how the alpha synchronization/desynchronization pattern, previously demonstrated in distractor-free trials (**Study I**), would be re-established after the presentation of a distracting sound. In order to ensure that we investigate a time period where several alpha cycles can occur, we have restricted our alpha analyses to the early distractors (offsetting 350-650ms before the onset of the target sound).

8.3.2 Material and Methods

8.3.2.1 Definition of Early Distractor-Related Alpha Activity: Sensor Level

Similarly, to the gamma activity analysis, the goal of this step was to define the time-frequency range of alpha activity of interest. First, to obtain a baseline clear of cue-related activity, we have created surrogate early distractors in the NoDIS trials. Afterwards, the oscillatory power, of early distractor and (surrogate distractor) trials was calculated using Morlet Wavelet decomposition with a width of four cycles per wavelet (m=7; Tallon-Baudry and Bertrand 1999) at center frequencies between 5 and 15 Hz, in steps of 1 Hz and 50 ms. Activity between -0.1 and 0.65s relative to distractor onset and 5-15Hz was contrasted between distractor and surrogate trials using a nonparametric cluster-based permutation analysis (Maris and Oostenveld 2007).

8.3.2.2 Definition of Early Distractor-Related Alpha Activity: Source Level

Based upon the previous step, we have defined a time-frequency window of interest (0.35-0.65 s post-distractor onset, 7 to 13Hz). We have utilized the frequency–domain adaptive spatial technique of dynamical imaging of coherent sources (DICS) in order to estimate the brain regions driving sensor-level distractor-related alpha activity. Data, from both surrogate and real distractors were concatenated, and cross-spectral density (CSD) matrix (-0.2 to 0.7 s, relative to real/surrogate distractor onset) were calculated using the multitaper method with a target frequency of **10** (±4) Hz. For each participant, an anatomically realistic single-shell headmodel based on the cortical surface was generated from individual head shapes (Nolte,

2003). A grid with 0.5 cm resolution was normalized on an MNI template, and then morphed into the brain volume of each participant. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was used to estimate the spatial distribution of power for time-frequency window of interest.

Afterwards, in order to characterize the brain areas activated in the alpha band following the presentation of the distracting sound, distractor-related alpha activity was contrasted to surrogate distractor-related alpha activity using non-parametric cluster-based permutation analysis (Maris and Oostenveld 2007). Please note, that for these tests, cluster-based permutations control for multiple comparisons in the source space dimension.

8.3.2.3 Early Distractor-Related Alpha Activity: Cue Modulation Effect

For each participant, we estimated source-level activity (0.35-0.65s post-early-distractor onset, 7 to 13Hz) for each cue category (left, right and uninformative). Afterwards, in order to investigate the interaction between early distractor alpha response and cue information, we have contrasted surrogate-corrected alpha activity between: (1) the left and right cue conditions, (2) the left and uninformative cue conditions, and (3) and the right and uninformative cue conditions. All three tests have been carried out using non-parametric cluster-based permutation analysis (Maris and Oostenveld 2007). For these tests, cluster-based permutations control for multiple comparisons in the source space dimension.

8.3.3 Results

8.3.3.1 Definition of Early Distractor-Related Alpha Activity: Sensor Level

Real early distractor alpha activity was contrasted to that of surrogate early distractor using non-parametric cluster-based permutation testing. As shown in the figure below, this contrast revealed one significant negative cluster ($p < 0.01$) centered spatially around left and right temporal sensors (see Figure 1), temporally between 0.35 and 0.65s post-early distractor onset and frequency-wise, between 7 and 13 Hz. Distracting sounds were followed by a decrease in alpha power (7-13 Hz) between 350 and 650ms.

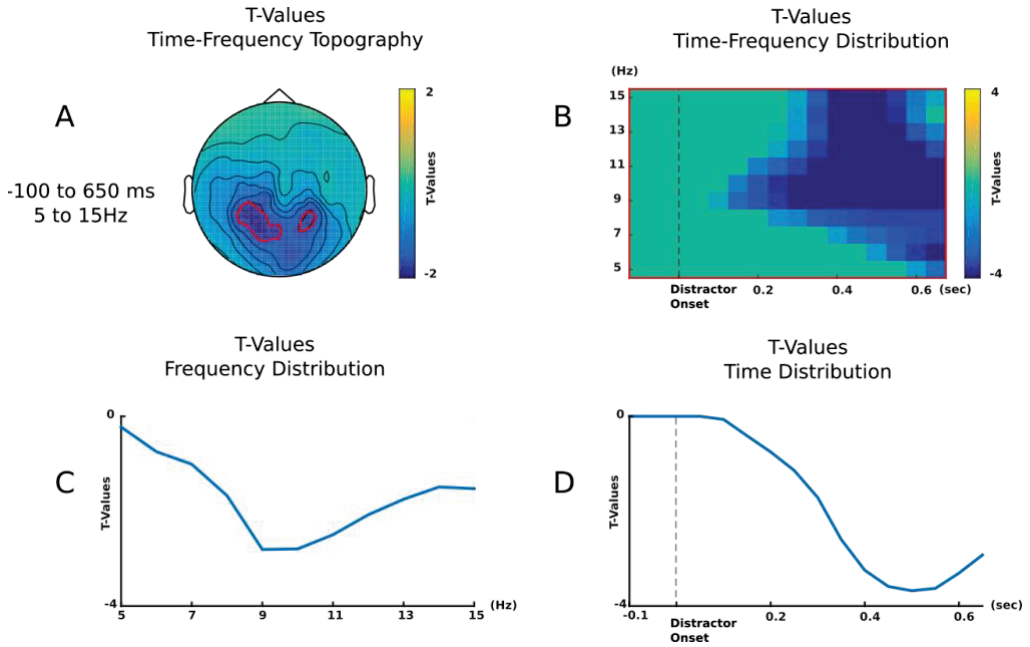


Figure 1. Topographical maps averaged between 5-15 Hz and -0.1-0.65 seconds (relative to distractor onset), of the t-values, masked at $p < 0.05$, of the baseline contrast between early distractor and surrogate distractor alpha activity. B. Time-frequency representations of the t-values (of the aforementioned test) of the sensors highlighted by red circles in A. C. Frequency distribution of t-values of the aforementioned sensors averaged across the time dimension. D. Time distribution of t-values of the aforementioned sensors averaged across the frequency dimension.

8.3.3.2 Definition of Early Distractor-Related Alpha Activity: Source Level

The aim of this test was to highlight regions possibly driving the aforementioned alpha activity observed on the sensor level. Thus, based upon the sensor level results, we have computed DICS beamformer sources for each participant between 7-13Hz and 0.35-0.65s post-distractor. Real early distractor alpha activity was contrasted to that of surrogate early distractors using non-parametric cluster-based permutation testing.

A significant cluster ($p < 0.01$) extended bilaterally, notably, to the Heschl, superior temporal, pre- and postcentral gyri. Other regions included left and right calcarine, inferior and middle temporal and occipital gyri.

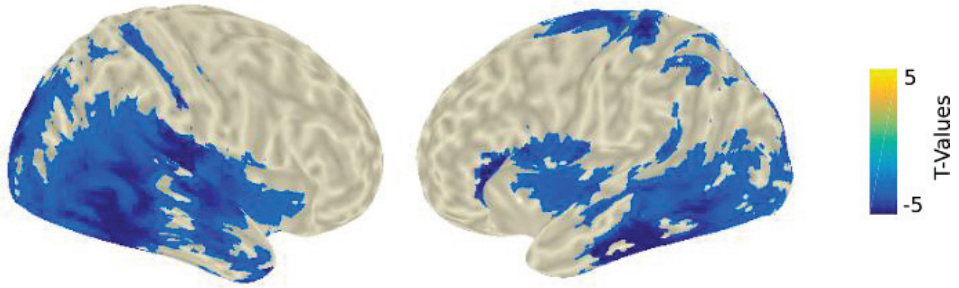


Figure 2. Distributions of T-values, masked at p<0.05, from Cluster Based Permutation tests contrasting real and surrogate early distractor alpha activity (7-13Hz and 0.35-0.65 post-distractor) at the source level

8.3.3.3 Early Distractor-Related Alpha Activity: Cue Modulation Effect

Only upon contrasting corrected early distractor alpha activity between the left and uninformative cue conditions, we have observed a significant cluster including the right auditory cortex which displayed a significantly lower activation when the distracting sound was preceded by an informative contralateral left cue rather than an uninformative cue. However, the p-value of the cluster did not resist Bonferroni correction for multiple comparisons ($p = 0.04$).

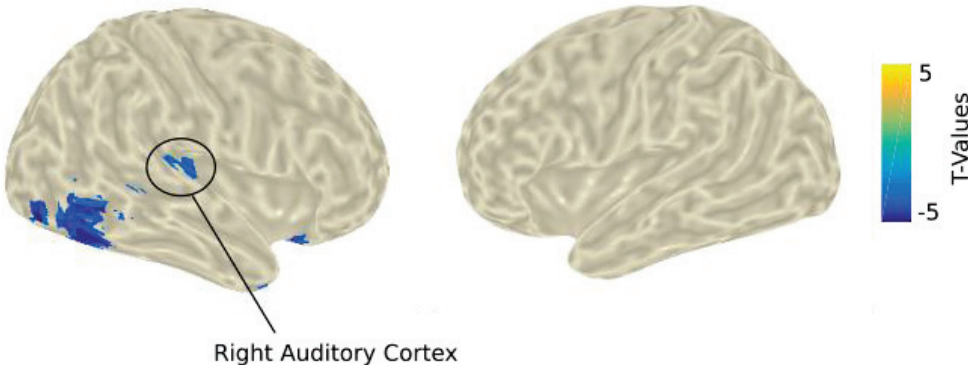


Figure 3. Distributions of T-values, masked at p<0.05, from Cluster Based Permutation tests contrasting surrogate-corrected early distractor alpha activity (7-13Hz and 0.35-0.65 post-distractor) between left cue and uninformative cue at the source level.

8.3.4 Discussion

In this study we have demonstrated that during the delay between the presentation of a distracting sound and the presentation of the auditory target alpha power decreases (desynchronization) in several regions notably the auditory cortices. This desynchronization was modulated by the cue information in the right auditory cortex where such desynchronization was more prominent for the contralateral (left) cue condition in comparison to the uninformative condition. Although, this modulation failed to reach significance, it suggests that the alpha activity observed here reflects top-down modulation by cue information rather than bottom-up processing of the distracting sounds which were presented binaurally. Future investigations shall probe the time-course of this auditory alpha activity in the source level using virtual electrodes.

The post-distracting sound alpha resembles the pattern of early alpha desynchronization described in **study I** in response to the cue. Interestingly, this desynchronization occurred later than gamma activity, previously observed in **study II** (350 ms vs 100ms after distracting sound onset, respectively). This fits well with our proposed oscillatory framework where gamma and alpha activity support bottom-up and top-down attentional mechanisms, respectively. In other words, once the distracting sound was processed (within the gamma band), top-down preparatory mechanisms were re-stablished (within the alpha band), in order to better process the upcoming auditory target.

Overall, this pattern of alpha activity corroborates our own findings in the absence of distracting sound (ElShafei et al. 2018) and previous findings from the auditory alpha literature (Muller and Weisz 2012; Frey et al. 2014; Weisz et al. 2014) and asserts the proposed role of alpha oscillations supporting top-down modulation of cortical excitability (Klimesch et al. 2007; Jensen and Mazaheri 2010).

9 Attention & Ageing

9.1 Study III: Impact of Ageing on Attentional Mechanisms (CAT 3.0)

Not Just A Number: Age-Related Modulations of Oscillatory Patterns Underlying Top-Down and Bottom-Up Attention.

Hesham A. ElShafei[1], Lesly Fornoni[1], Olivier Bertrand[1] and Aurélie Bidet-Caulet[1].

In preparation.

[1] Brain Dynamics and Cognition Team, Lyon Neuroscience Research Center; CRNL, INSERM U1028, CNRS UMR5292, University of Lyon 1, Université de Lyon, Lyon, France

Abstract

Attention operates through top-down (TD) and bottom-up (BU) mechanisms. Recently, it has been suggested that these mechanisms are supported by distinct frequency bands with slower (alpha) frequencies indexing facilitatory and suppressive mechanisms of TD attention and faster (gamma) frequencies indexing BU attentional capture. It has been well-demonstrated that ageing is characterized by increased distractibility, which can result from either a reduced efficiency of TD attention, or an enhanced triggering of BU attention. However, only a few of studies have investigated the impact of ageing on the balance between TD and BU attentional mechanisms and its oscillatory correlates. MEG data were collected from 14 elderly (mean age = 67) and 14 matched young (mean age = 25) healthy human participants while performing a modified version of the Competitive Attention Task in which they performed a pitch discrimination task. TD attention was manipulated by a visual cue that was either informative or not of the side of the monaural target sound. BU attention was triggered by binaural distracting sounds that were played (25% of trials) between the cue and the target. Behaviorally, older participants' performances were comparable to the young group, except for an exacerbated attentional capture by late distractors. Electrophysiologically, in comparison to young participants, they exhibited (1) deficits in the suppressive mechanisms of TD attention, as indexed by a reduced alpha synchronization in task-irrelevant visual regions, (2) less prominent alpha peak frequency differences between cortical regions, (3) a similar BU system activation indexed by distractor-induced gamma responses, and (4) a reduced activation of prefrontal inhibitory control regions. These results suggest that the ageing-related increased distractibility is of TD origin.

1 Introduction

Ageing is characterized by attentional difficulties, in particular a reduced capability to inhibit irrelevant information (Guerreiro et al., 2010; Zanto and Gazzaley, 2014). This exacerbated distractibility has been attributed to a degradation of inhibitory mechanisms (inhibitory deficit hypothesis, Hasher and Zacks, 1988) and a deterioration in the functioning of the frontal lobe (frontal aging hypothesis, West, 1996).

Attention operates through top-down (TD) and bottom-up (BU) mechanisms (James, 1890; Corbetta and Shulman, 2002). TD processes promote the processing of relevant stimuli through facilitatory and suppressive mechanisms, resulting in enhanced processing of relevant information and reduced brain responses to unattended inputs, respectively (review in Hillyard et al., 1998). Attention can also be oriented in a BU fashion by task-irrelevant unexpected salient stimuli (Corbetta et al., 2000). A good balance between BU and TD mechanisms is thus crucial: enhanced distractibility can result from either a reduced efficiency of TD mechanisms, or an enhanced triggering of BU attentional capture. TD and BU processes are supported by partially overlapping networks: TD processes are supported by a dorsal fronto-parietal network, including the intraparietal sulcus, and the frontal eye fields, whereas BU processes are supported by a ventral fronto-parietal network, including the temporo-parietal junction, and the ventral frontal cortex, with the two networks overlapping mainly in the lateral prefrontal cortex (Corbetta and Shulman, 2002; Corbetta et al., 2008). Recently, it has been suggested that signals in these networks are propagated via distinct frequency bands with slower (alpha) frequencies supporting long-range interareal interactions along the TD network and faster (gamma) frequencies supporting local interactions in the BU network (Buschman and Miller, 2007).

Alpha oscillations (8–14 Hz) have been proposed to play a crucial role in TD anticipatory attention (review in Foxe and Snyder, 2011; Frey et al., 2015). More precisely, they play an active inhibitory role (Klimesch et al., 2007; Jensen and Mazaheri, 2010): reduced and enhanced alpha power reflect increased and decreased cortical excitability in task relevant and irrelevant areas, respectively (e.g. Kelly et al., 2006; Gomez-Ramirez et al., 2011; Weisz et al., 2011). Therefore, alpha rhythm is a suitable candidate for supporting facilitatory and suppressive mechanisms of anticipatory attention (ElShafei et al., 2018). With ageing, TD attentional facilitatory processes, as indexed by alpha desynchronization, has been found to

be either reduced (Deiber et al., 2013; Hong et al., 2015; van der Waal et al., 2017), reserved (Leenders et al., 2018) or even enhanced (Heideman et al., 2018). However, TD suppressive processes indexed by alpha synchronization seem to deteriorate (Vaden et al., 2012).

Gamma oscillations (>30 Hz) have also been associated with attention (review in Fries, 2009) with evidence suggesting that BU feedforward signaling propagates pre-dominantly via these oscillations in primate sensory areas (Bastos et al., 2015; Michalareas et al., 2016). Moreover, gamma activity has been found in frontal regions of the ventral network in response to novel sounds (e.g. Lee et al., 2007; Akimoto et al., 2013). To our knowledge, no study has investigated the impact of ageing on gamma oscillatory activity supporting BU attention. In addition, no study has investigated how ageing would impact the balance between TD and BU mechanisms of attention, supported by activity in different oscillatory bands.

Thus, the aim of the present study was to characterize the brain origins of the exacerbated distractibility in elderly by investigating the impact of ageing on oscillatory activities supporting the balance between TD and BU attention. For this purpose, we recorded MEG activity from young and elderly participants while performing the Competitive Attention Task (Bidet-Caulet et al., 2014), a novel paradigm that permits the assessment of BU and TD mechanisms of auditory attention and the interaction between them.

We hypothesized that ageing would be characterized by an (1) exacerbated behavioral distractibility, (2) reduced TD filtering of irrelevant information, indexed by alterations in the alpha band, and (3) impaired gamma responses to distracting sounds and/or impaired modulation of these responses by TD attention.

2 Material & METHODS

2.1. Participants

Participants were 14 young (mean age = 25 ± 0.67 Standard Error of Mean (SEM); range: 20—29 years; 5 females) and 14 elderly (mean age = 67 ± 1.08 SEM; range: 61—75 years; 5 females) adults. The two groups were matched for sex, handedness, scholar and musical education (see Table 1). As expected, the 2 groups significantly differ in age (non-paired t-test $p < 0.001$) but did not significantly differ in scholar (non-paired t -test $p = 0.67$) and musical (non-paired t -test $p = 0.32$) education. All participants were healthy, right-handed, free from any neurological or psychiatric disorders and reported normal hearing, and normal or corrected-to-normal vision. The study was approved by the local ethical committee, and subjects gave written informed consent, according to the Declaration of Helsinki, and they were paid for their participation. Please note that data from all young participants are included in the analysis presented in a previous study of gamma activity in young adults (ElShafei et al., in prep).

	Elderly group	***Young Group***
Age (years ± SEM)	67 ± 1.08	25 ± 0.67
Gender	5F, 8M	5F, 8M
Handedness	14R	14R
Scholar Education (years ± SEM)	15 ± 0.71	15 ± 0.57
Musical Education (years ± SEM)	1 ± 0.45	2 ± 0.68

Table1. Group demographics. SEM, standard error of the mean; F, Female; M, Male; R, right-handed.

2.2. Stimuli and tasks

2.2.1. Competitive Attention Task (CAT)

In 75 % of the trials, a target sound (100 ms duration) followed a central visual cue (200 ms duration) with a fixed delay of 1000 ms (see Figure 1). The cue was a green arrow, presented on a grey-background screen, pointing either to the left, right, or both sides. Target sounds were monaural pure tones (carrier frequency between 512 and 575 Hz; 5 ms rise-time, 5 ms fall-time). In the other 25 %, the same structure was retained, however, a binaural distracting sound (300 ms duration) was played during the cue-target delay (50-650 ms range after cue offset). Trials with a distracting sound played from 50 ms to 350 ms after the cue offset were classified as DIS1, those with a distracting sound played from 350 ms to 650 ms after the cue offset were classified as DIS2, those with no distracting sound were classified as NoDIS. A total of 40 different ringing sounds were used as distracting sounds (clock-alarm, door-bell, phone ring, etc.) for each participant.

The cue and target categories were manipulated in the same proportion for trials with and without distracting sound. In 25% of the trials, the cue was pointing left, and the target sound was played in the left ear, and in 25% of the trials, the cue was pointing right, and the target sound was played in the right ear, leading to a total of 50% of *informative* trials. In the other 50% of the trials, the cue was *uninformative*, pointing in both directions, and the target sound was played in the left (25%) or right (25%) ear. To compare brain responses to acoustically matched sounds, the same distracting sounds were played in each combination of cue category (informative, uninformative) and distractor condition (DIS1 or DIS2). Each distracting sound was thus played 4 times during the whole experiment, but no more than once during each single block to limit habituation.

Participants were instructed to categorize two target sounds as either high- or low-pitched sound, by either pulling or pushing a joystick. The target type (high or low) was manipulated in the same proportion in all conditions. The mapping between the targets (low or high) and the responses (pull or push) was counterbalanced across participants, but did not change across the blocks, for each participant. In order to account for the participants' pitch-discrimination capacities, the pitch difference between the two target sounds was defined in a Discrimination Task (see below). Participants were informed that informative cues were 100 % predictive and that a distracting sound could be sometimes played. They were asked to allocate their attention to the cued side in the case of informative cue, to ignore the

distractors and to respond as quickly and correctly as possible. Participants had a 3.4 second response window. In the absence of the visual cue, a blue fixation cross was presented at the center of the screen. Subjects were instructed to keep their eyes fixated on the cross.

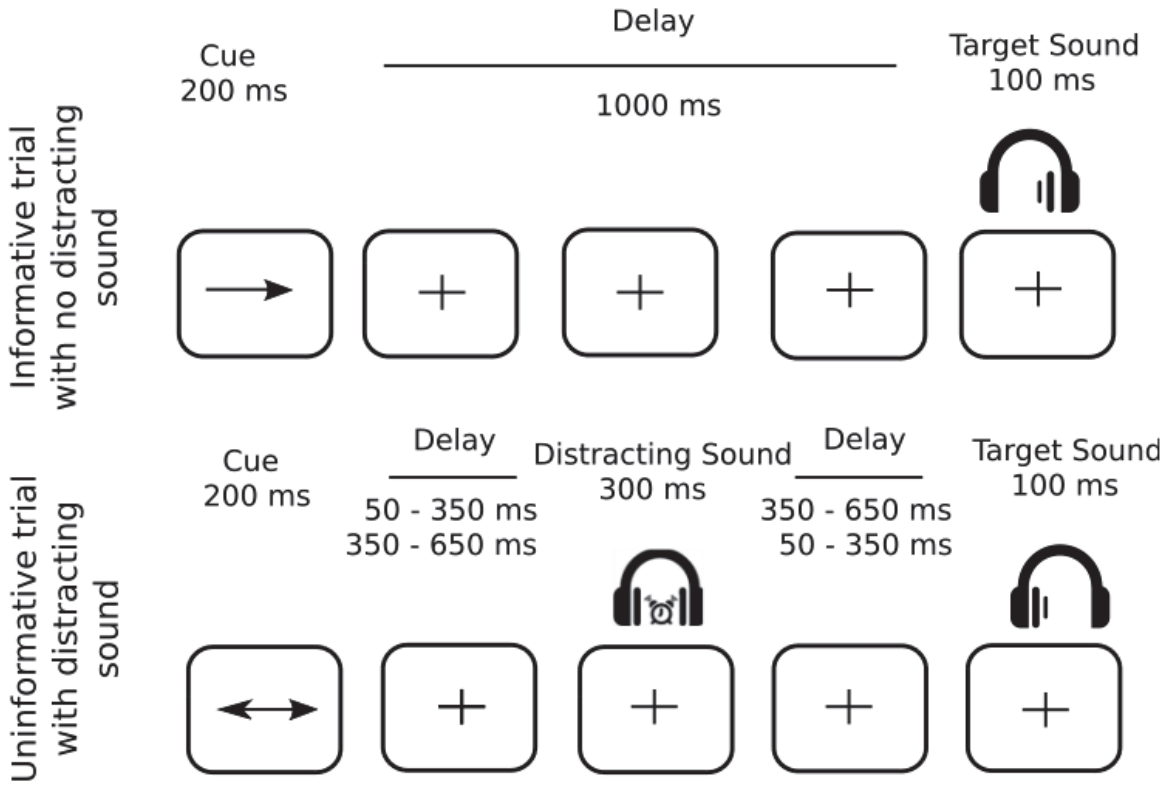


Figure 1. Protocol. Top row. Example of an informative trial with no distracting sound: a one-sided visual cue (200 ms duration) indicated in which ear (left or right) the target sound would be played (100 ms duration) after a fixed 1000-ms delay. Bottom row. Example of an uninformative trial with a distracting sound: a two-sided visual cue (200 ms duration) did not provide any indication in which ear (left or right) the target sound will be played. In 25 % of the trials, a binaural distracting sound (300 ms duration), such as a clock ring, was played during the delay between cue and target. The distracting sound could equiprobably onset in two different time periods after the cue offset: in the 50–350 ms range, or in the 350–650 ms range.

2.2.2. Discrimination Task

Participants were randomly presented with one of two target sounds: a low-pitched sound (512 Hz) and a high-pitched sound (575 Hz; two semitones higher), equiprobably in each ear (four trials per ear and per pitch). As described above, participants were asked to categorize the target sounds as either high- or low-pitched sound within 3 seconds.

2.2.3. Procedure

Participants were seated in a sound-attenuated, magnetically shielded recording room, at a 50 cm distance from the screen. The response device was an index-operated joystick that participants moved either towards them (when instructed to pull) or away from them (when instructed to push). All stimuli were delivered using Presentation software (Neurobehavioral Systems, Albany, CA, USA). All sounds were presented through air-conducting tubes using Etymotic ER-3A foam earplugs (Etymotic Research, Inc., USA).

First, the auditory threshold was determined for the two target sounds differing by 2 semitones (512 and 575 Hz), for each ear, for each participant using the Bekesy tracking method (Von Békésy and Wever, 1960). The target sounds were then presented at 25 dB sensation (between 30 and 69.5 dB A in old, and between 37.5 and 50.75 dB A in young participants) level while the distracting sounds were played at 55 dB sensation level (between 40 and 79.5 dB A in old, and between 47.5 and 60.75 dB A in young participants), above the target sound thresholds. Second, participants performed the discrimination task. If participants failed to respond correctly to more than 85% of the trials, the pitch of the high target sound was augmented, by half a semitone with a maximum difference of 3 semitones between the two targets (auditory thresholds were then measured with the new targets). Afterwards, participants were trained with a short sequence of the Competitive Attention Task. Finally, MEG and EEG were recorded while subjects performed 10 blocks (64 trials each) leading to 240 trials in the NoDIS and 80 in the DIS conditions, for informative and uninformative cues, separately. The whole session lasted around 80 minutes. After the MEG/EEG session, participants' subjective reports regarding their strategies were collected.

2.3. Behavioral Data Analysis

For behavioral data analysis, a button press before target onset was considered as a false alarm (FA). A trial with no button-press after target onset and before the next cue onset was considered as a miss trial. A trial with no FA and with a button-press after target onset was counted as correct if the pressed button matched the response mapped to the target sound, and as incorrect if otherwise. Reaction-times (RTs) to targets were analyzed in the correct trials only. The influence of (1) age group (2 levels: young and elderly), (2) cue condition (2 levels: informative and uninformative), and (3) distractor condition (3 levels: NoDis, DIS1 and DIS2) on percentage of incorrect responses and median reaction times (RTs) of correct responses was tested using a linear mixed-effects models (lme4 package, Bates et al., 2014 for R Team, 2014). A random effect was included for each participant, allowing us to model variability between participants. For post-hoc analysis we used the Lsmean package (Lsmean version 2.20-23; Searle et al., 1980) where p-values were considered as significant at $p<0.05$ and adjusted for the number of comparisons performed (Tukey method).

Moreover, planned analyses of the CUE BENEFIT were carried out between groups on the differences in RTs Uninformative NoDIS – Informative NoDIS and of distractor effects on the differences in RTs NoDIS – DIS1 (as a measure of the AROUSAL BENEFIT) or DIS2 – DIS1 (as a measure of ATENTION CAPTURE COST), using non-paired t-tests (Bidet-Caulet et al. 2014; Masson and Bidet-Caulet 2018).

2.4. Brain Recordings

Simultaneous EEG and MEG data were recorded, although the EEG data will not be presented here. The MEG data were acquired with a 275-sensor axial gradiometer system (CTF Systems Inc., Port Coquitlam, Canada) with continuous sampling at a rate of 600Hz, a 0–150Hz filter bandwidth, and first-order spatial gradient noise cancellation. Moreover, eye-related movements were measured using vertical and horizontal EOG electrodes. Head position relative to the gradiometer array was acquired continuously using coils positioned at three fiducial points; nasion, left and right pre-auricular points. Head position was checked at the beginning of each block to control head movements.

In addition to the MEG/EEG recordings, T1-weighted three-dimensional anatomical images were acquired for each participant using a 3T Siemens Magnetom whole-body scanner

(Erlangen, Germany). These images were used for reconstruction of individual head shapes to create forward models for the source reconstruction procedures. The processing of these images was carried out using CTF's software (CTF Systems Inc., Port Coquitlam, Canada).

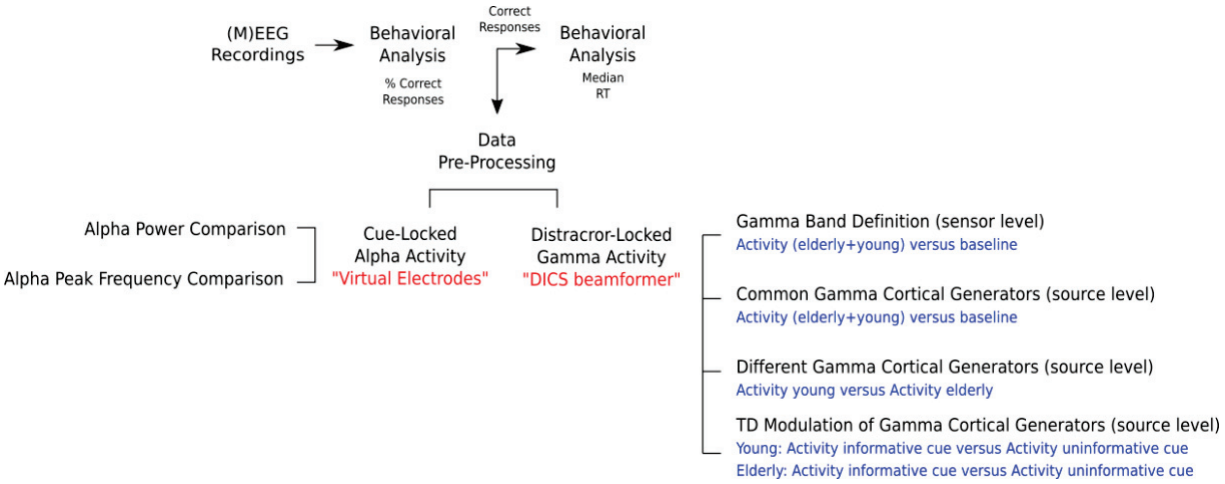


Figure 2. Outline of the analysis pipeline.

2.5. Data Pre-processing (Figure 2)

Only correct trials were considered for electrophysiological analyses. Data segments for which the head position differed for more than 10 mm from the median position during the 10 blocks were excluded. In addition, data segments contaminated with muscular activity or sensor jumps were excluded semi-manually using a threshold of 2200 and 10000 femtoTesla respectively. For all participants, more than 75 % of trials remained after rejection for further analyses. Independent component analysis was applied on the band-pass filtered (0.1-40Hz) data in order to remove eye-related (blink and saccades) and heart-related artefacts. Subsequently, components (four on average) were removed from the non-filtered data via the inverse ICA transformation. Data were further notch filtered at 50, 100 and 150Hz and high-pass filtered at 0.2Hz.

2.6. Cue-Locked Alpha Activity (Distractor-Free Trials)

Region of interests, time-window and frequency bands for the analysis of cue-locked alpha activity was based on previous results in young healthy adults obtained using a similar paradigm (ElShafei et al., 2018).

2.6.1. Virtual-Electrode Level Analysis and Defining ROIs

The source space was subdivided into 69 anatomically defined brain parcels according to the Talairach Tournoux atlas (Talairach and Tournoux, 1988; Lancaster et al., 1997). Broadmann areas 17, 18 and 19 were defined as the visual regions of interest (ROIs) while areas 22, 41 and 42 were defined as the auditory ROIs and areas 4 and 6 were defined as the motor ROIs, in each hemisphere.

2.6.2. Reconstruction of Source Activity

In order to reconstruct activity at the source level, we computed the time-frequency signal of the ROIs defined above at the virtual electrode level. Using the linearly constrained minimum variance (LCMV) beamformer (Van Veen et al., 1997) beamformer, spatial filters were constructed from the covariance matrix of the averaged single trials at sensor level (-0.8 – 2s, relative to cue onset, 1-20 Hz, lambda 5%) and the respective leadfield. Spatial filters were multiplied by the sensor level data in order to obtain the time course activity at each voxel of interest.

Activity was averaged across all voxels within each ROI in both hemispheres. Thus, limiting our analysis to three ROIs (one auditory, one visual and one motor). For each ROI, the evoked potential (i.e., the signal averaged across all trials) was subtracted from each trial. Subsequently, the oscillatory power, of distractor-free trials, was calculated using Morlet Wavelet decomposition with a width of four cycles per wavelet (m=7; Tallon-Baudry and Bertrand, 1999) at center frequencies between 5 and 18 Hz, in steps of 1 Hz and 50 ms.

2.6.3. Impact of Age on Alpha Activity: Power differences

In order to investigate differences between groups in low and high alpha sub-bands, baseline-corrected (-0.6 to -0.2s pre-cue) alpha power (computed using Morlet Wavelets) was averaged between 7 and 11Hz, and between 11 and 15Hz, separately, in each ROI. Subsequently, alpha activity (0.6 to 1s post-cue by step of 50 ms) within each alpha sub-band was contrasted between groups using a non-parametric cluster-based permutation analysis (Maris and Oostenveld, 2007). Please note, that for this test, cluster-based permutations control for multiple comparisons in the time dimension.

2.6.4. Impact of Age on Alpha Activity: Alpha Peak Frequency

Alpha power (computed using Morlet Wavelets) was averaged between 0.6 and 1s for each ROI, to extract the power spectrum in each subject. Afterwards, individual alpha peak frequency (iAPF) was defined separately for each ROI, in each subject. For auditory and motor ROIs, the peak was defined as the frequency with the maximum alpha power decrease relative to the *baseline* (-0.6 to -0.2s pre-cue onset) between 5 and 15 Hz. For visual virtual electrodes, the peak was defined as the frequency with the maximum alpha power increase relative to the baseline.

The APFs were fit into a linear mixed-effects model (lme) with the following factors as fixed effect: (1) age group (2 levels: young and elderly), (2) ROI (3 levels: auditory, visual and motor). A random effect was included for each participant, allowing us to model variability between participants. Similarly to previous analysis, for post-hoc analysis, we used the Lsmean package.

2.7. Distractor-locked Gamma Activity

2.7.1. Gamma Band (Sensor level): Definition

This analysis was done to define the time-frequency range of gamma activity of interest. First, for each distractor onset time-range, we have created surrogate distractors in the NoDIS trials with similar distribution over time than the real distractors. Afterwards, the oscillatory power, of distractor and (surrogate distractor) trials was calculated using Morlet Wavelet decomposition with a width of four cycles per wavelet (m=7; Tallon-Baudry and Bertrand, 1999) at center frequencies between 40 and 150 Hz, in steps of 1 Hz and 10 ms. Data from both groups were pooled together and activity of interest (defined between 0 and 0.35s post-distractor onset and 50-110Hz) was contrasted between distractor and surrogate trials using a nonparametric cluster-based permutation analysis (Maris and Oostenveld, 2007). This contrast extracts distractor-related activity clear of cue-related activity.

2.7.2. Gamma Band (Source level): Computation

In order to estimate the brain regions driving the sensor-level distractor-locked gamma activity (0.1-0.3 s post-distractor onset, 60 to 100Hz), we have utilized the frequency–domain adaptive spatial technique of dynamical imaging of coherent sources (DICS; Gross et al., 2001).

Data, from both surrogate and real distractors were concatenated, and cross-spectral density (CSD) matrix (-**0.2 to 0.6 s**, relative to real/surrogate distractor onset) were calculated using the multitaper method with a target frequency of **80 (±30) Hz.** For each participant, an anatomically realistic single-shell headmodel based on the cortical surface was generated from individual head shapes (Nolte, 2003). A grid with 0.5 cm resolution was normalized on an MNI template, and then morphed into the brain volume of each participant. Leadfields for all grid points along with the CSD matrix were used to compute a common spatial filter that was used to estimate the spatial distribution of power for time-frequency windows of interest.

2.7.3. Gamma Power Source Level Analysis

For each participant, we estimated source-level activity (0.1-0.3 s post-distractor onset, 60 to 100Hz) for each cue category (informative and uninformative) and for both cue categories concatenated. We performed three analyses:

(1) To characterize the brain areas activated in the gamma band during the distracting sound presentation, data from both groups were pooled together and distractor-locked gamma activity was contrasted to surrogate distractor-locked gamma activity.

(2) To investigate group differences in distracting sound processing in the gamma band, surrogate-corrected gamma activity (surrogate distractor-locked gamma activity was subtracted from distractor-locked gamma activity) was compared between groups.

(3) To investigate a potential interaction between groups and the use of the cue information, for each group separately, surrogate-corrected gamma activity in the informative cue condition was contrasted to surrogate-corrected gamma activity in the uninformative cue condition.

All tests have been carried out using non-parametric cluster-based permutation analysis (Maris and Oostenveld, 2007). Please note, that for these tests, cluster-based permutations control for multiple comparisons in the source space dimension.

3 Results

3.1 Behavioral Analysis

Participants correctly performed the discrimination task in 95.37 ± 0.29 SEM % of the trials. The remaining trials were either incorrect trials (4.62 ± 0.29 SEM %), missed trials (0.49 ± 0.09 %) or trials with FAs (0.14 ± 0.03 %). In order to investigate behavioral performances (percentage of incorrect responses and RTs), a lme model was used with 3 factors: (1) age group (2 levels: young and elderly), (2) cue condition (2 levels: informative and uninformative), and (3) distractor condition (3 levels: NoDis, DIS1 and DIS2).

2.7.4. Behavioral Analysis: Incorrect Response Percentage (Figure 3)

Only a significant main effect of the distractor condition ($F(2, 52) = 8.9$, $p < 0.01$, $\eta^2 = 0.21$) was found on the percentage of incorrect responses, with no main effect of group ($F(1, 15) = 2.1$, $p = 0.15$, $\eta 2 = 0.07$). Post-hoc tests indicated that participants, from both groups, committed more errors in the late DIS2 condition in comparison to the early DIS1 ($p < 0.01$) and the NoDIS ($p < 0.001$) conditions.

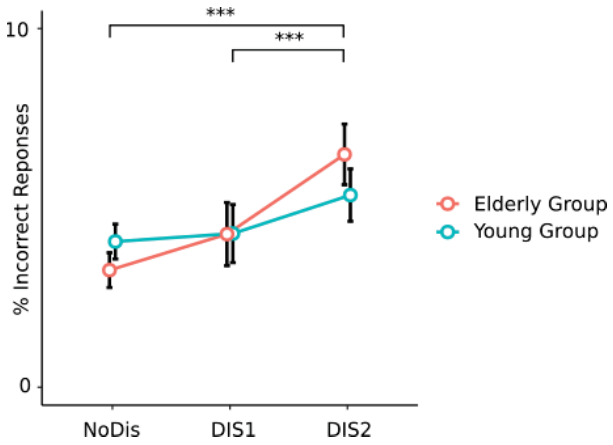


Figure 3. Percentage of Incorrect Responses averaged across cue conditions, according to distractor conditions, for both groups. $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Error bars represent SEM.

2.7.5. Behavioral Analysis: Median Reaction Times (Figure 4)

A main effect of cue category ($F(1, 26) = 3.7$, $p < 0.01$, $\eta^2 = 0.22$) was found on reaction times. Participants were faster when the cue was informative in comparison to the uninformative cue. In addition we found a main effect of the distractor condition ($F(2, 52) = 95.2$, $p < 0.01$,

η^2 = 0.64). Post-hoc tests indicated that in comparison to the NoDIS condition, participants were faster in the early DIS1 condition ($p < 0.001$) but slower in the late DIS2 condition ($p<0.001$). In addition, participants were faster in the early DIS1 condition in comparison to the late DIS2 condition ($p<0.01$). Most interestingly, we have found a significant interaction between age and distractor factors ($F(2, 52) = 10.9$, $p < 0.01$, $\eta^2 = 0.17$). Post-hoc tests indicated that elderly participants were slower than the young ones in the late DIS2 condition ($p= 0.04$).

Unpaired t-test between groups confirmed that the attention capture effect (DIS2 – DIS1) was significantly more pronounced for the elderly group ($p < 0.01$); whereas the arousal facilitation effect (NoDIS – DIS1; $p = 0.29$) and the cue benefit effect ($p = 0.83$) was similar in both groups.

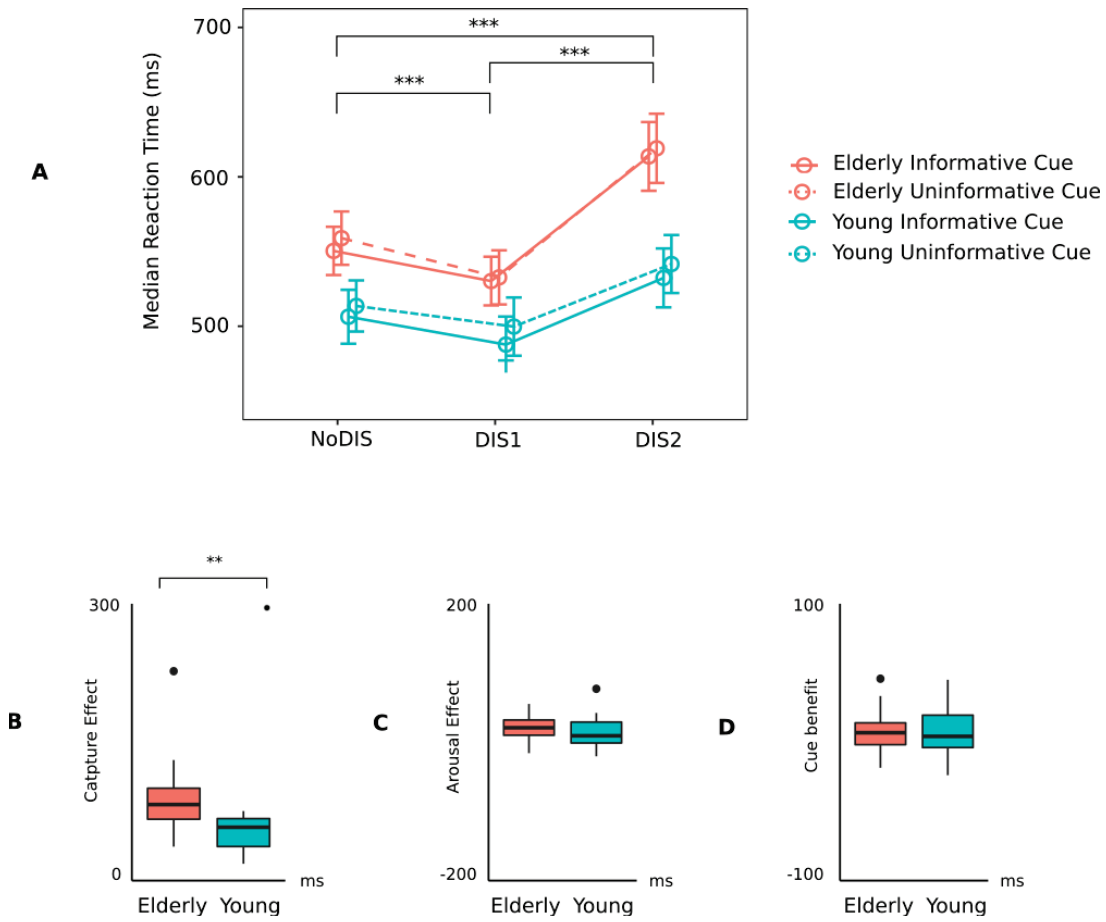


Figure 4. (A). Median RTs in each group according to cue information and distractor conditions. Error bars represent SEM. Boxplot of the Attention capture effect (B), the Arousal effect (C), and the Cue benefit effect (D), for each group. *P* < 0.05, ** *P* < 0.01, *** *P* < 0.001.

3.2 Cue-Locked Alpha Analysis

3.2.1 Ageing and Alpha Power Modulations (source level)

Upon contrasting post-cue activity between both groups in each ROI (motor, auditory or visual), no differences were found in the low alpha sub-band (7-11 Hz). However, in the high alpha sub-band (11-15 Hz), we found two significant positive clusters: one in the visual ROI ($p = 0.02$) and another in the motor ROI ($p = 0.01$). In the visual ROI, as shown in Figure 5, alpha power was significantly lower (less alpha synchronization) in the elderly than in the young participants between 600 ms and 1000 ms. In the motor ROI, the elderly displayed lower alpha power (more alpha desynchronization) than young participants between 600 ms and 800 ms.

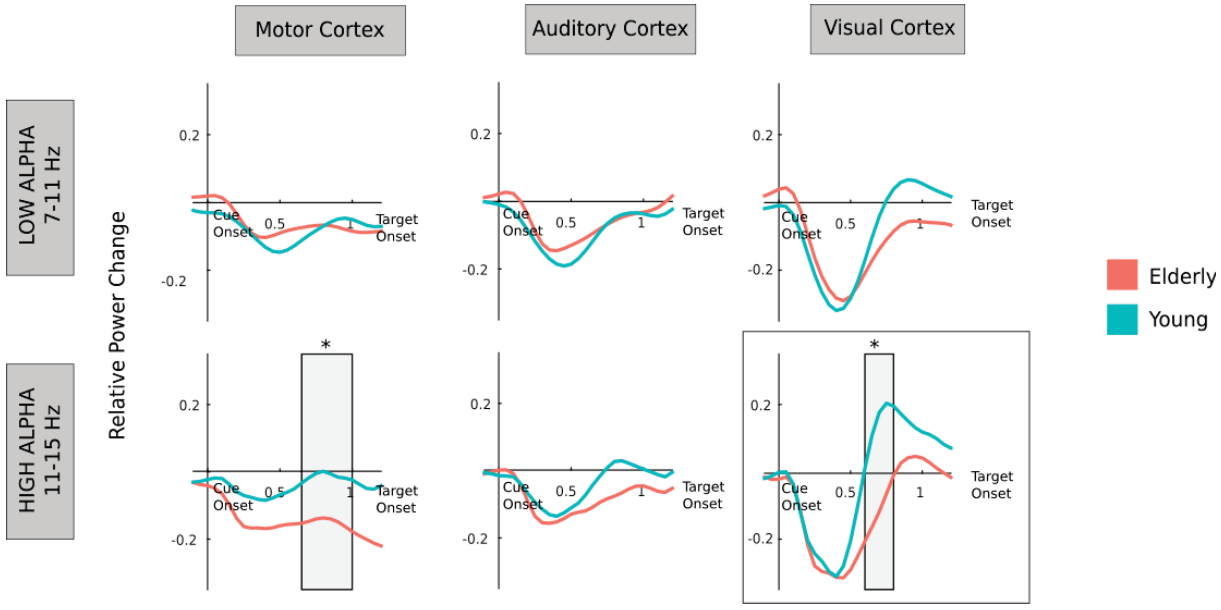


Figure 5. Time-course of alpha activity averaged between 7-11Hz and 11-15Hz across virtual ROIs. Grey Rectangles represent time-windows of significant group differences based upon cluster-based permutation testing. * $p < 0.05$.

2.7.6. Ageing and Alpha peak frequency (source level)

In order to investigate the alpha peak frequency in virtual ROIs, a lme model was used with 2 factors: (1) age (2 levels: young and elderly), and (2) ROI (3 levels: auditory, visual and motor). The lme model yielded a significant interaction between age and ROI ($F(2,52) = 4.1$, $p < 0.01$, $\eta^2 = 0.11$). Post-hoc tests indicated that, only in the young group, the alpha peak frequency was significantly higher in the visual ROI (mean = 12.32 Hz ± 0.44 SEM) than in the auditory

(mean = 9.39 Hz ± 0.58 SEM) and the motor ROIs (mean = 10 Hz ± 0.58 SEM) ($p < 0.001$ and $p = 0.01$, respectively), as shown in Figure 6.

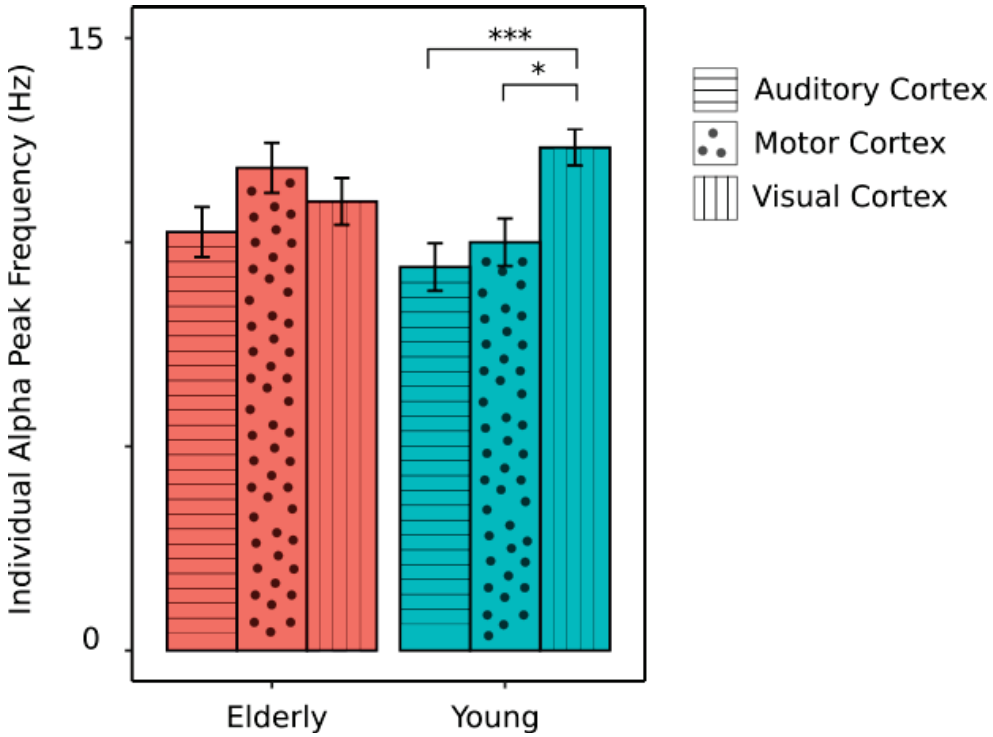


Figure 6. Individual Alpha Peak Frequency across virtual ROIs for each group. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Error bars represent SEM.

3.3 Distractor-Locked Gamma Activity

3.3.1 Gamma-band definition (sensor level)

Oscillatory data were pooled from both groups and real-distractor high-frequency activity was contrasted to that of surrogate-distractor using non-parametric cluster-based permutation testing. As shown in Figure 7, this contrast revealed one significant positive cluster (p = 0.001) indicating an increase in gamma activity centered spatially around left and right temporal sensors (Fig 7A), temporally between 0.1 and 0.3s post-distractor onset (Fig 7B & C), and frequency-wise between 60 and 100 Hz (Fig 7B & D).

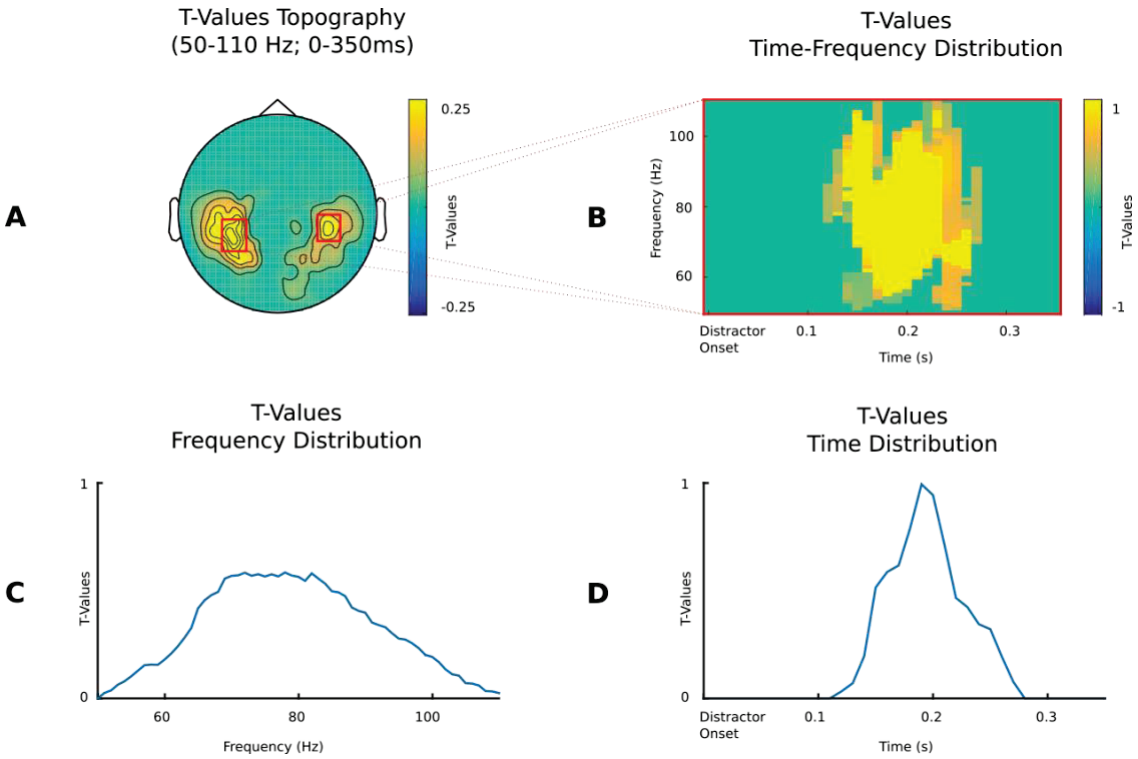


Figure 7. Common sensor level gamma activity to distractor. A. Topographical maps averaged between 50-110 Hz and 0-0.35 seconds post-distractor onset, of the t-values, masked at $p < 0.05$ of the contrast between distractor and surrogate distractor gamma activity. **B.** Time-frequency representations of t-values (of the aforementioned test) of the sensors highlighted by red boxes in A. **C.** Frequency distribution of t-values of the aforementioned sensors averaged across the time dimension. **D.** Time distribution of t-values of the aforementioned sensors averaged across the frequency dimension.

3.3.2 Gamma Activity: Common Activation (source level)

Based upon sensor level results, we have computed DICS beamformer sources for each participant between 60-100Hz and 0.1-0.3s post-distractor. Once again, source-level data was

pooled from both groups and real-distractor gamma activity was contrasted to that of surrogate distractors using non-parametric cluster-based permutation testing.

The aim of this test was to highlight the brain regions that are commonly activated in both groups in the gamma band. A significant positive cluster ($p < 0.01$) indicating a bilateral increase in gamma activity notably in (1) the auditory cortices, and (2) the tempo-parietal junctions and the ventrolateral prefrontal cortices (Figure 8). Other regions included the middle and posterior cingulate gyri, pre- and post-central gyri, the Precuneus, and the inferior temporal gyrus.

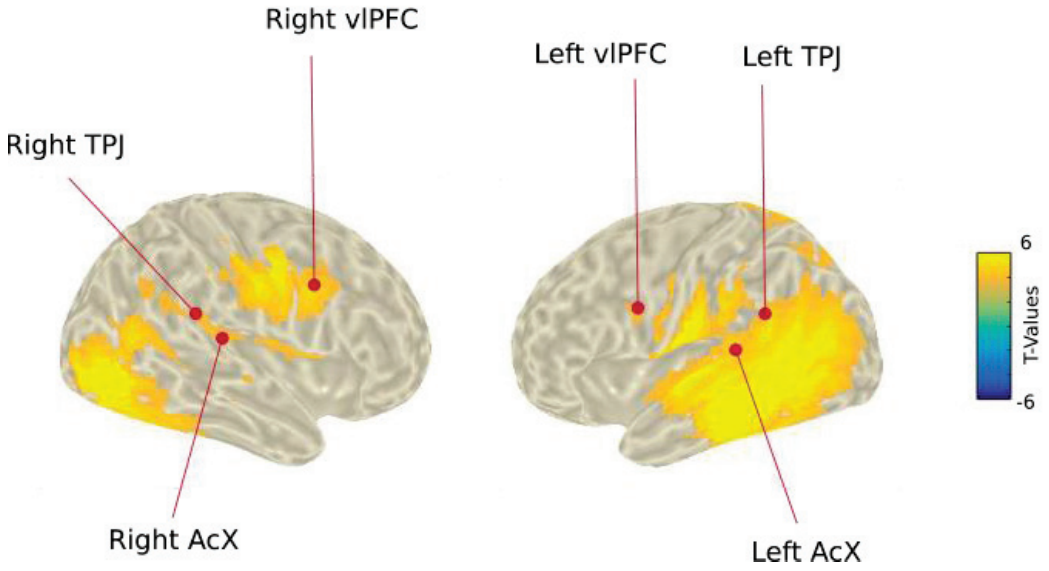


Figure 8. Common source level gamma activity to distractor. Distributions of T-values, masked at *p<0.05*, from Cluster Based Permutation tests contrasting real and surrogate distractor gamma activity (60-100Hz and 0.1-0.3 post-distractor) pooled from both groups at the source level. TPJ: temporo-parietal junction. vlPFC: ventro-lateral prefrontal cortex.

2.7.7. Gamma Activity: Group Comparison (source level)

The aim of this test was to highlight the brain regions that are differentially activated in the elderly and young groups, in the gamma band. For each participant, real distractor source-level data (60-100 Hz, 0.1-0.3s) were corrected by subtracting surrogate-distractor activity. Corrected distractor gamma activity was contrasted between groups using non-parametric cluster-based permutation testing. A significant positive cluster ($p = 0.01$) was found notably in (1) the left dorso- and ventromedial prefrontal cortices, and (2) the left anterior cingulate gyrus (Figure 9A). Other regions included the left pre- and post- central gyri, the left supplementary motor area, the left superior parietal lobule. All these regions displayed a higher gamma activation for the young group compared to the elderly group.

3.3.3 Gamma Activity: Modulation by Cue Information

To investigate the effect of top-down attention on bottom-up processing, we analyzed the effect of cue information on the gamma response to distracting sounds, in each group separately. For each participant, real distractor source-level data (60-100 Hz, 0.1-0.3s) were baseline corrected by subtracting surrogate-distractor activity. For each group separately, corrected distractor gamma activity was contrasted between the two cue categories (informative vs. uninformative) using non-parametric cluster-based permutation testing. Only for the young group, a significant positive cluster ($p = 0.02$) was found in regions highly similar to that of the previous analysis the dorso- and ventromedial prefrontal cortices, the left anterior cingulate gyrus, the left pre- and post- central gyri, the left supplementary motor area, the left superior parietal lobule, in the left hemisphere (Figure 9B). All regions displayed a significantly higher gamma activation for trials when the distracting sound was preceded by an informative cue rather than an uninformative cue.

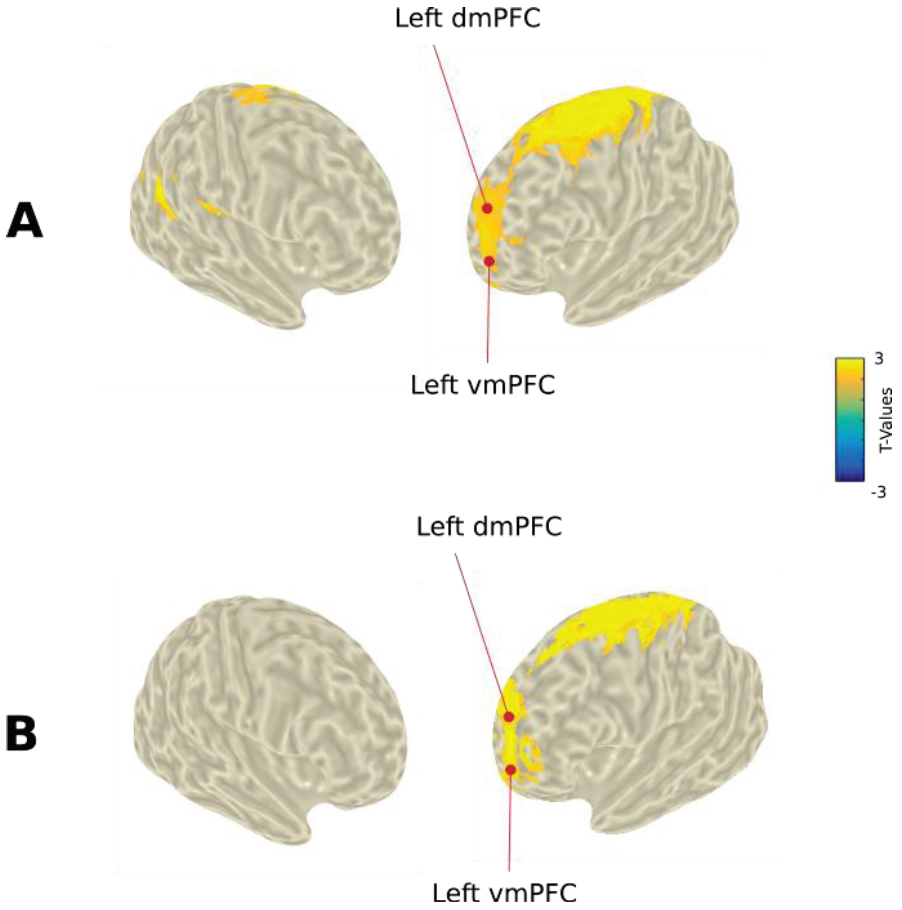


Figure 9. A. Between group comparison of gamma activity to distractor. Distributions of T-values, masked at *p<0.05*, from Cluster Based Permutation tests contrasting surrogate-corrected distractor gamma activity (60-100Hz and 0.1-0.3 post-distractor) between groups at the source level. **B. Top-down modulation of gamma activity to distractor in the young group.** Distributions of T-values, masked at *p<0.05*, from Cluster Based Permutation tests contrasting surrogate-corrected distractor gamma activity (60-100Hz and 0.1-0.3 post-distractor) within informative and uninformative cue conditions for the young group.

4 Discussion

In the present study, we have demonstrated that ageing differently impacts TD and BU attentional processes. Behavioral measures of TD attention seemed unchanged while distractibility was exacerbated with ageing. Electrophysiologically, during expectation of a visually-cued target sound, the alpha power decrease in the relevant auditory cortices was preserved; whereas the alpha increase in the irrelevant visual areas was reduced, in elderly compared to young adults. Moreover, in response to a distracting sound, a similar activation of the ventral BU attentional network in the gamma band, but a reduced recruitment of medial frontal regions was observed with ageing.

4.1 Impact of Ageing on Behavioral Measures of Bottom-up and Top-down Attention

Behaviorally, we have capacity to benefit from the cue information to identify the target pitch faster, in both groups. This equivalence in performance is in line with previous studies suggesting that TD attentional orienting is not affected by ageing (Greenwood et al., 1993; Curran et al., 2001; Olk and Kingstone, 2015; Erel and Levy, 2016).

In trials with targets preceded by distracting sounds, both groups displayed a similar reaction time (RT) pattern: participants were faster in trials with early distracting sounds rather than with late distracting sounds. This pattern could be explained in light of the effects triggered by a distracting sound (review in Bidet-Caulet et al., 2014; Masson and Bidet-Caulet, 2018): (1) a persistent increase in arousal resulting in RT reduction (behavioral benefit) and (2) a stronger transient attentional capture (orienting) effect leading to RT augmentation (behavioral cost). The behavioral net effect of distracting sound varies according to the time interval between the distracting and the target sounds. Thus, in the present paradigm, the difference in reaction time to targets between trials with late distracting sounds (DIS2) and trials with early distracting sounds (DIS1) provides a good approximation of the attentional capture effect with no or little contamination by the increase in arousal. Importantly, in comparison to the young group, elderly participants displayed a larger attentional capture effect. This increased susceptibility to task-irrelevant distractors is a recurrent finding in the literature using unimodal (visual or auditory) or cross-modal paradigms (e.g. Gazzaley et al., 2005; Parmentier and Andrés, 2009; Bélanger et al., 2010; Li and Zhao, 2015; Mevorach et al., 2016).

4.2 Impact of Ageing on TD Attentional Mechanisms Revealed by Alpha Activity

In a recent study (ElShafei et al., 2018), we have found in young adults, during the anticipation of a visually-cued auditory target, (1) an increase in alpha power around 13 Hz in task-irrelevant visual regions, (2) a simultaneous alpha decrease around 9Hz in task-relevant auditory regions. This suggests that alpha desynchronization and synchronization reflect facilitatory and suppressive mechanisms of TD attention, respectively, by augmenting and reducing cortical excitability, in agreement with an inhibitory role of alpha oscillations (Klimesch et al., 2006; Jensen and Mazaheri, 2010; Foxe and Snyder 2011). In the present study, we have replicated these findings among the young group with a slightly different protocol.

In addition, we have observed that elderly participants, compared to young adults, seem to display a similar alpha desynchronization in the relevant auditory cortices, but present a reduced alpha synchronization in the irrelevant visual cortices. These findings suggest that with ageing, suppressive TD attentional mechanisms become defect, while facilitatory mechanisms would be preserved, in line with previous studies of alpha oscillations during visual attention (Vaden et al., 2012; Leenders et al., 2018). This result is consistent with several previous studies using fMRI showing that the capability to filter out task-irrelevant information is reduced with ageing (e.g. Gazzaley et al., 2005).

Moreover, we found a larger alpha desynchronization in the motor areas in elderly, in agreement with a stronger recruitment of motor regions during response preparation with ageing (e.g. Naccarato et al., 2006; Deiber et al., 2013). Elderly could rely more on motor preparation processes as a compensatory mechanism to their reduced attention filtering of irrelevant information, resulting in comparable performances to younger adults at the behavioral level.

Finally, a novel finding in the present study is the decreased differentiation between alpha peak frequency of different sensory regions, with ageing. This finding is in line with studies investigating the development of alpha peak frequency across the life-span and suggesting a general decline in alpha frequency with age (e.g. Chiang et al., 2011; Gómez et al., 2013). Yet, this begs the question: is this decreased differentiation causal to the failure of older participants to filter out irrelevant visual information? In other words, would the reduction in alpha frequency specialization in the ageing brain lead to reduced suppressive mechanisms of TD attention? Another possibility would be that the alteration of suppressive

attentional mechanisms results in a reduced alpha frequency specificity in the ageing brain. This question remains for future investigation to answer.

4.3 Impact of Ageing on Gamma Activation during BU Attention

To the best of our knowledge, this is the first study to investigate gamma activity to highlight the impact of ageing on auditory BU attentional processes. Gamma activity has been linked to both sensory and non-sensory cortical activation in both the visual (Akimoto et al., 2013, 2014) and auditory (Lee et al., 2007; Ahveninen et al., 2013) modalities. In both the young and elderly groups, a gamma activation in bilateral auditory cortices, and several other brain regions including the temporo-parietal junctions and the right ventro-lateral prefrontal cortex, was observed in response to an unexpected salient distracting sound. These regions are part of the well-established ventral BU attentional network from studies using functional (Salmi et al., 2009; Alho et al., 2014; Salo et al., 2017; Long and Kuhl, 2018) and electrophysiological (e.g. Ahveninen et al., 2013) recordings. Therefore, these present results suggest a similar activation of the ventral BU attentional network in the gamma band in elderly and young adults. Nevertheless, in the literature it is rather unclear how ageing impacts the BU network with evidence of reserved (Deslauriers et al., 2017), reduced (Li et al., 2015) and even augmented (Kurth et al., 2016) activation with ageing.

Importantly, younger participants demonstrated higher gamma activation in several regions mainly in the ventro- and dorso- medial prefrontal cortices and the anterior cingulate cortex, in the left hemisphere. Interestingly, modulation of gamma activity according to the preceding cue information was found in the same brain regions: gamma activity was larger after an informative cue in comparison to an uninformative cue in young participants, only. This gamma modulation by cue information in medial frontal regions in young adults is consistent with previous results (ElShafei et al., in prep)

The ventro- and dorso- medial prefrontal cortices (PFC) and the anterior cingulate cortex constitute the hub of the inhibitory control system. Indeed, the activation of these regions is increased during presentation of irrelevant salient stimuli (e.g. Rule et al., 2002; Salmi et al., 2009). In the non-human primate auditory system, such role could be established through connections between these regions (the medial PFC and the ACC) and inhibitory neurons in auditory association regions in order to suppress irrelevant signals (Matsumoto and Tanaka, 2004; Barbas et al., 2005, 2012; Medalla et al., 2007). In addition, these regions

seem to play a role in the interaction between top-down and bottom-up networks of attention either directly (Salmi et al., 2009; Chadick et al., 2014) or indirectly via connections to the lateral prefrontal cortex (Medalla and Barbas, 2010).We posit that, in the present study, gamma activation of the medial PFC regions and the ACC during the presentation of distracting sounds reflects a strong and fast inhibitory signal to regions involved in the processing of task-irrelevant information. A larger gamma activation of these regions in trials with an informative cue suggest a stronger inhibition of distracting sound processing, resulting from an increased top-down attention load with informative cues. We found that with ageing the amplitude of this top-down inhibitory signal and the capacity to modulate it decline. This is consistent with the proposal that structural alterations in the prefrontal cortex with ageing might disrupt functional connectivity between the prefrontal cortex and sensory regions processing task-irrelevant stimuli (Chadick and colleagues (2014).

4.4 Impact of Ageing on BU/TD Attention balance

Taken together, our findings suggest that with ageing, the integrity of the BU attentional network might remain intact, while TD inhibitory processes in the gamma and alpha bands are altered. Therefore, the exacerbated distractibility exhibited by elderly participants on the behavioral level would rather be related to a reduced activation of TD inhibitory processes than to an enhanced activation of the ventral BU attention network. Elderly participants seem to deploy less TD control in comparison to younger participants. This potentially frontally-driven deterioration of attentional control lies on the cross-roads of the two leading hypotheses accounting for the increased distractibility often observed with ageing: the inhibitory deficit hypothesis (Hasher and Zacks, 1988) and the frontal ageing hypothesis (West, 1996). In line with previous findings (Chadick et al., 2014; Amer et al., 2016) and with the proposition made by Gazzaley and D'Esposito (2007), our findings reconcile both hypotheses: the decrease in the functioning of the frontal control network might be the origin of the ageing-related deficit in inhibitory mechanisms. Thus, the exacerbated behavioral distractibility in ageing might actually be of TD origin.

5 Conclusion

To our knowledge, the current study is the first to utilize oscillatory modulations in the alpha and gamma bands in an attempt to outline how ageing affects TD and BU attentional mechanisms and the interplay between them in the same experiment. Behaviorally, distractibility to distracting sounds is exacerbated with ageing. Electrophysiologically, modulations in alpha oscillations reveal that while facilitatory processes of TD attention seem intact, suppressive processes are reduced with ageing, showing a less efficient TD filtering of task-irrelevant information. This deficit might be compensated by enhanced motor preparation. Moreover, modulations in gamma activity reveal that in comparison to younger adults, elderly participants similarly activate the ventral BU attentional network but display a weaker activation of inhibitory frontal regions in response to distracting sounds.

Therefore, the exacerbated distractibility exhibited by elderly participants on the behavioral level would rather be related to a reduced activation of TD inhibitory processes than to an enhanced activation of the ventral BU attentional network. Importantly, TD inhibitory processes are altered during both attentional preparation and capture, leading to an attentional imbalance towards an enhanced impact of BU attention.

While the present study is focused on the power of oscillatory activity, future investigations should explore how these oscillations would support the connectivity between different cortical regions during the deployment of TD and BU attentional processes in the elderly.

6 References

Ahveninen J, Huang S, Belliveau JW, Chang W-T, Hämäläinen M (2013) Dynamic oscillatory processes governing cued orienting and allocation of auditory attention. Psychologist 26:194–198.

Akimoto Y, Kanno A, Kambara T, Nozawa T, Sugiura M, Okumura E, Kawashima R (2013) Spatiotemporal Dynamics of High-Gamma Activities during a 3-Stimulus Visual Oddball Task. PLoS One 8:1–12.

Akimoto Y, Nozawa T, Kanno A, Ihara M, Goto T, Ogawa T, Kambara T, Sugiura M, Okumura E, Kawashima R (2014) High-gamma activity in an attention network predicts individual differences in elderly adults' behavioral performance. Neuroimage 100:290–300 Available at: http://dx.doi.org/10.1016/j.neuroimage.2014.06.037.

Alho K, Salmi J, Koistinen S, Salonen O, Rinne T (2014) Top-down controlled and bottom-up triggered orienting of auditory attention to pitch activate overlapping brain networks. Brain Res 1626:1–10 Available at: http://dx.doi.org/10.1016/j.brainres.2014.12.050.

Amer T, Anderson JAE, Campbell KL, Hasher L, Grady CL (2016) Age differences in the neural correlates of distraction regulation: A network interaction approach. Neuroimage 139:231–239 Available at: http://dx.doi.org/10.1016/j.neuroimage.2016.06.036.

Barbas H, Bunce JG, Medalla M (2012) Prefrontal pathways that control attention. Princ Front lobe Funct:31–48.

Barbas H, Medalla M, Alade O, Suski J, Zikopoulos B, Lera P (2005) Relationship of prefrontal connections to inhibitory systems in superior temporal areas in the rhesus monkey. Cereb Cortex 15:1356–1370 Available at: http://academic.oup.com/cercor/article/15/9/1356/288682/Relationship-of-Prefrontal-Connections-to [Accessed August 23, 2018].

Bastos AM, Vezoli J, Bosman CA, Schoffelen J-MM, Oostenveld R, Dowdall JR, DeWeerd P, Kennedy H, Fries P, De Weerd P, Kennedy H, Fries P (2015) Visual areas exert feedforward and feedback influences through distinct frequency channels. Neuron 85:390–401 Available at: http://www.ncbi.nlm.nih.gov/pubmed/25556836 [Accessed June 13, 2018].

Bates D, Mächler M, Bolker B, Walker S (2014) Fitting linear mixed-effects models using lme4. arXiv Prepr arXiv14065823.

Bélanger S, Belleville S, Gauthier S (2010) Inhibition impairments in Alzheimer's disease, mild cognitive impairment and healthy aging: Effect of congruency proportion in a Stroop task. Neuropsychologia 48:581–590 Available at: http://www.ncbi.nlm.nih.gov/pubmed/19879885 [Accessed September 13, 2018].

Bidet-Caulet A, Bottemanne L, Fonteneau C, Giard M-H, Bertrand O (2014) Brain Dynamics of Distractibility: Interaction Between Top-Down and Bottom-Up Mechanisms of Auditory Attention. Brain Topogr 28:423–436 Available at: http://link.springer.com/10.1007/s10548-014-0354-x.

Buschman TJ, Miller EK (2007) Top-Down Versus Bottom-Up Control of Attention in the Prefrontal and Posterior Parietal Cortices. Science (80-):8–11.

Chadick JZ, Zanto TP, Gazzaley A (2014) Structural and functional differences in medial prefrontal cortex underlies distractibility and suppression deficits in aging. :69–81.

Chiang AKI, Rennie CJ, Robinson PA, van Albada SJ, Kerr CC (2011) Age trends and sex differences of alpha rhythms including split alpha peaks. Clin Neurophysiol 122:1505–1517 Available at: http://dx.doi.org/10.1016/j.clinph.2011.01.040.

Corbetta M, Kincade JM, Ollinger JM, McAvoy MP, Shulman GL (2000) Voluntary orienting is

dissociated from target detection in human posterior parietal cortex. Nat Neurosci 3:292.
Corbetta M, Patel G, Shulman G (2008) The reorineting system of the human brain: From environment to theory of mind. Neuron 58:306–324.
Corbetta M, Shulman GL (2002) Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci 3:201.
Curran T, Hills A, Patterson MB, Strauss ME (2001) Effects of aging on visuospatial attention: an ERP study. Neuropsychologia 39:288–301.
Deiber MP, Ibañez V, Missonnier P, Rodriguez C, Giannakopoulos P (2013) Age-associated modulations of cerebral oscillatory patterns related to attention control. Neuroimage 82:531–546 Available at: http://dx.doi.org/10.1016/j.neuroimage.2013.06.037.
Deslauriers J, Ansado J, Marrelec G, Provost JS, Joanette Y (2017) Increase of posterior connectivity in aging within the Ventral Attention Network: A functional connectivity analysis using independent component analysis. Brain Res 1657:288–296 Available at: http://dx.doi.org/10.1016/j.brainres.2016.12.017.
ElShafei HA, Bouet R, Bertrand O, Bidet-Caulet A (2018) Two Sides of the Same Coin: Distinct Sub-Bands in the Alpha Rhythm Reflect Facilitation and Suppression Mechanisms during Auditory Anticipatory Attention. Eneuro:ENEURO.0141-18.2018 Available at: http://eneuro.sfn.org/lookup/doi/10.1523/ENEURO.0141-18.2018.
Erel H, Levy DA (2016) Orienting of visual attention in aging. Neurosci Biobehav Rev 69:357–380 Available at: http://dx.doi.org/10.1016/j.neubiorev.2016.08.010.
Fontolan L, Morillon B, Liegeois-Chauvel C, Giraud A-L (2014) The contribution of frequency-specific activity to hierarchical information processing in the human auditory cortex. Nat Commun 5:4694.
Foxe JJ, Snyder AC (2011) The role of alpha-band brain oscillations as a sensory suppression mechanism during selective attention. Front Neurosci 2:1–13.
Frey JN, Ruhnau P, Weisz N (2015) Not so different after all: The same oscillatory processes support different types of attention. Brain Res 1626:183–197 Available at: http://dx.doi.org/10.1016/j.brainres.2015.02.017.
Fries P (2009) Neuronal Gamma-Band Synchronization as a Fundamental Process in Cortical Computation. Annu Rev Neurosci 32:209–224 Available at: http://www.annualreviews.org/doi/10.1146/annurev.neuro.051508.135603.
Gazzaley A, Cooney JW, Rissman J, D'Esposito M, McEvoy K, Knight RT, D'Esposito M (2005) Top-down suppression deficit underlies working memory impairment in normal aging. Nat Neurosci 8:1298–1300.
Gazzaley A, D'esposito M (2007) Top-down modulation and normal aging. Ann N Y Acad Sci 1097:67–83.
Gomez-Ramirez M, Kelly SP, Molholm S, Sehatpour P, Schwartz TH, Foxe JJ (2011) Oscillatory sensory selection mechanisms during intersensory attention to rhythmic auditory and visual inputs: a human electrocorticographic investigation. J Neurosci 31:18556–18567.
Gómez C, M Pérez-Macías J, Poza J, Fernández A, Hornero R (2013) Spectral changes in spontaneous MEG activity across the lifespan. J Neural Eng 10.
Greenwood PM, Parasuraman R, Haxby J V (1993) Changes in visuospatial attention over the adult lifespan. Neuropsychologia 31:471–485.
Gross J, Kujala J, Hämäläinen M, Timmermann L, Schnitzler A, Salmelin R (2001) Dynamic imaging of coherent sources: studying neural interactions in the human brain. Proc Natl Acad Sci 98:694–699.
Guerreiro MJSS, Murphy DR, Van Gerven PWMM (2010) The Role of Sensory Modality in Age-

Related Distraction: A Critical Review and a Renewed View. Psychol Bull 136:975–1022.
Hasher L, Zacks RT (1988) Working memory, comprehension, and aging: A review and a new view. In: Psychology of learning and motivation, pp 193–225. Elsevier.
Heideman SG, Rohenkohl G, Chauvin JJ, Palmer CE, Ede F van, Nobre AC (2018) Anticipatory neural dynamics of spatial-temporal orienting of attention in younger and older adults. Neuroimage Available at: http://dx.doi.org/10.1016/j.dyepig.2015.02.007.
Hillyard SA, Vogel EK, Luck SJ (1998) Sensory gain control (amplification) as a mechanism of selective attention: electrophysiological and neuroimaging evidence. Philos Trans R Soc London B Biol Sci 353:1257–1270.
Hong X, Sun J, Bengson JJ, Mangun GR, Tong S (2015) Normal aging selectively diminishes alpha lateralization in visual spatial attention. Neuroimage 106:353–363 Available at: http://linkinghub.elsevier.com/retrieve/pii/S1053811914009367.
James W (1890) The Principles of Psychology. 2:94.
Jensen O, Mazaheri A (2010) Shaping Functional Architecture by Oscillatory Alpha Activity: Gating by Inhibition. Front Hum Neurosci 4:1–8 Available at: http://journal.frontiersin.org/article/10.3389/fnhum.2010.00186/abstract.
Kelly SP, Lalor EC, Reilly RB, Foxe JJ (2006) Increases in alpha oscillatory power reflect an active retinotopic mechanism for distracter suppression during sustained visuospatial attention. J Neurophysiol 95:3844–3851 Available at: http://www.ncbi.nlm.nih.gov/pubmed/16571739.
Klimesch W, Sauseng P, Hanslmayr S (2007) EEG alpha oscillations: The inhibition–timing hypothesis. Brain Res Rev 53:63–88 Available at: https://www.sciencedirect.com/science/article/pii/S016501730600083X.
Kurth S, Majerus S, Bastin C, Collette F, Jaspar M, Bahri MA, Salmon E (2016) Effects of aging on task- and stimulus-related cerebral attention networks. Neurobiol Aging 44:85–95 Available at: http://dx.doi.org/10.1016/j.neurobiolaging.2016.04.015.
Lancaster JL, Rainey LH, Summerlin JL, Freitas CS, Fox PT, Evans AC, Toga AW, Mazziotta JC (1997) Automated labeling of the human brain: a preliminary report on the development and evaluation of a forward-transform method. Hum Brain Mapp 5:238.
Lee B, Park KS, Kang D-H, Kang KW, Kim YY, Kwon JS (2007) Generators of the gamma-band activities in response to rare and novel stimuli during the auditory oddball paradigm. Neurosci Lett 413:210–215.
Leenders MP, Lozano-Soldevilla D, Roberts MJ, Jensen O, De Weerd P (2018) Diminished Alpha Lateralization During Working Memory but Not During Attentional Cueing in Older Adults. Cereb Cortex 28:21–32 Available at: http://academic.oup.com/cercor/article/28/1/21/2557349.
Li HJ, Hou XH, Liu HH, Yue CL, Lu GM, Zuo XN (2015) Putting age-related task activation into large-scale brain networks: A meta-analysis of 114 fMRI studies on healthy aging. Neurosci Biobehav Rev 57:156–174 Available at: http://dx.doi.org/10.1016/j.neubiorev.2015.08.013.
Li L, Zhao D (2015) Age-related inter-region EEG coupling changes during the control of bottom-Up and top-Down attention. Front Aging Neurosci 7:1–14.
Long NM, Kuhl BA (2018) Bottom-up and top-down factors differentially influence stimulus representations across large-scale attentional networks. J Neurosci:2724–17 Available at: http://www.jneurosci.org/lookup/doi/10.1523/JNEUROSCI.2724-17.2018.
Maris E, Oostenveld R (2007) Nonparametric statistical testing of EEG- and MEG-data. J Neurosci Methods 164:177–190.

Masson R, Bidet-Caulet A (2018) Fronto-central P3a to distracting sounds: an index of their arousing properties. bioRxiv:333419 Available at: https://www.biorxiv.org/content/early/2018/05/30/333419 [Accessed June 19, 2018].

Matsumoto K, Tanaka K (2004) The role of the medial prefrontal cortex in achieving goals. Curr Opin Neurobiol 14:178–185 Available at: http://www.ncbi.nlm.nih.gov/pubmed/15082322 [Accessed August 23, 2018].

Medalla M, Barbas H (2010) Anterior cingulate synapses in prefrontal areas 10 and 46 suggest differential influence in cognitive control. J Neurosci 30:16068–16081 Available at: http://www.ncbi.nlm.nih.gov/pubmed/21123554 [Accessed August 23, 2018].

Medalla M, Lera P, Feinberg M, Barbas H (2007) Specificity in Inhibitory Systems Associated with Prefrontal Pathways to Temporal Cortex in Primates. Cereb Cortex 17:i136–i150 Available at: http://www.ncbi.nlm.nih.gov/pubmed/17725996 [Accessed August 23, 2018].

Mevorach C, Spaniol MM, Soden M, Galea JM (2016) Age-dependent distractor suppression across the vision and motor domain. J Vis 16:27 Available at: http://jov.arvojournals.org/article.aspx?doi=10.1167/16.11.27.

Michalareas G, Vezoli J, Van Pelt S, Schoffelen J-M, Kennedy H, Fries P (2016) Alpha-beta and gamma rhythms subserve feedback and feedforward influences among human visual cortical areas. Neuron 89:384–397.

Naccarato M, Calautti C, Jones PS, Day DJ, Carpenter TA, Baron J-C (2006) Does healthy aging affect the hemispheric activation balance during paced index-to-thumb opposition task? An fMRI study. Neuroimage 32:1250–1256 Available at: http://www.ncbi.nlm.nih.gov/pubmed/16806984 [Accessed August 5, 2018].

Nolte G (2003) The magnetic lead field theorem in the quasi-static approximation and its use for magnetoencephalography forward calculation in realistic volume conductors. Phys Med Biol 48:3637.

Olk B, Kingstone A (2015) Attention and ageing: Measuring effects of involuntary and voluntary orienting in isolation and in combination. Br J Psychol 106:235–252.

Parmentier FBR, Andrés P (2009) The involuntary capture of attention by sound: Novelty and postnovelty distraction in young and older adults. Exp Psychol 57:68–76 Available at: http://www.ncbi.nlm.nih.gov/pubmed/20178965 [Accessed September 13, 2018].

Rule RR, Shimamura AP, Knight RT (2002) Orbitofrontal cortex and dynamic filtering of emotional stimuli. Cogn Affect Behav Neurosci 2:264–270.

Salmi J, Rinne T, Koistinen S, Salonen O, Alho K (2009) Brain networks of bottom-up triggered and top-down controlled shifting of auditory attention. Brain Res 1286:155–164 Available at: http://dx.doi.org/10.1016/j.brainres.2009.06.083.

Salo E, Salmela V, Salmi J, Numminen J, Alho K (2017) Brain activity associated with selective attention, divided attention and distraction. Brain Res 1664:25–36 Available at: http://dx.doi.org/10.1016/j.brainres.2017.03.021.

Searle SR, Speed FM, Milliken GA (1980) Population marginal means in the linear model: an alternative to least squares means. Am Stat 34:216–221.

Talairach J, Tournoux P (1988) Co-planar stereotaxic atlas of the human brain: 3-dimensional proportional system: an approach to cerebral imaging.

Tallon-Baudry, Bertrand (1999) Oscillatory gamma activity in humans and its role in object representation. Trends Cogn Sci 3:151–162 Available at: http://www.ncbi.nlm.nih.gov/pubmed/10322469.

Team RC (2014) R: A Language and Environment for Statistical Computing. Vienna: R

Foundation for Statistical Computing. Available online at: h ttp. www R-project org.
Vaden RJ, Hutchesona NL, McColluma LA, Kentrosa JG, M. VK (2012) Older adults, unlike younger adults, do not modulate alpha power to suppress irrelevant information. North 29:1883–1889.
van der Waal M, Farquhar J, Fasotti L, Desain P (2017) Preserved and attenuated electrophysiological correlates of visual spatial attention in elderly subjects. Behav Brain Res 317:415–423 Available at: http://dx.doi.org/10.1016/j.bbr.2016.09.052.
Van Veen BD, van Drongelen W, Yuchtman M, Suzuki A (1997) Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. Biomed Eng IEEE Trans 44:867–880.
Von Békésy G, Wever EG (1960) Experiments in hearing. McGraw-Hill New York.
Weisz N, Hartmann T, Müller N, Lorenz I, Obleser J (2011) Alpha rhythms in audition: Cognitive and clinical perspectives. Front Psychol 2:1–15.
West RL (1996) An application of prefrontal cortex function theory to cognitive aging. Psychol Bull 120:272.
Zanto TP, Gazzaley A (2014) Attention and ageing. Oxford Handb Atten:927–971.

10 Attention & Frontal Damage

10.1 Study IV: Impact of Frontal Damage on Attentional Mechanisms (CAT 3.0)

10.1.1 Introduction

In chapter 4, we have discussed how lesions in the lateral prefrontal cortex (lPFC) could impact various attentional mechanisms. For example, Bidet-Caulet and colleagues (2015) demonstrated that only the facilitatory but not the inhibitory top-down mechanisms of auditory selective attention are negatively impacted by lPFC lesions. In addition, lPFC lesions have been also accompanied by an increased susceptibility to distracting information (e.g. Chao and Knight 1995).

The purpose of this study was to shed more light on the impact of lPFC lesions on anticipatory top-down attention, bottom-up attentional capture and the balance between the two; and in turn to highlight the role of the lPFC in all of these processes. However, the recruitment of a homogeneous cohort of patients with relatively circumscribed unilateral lesion resulting from ischemic stroke is slow and still underway. Thus, in this chapter we shall present and discuss preliminary behavioral results. In addition, we shall lay out the analyses that we are planning once the recruitment will be over.

10.1.2 Materials and Methods

10.1.2.1 Participants

Eight LPFC patients (mean age = 58 ± 4.53 Standard Error of Mean (SEM); range: 39—74 years; 4 females) were selected on the basis of a unilateral focal lesion to their dorsolateral PFC (4 right and 4 left). All lesions were due to ischemic stroke. Maximal lesion overlap comprised Brodmann's areas 9, 44, 45 and 46, with variable amount of damage in Brodmann's areas 4, 6, 8 and 47, as well as some part of the insula but auditory cortices were always preserved (see Figure 1). All patients were right-handed and reported no motor weakness. Recordings took place at least 1 year and a half after the injury. The patients were free of medical complications, psychiatric disorders, substance abuse, psychoactive drug treatment, or other neurological diseases. Eight healthy controls (mean age = 58 ± 4.69 SEM; range: 35—79 years; 4 females) free of neurological or psychiatric disease, were chosen to individually match the patients in age, gender, handedness, education level and music training. As expected, the two groups did not significantly differ in age (T-test p = 0.94), in education level (T-test p = 0.71), nor in music training (T-test p = 0.49). The study was approved by the local ethical committee, and subjects gave written informed consent, according to the Declaration of Helsinki, and they were paid for their participation.

	Patient group	***Control Group***
Age (years ± SEM)	58 ± 4.53	58 ± 4.69
Gender	4F, 4M	4F, 4M
Handedness	8R	8R
Scholar Education (years ± SEM)	14 ± 1.15	15 ± 0.98
Musical Education (years ± SEM)	3 ± 1.42	1 ± 0.88

Table1. Group demographics. SEM, standard error of the mean; F, Female; M, Male; R, right-handed.

10.1.2.2 Lesion Reconstruction

We have utilized the reconstruction pipeline described by Hirel and colleagues (2017). Participant lesions were imaged with 3D MRI scans (Magnetom Prisma Siemens 3T MRI equipped with a 64-channel head/neck coil), with T1, T2 and T2FLAIR sequences (Fluid-Attenuated Inversion Recovery scan: TR = 5000 ms, TE = 349 ms, TI = 1008 ms, FOV = 224x224 mm, sagittal acquisition, slice thickness = 0.9 mm,192 slices). Lesions were drawn manually by a trained neurologist on the individual's T2-FLAIR MRI images in native space, using MITK 3M3 (Mint Medical Ins, USA). MRI images and lesions masks were normalized into the MNI (Montreal Neurological Institute) space, using the standard linear spatial normalization procedure from SPM12 (Functional Imaging Laboratory, London, UK) in Matlab.

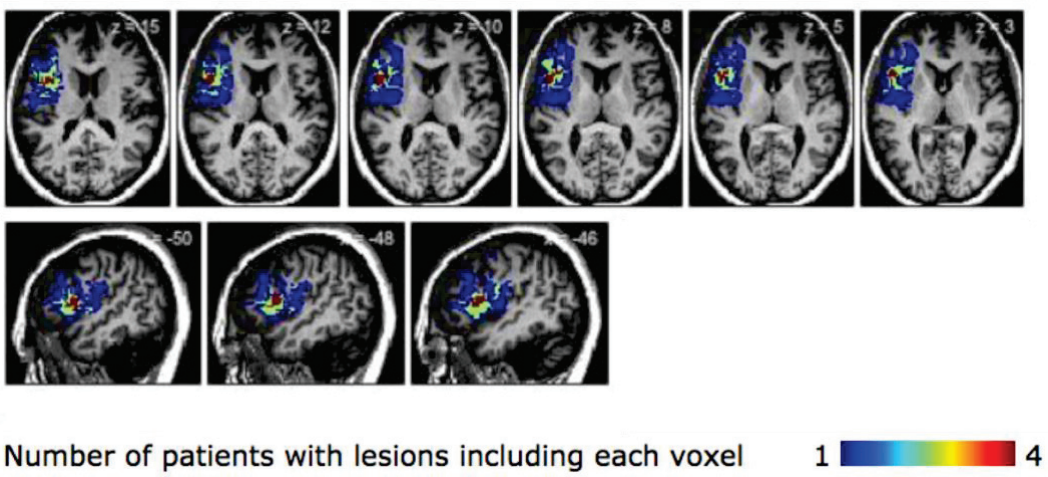


Figure 1. Overlay of the 8 lesions. The number of patients having a lesion at each voxel is color-coded. The four lesions in the right hemisphere have been flipped on left hemisphere. There is a maximum of four patients having a lesion in the same voxel.

10.1.3 Stimuli and tasks

10.1.3.1 Competitive Attention Task (CAT)

A complete description of the paradigm used (CAT 3.0) has been previously provided (please refer to section 5.1 and 5.3 and Figure 2 below).

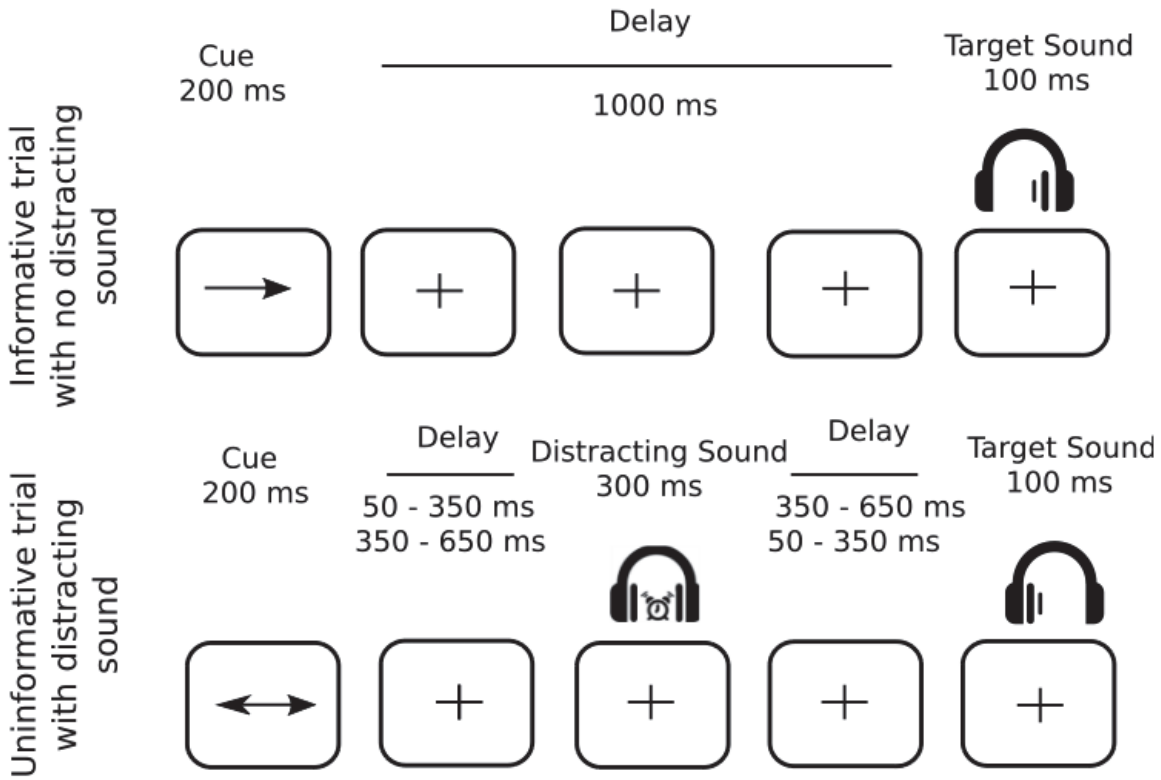


Figure 2. Protocol. Top row. In informative trials, a one-sided visual cue (200 ms duration) indicated in which ear (left or right) the target sound would be played (100 ms duration) after a fixed 1000-ms delay. Bottom row. In uninformative trials, a two-sided visual cue (200 ms duration) did not provide any indication in which ear (left or right) the target sound will be played. In 25 % of the trials a binaural distracting sound (300 ms duration), such as a clock ring, was played during the delay between cue and target. The distracting sound could equiprobably onset in two different time periods after the cue offset: in the 50–350 ms range, or in the 350–650 ms range.

10.1.3.2 Discrimination Task

Participants were randomly presented with one of two target sounds: a low-pitched sound (512 Hz) and a high-pitched sound (575 Hz; two semitones higher), equiprobably in each ear (four trials per ear and per pitch). Participants were asked to categorize the target sounds as either high- or low-pitched sound within 3 seconds.

10.1.3.3 Procedure

Participants were seated in a sound-attenuated, magnetically shielded recording room, at a 50 cm distance from the screen. The response device was an index-operated joystick that participants moved either towards them (when instructed to pull) or away from them (when instructed to push). All stimuli were delivered using Presentation software (Neurobehavioral Systems, Albany, CA, USA). All sounds were presented through air-conducting tubes using Etymotic ER-3A foam earplugs (Etymotic Research, Inc., USA).

First, the auditory threshold was determined for the two target sounds differing by 2 semitones (512 and 575 Hz), for each ear, for each participant using the Bekesy tracking method (Von Békésy and Wever 1960). The target sounds were then monaurally presented at 25 dB SL (58.9 ± 2.9; mean dBA ± SEM) while the distracting sounds were binaurally played at 55 dB SL (68.9 ± 2.9; mean dBA ± SEM). Second, participants performed the discrimination task. If participants failed to respond correctly to more than 85% of the trials, the pitch of the high target sound was augmented, by half a semitone with a maximum difference of 3 semitones between the two targets (auditory thresholds were then measured with the new targets). Afterwards, participants were trained with a short sequence of the Competitive Attention Task (CAT). Finally, MEG and EEG were recorded while subjects performed 10 blocks (64 trials each): the whole session lasted around 80 minutes. After the MEG/EEG session, participants' subjective reports regarding their strategies were collected.

10.1.4 Behavioral Data Analysis

For behavioral data analysis, a response was considered correct, if it matched the response mapped to the target sound and was executed before the apparition of the following cue. Trials with an incorrect, or precocious or no response were excluded from further analysis. The influence of (1) group (2 levels: patients and controls), (2) cue condition (2 levels: informative and uninformative), and (3) distractor condition (3 levels: NoDis, DIS1 and DIS2) on percentage of incorrect responses and median reaction times (RTs) of correct responses was tested using a linear mixed-effects models (lme4 package, Bates et al., 2014 for R Team, 2014). A random effect was included for each participant, allowing us to model variability between participants. For post-hoc analysis we used the Lsmean package (Lsmean version 2.20-23; Searle et al., 1980) where p-values were considered as significant at $p<0.05$ and adjusted for the number of comparisons performed (Tukey method).

Moreover, planned analyses of the CUE BENEFIT were carried out between groups on the differences in RTs Uninformative NoDIS – Informative NoDIS and of distractor effects on the differences in RTs NoDIS – DIS1 (as a measure of the AROUSAL BENEFIT) or DIS2 – DIS1 (as a measure of ATENTION CAPTURE COST), using non-parametric Kruskal–Wallis tests (Bidet-Caulet et al. 2014; Masson and Bidet-Caulet 2018). As a final step, these three measures were tested separately in each group, using non-parametric one-sample Wilcoxon tests.

10.2 Results

Participants correctly performed the discrimination task in 92.05 ± 0.58 SEM % of the trials. The remaining trials were either incorrect trials (6.48 ± 0.50 SEM %), missed trials (0.63 ± 0.13 %) or trials with FAs (0.42 ± 0.09 %).

10.2.1 Behavioral Analysis: Incorrect Response Percentage (Figure)

Only a significant main effect of the distractor condition ($F(2, 30) = 6.4$, $p < 0.01$, $\eta^2 = 0.25$) was found on the percentage of incorrect responses. Post-hoc tests indicated that participants, from both groups, committed more errors in the late DIS2 condition in comparison to the NoDIS ($p < 0.01$) conditions.

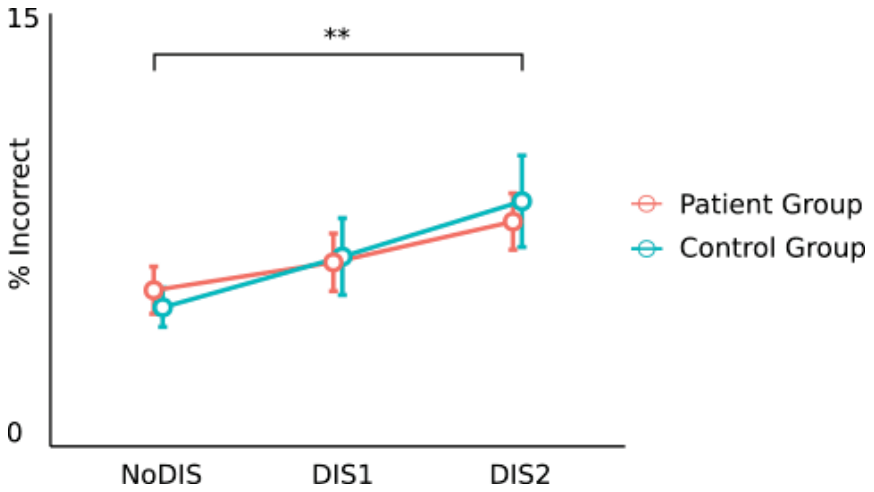


*Figure 3. Percentage of Incorrect Responses averaged across cue conditions for patient (red) and control (blue) groups. P < 0.05, ** P < 0.01. Error bars represent SEM.*

10.2.2 Behavioral Analysis: Median Reaction Times (Figure)

We have only found a main effect of the distractor condition ($F(2, 30) = 71.9$, $p < 0.001$, $\eta^2 = 0.25$) with no main effect of group ($F(1, 15) = 2.7$, $p = 0.12$, $\eta^2 = 0.16$). Post-hoc tests indicated that in comparison to the NoDIS condition, participants were faster in the early DIS1 condition ($p = 0.029$) but slower in the late DIS2 condition ($p < 0.001$). In addition, participants were faster in the early DIS1 condition in comparison to the late DIS2 condition ($p < 0.001$).

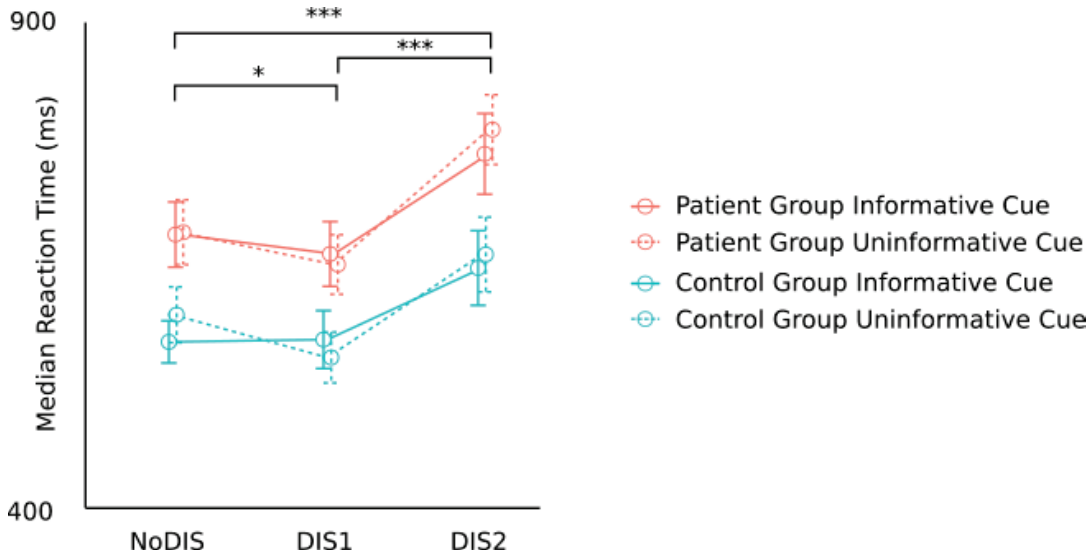


*Figure 4. Left Panel: Median RTs for both groups. Right Panel: Attentional Capture effect on RTs for both groups. P < 0.05, ** P < 0.01, *** P < 0.001. Error bars represent SEM.*

10.2.3 Planned Behavioral Analysis (Figure 5)

Non-parametric Kruskal–Wallis tests between groups demonstrated that the cue benefit effect (Uninformative NoDIS – Informative NoDIS; p=0.24), the attention capture effect (DIS2 – DIS1; p = 0.09) and the arousal effect (NoDIS – DIS; p = 0.46) were similar between groups.

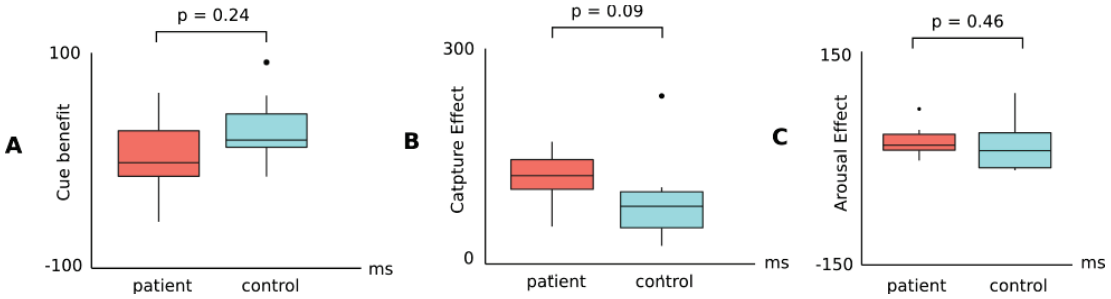


Figure 5. Boxplot of (A) the Cue benefit effect, (B) the Attention capture effect, and (C) the Arousal effect, according to groups.

Below is a table with all the results from the one-sample Wilcoxon test (see **Table** 1).

	Patient Group	***Control Group***
Cue benefit effect	*p = 0.84*	*p = 0.04*
Attention capture effect	*p = 0.007*	*p = 0.007*
Arousal effect	*p = 0.01*	*p = 0.3*

Table 1. List of p-values from the one-sample Wilcoxon tests for the three behavioral measures.

10.3 Discussion

Below we will discuss the preliminary behavioral results. However, due to the small group size, these results and their interpretation should be treated with caution.

10.3.1 Impact of lPFC Lesions on Top-Down Mechanisms of Attention

Preliminarily, according to the GLM analysis, neither group seemed to benefit from the cue information to faster identify the target pitch. However, visually, a difference between the two groups could be observed, while not significant (see **Figure** and **Figure** 5**A** and **Table1**). However, in the absence of distracting sounds, only the control group was faster in the informative cue condition in comparison to the uninformative condition. This potential failure to use top-town anticipation in patients with frontal damage would be in line with previous studies (1) in patients suffering from dorsolateral frontal lesions performing a forewarned reaction-time task in the visual modality (Zappoli et al. 2000) and (2) in patients suffering from lateral prefrontal lesions performing an auditory Go/NoGo delayed response task (Funderud et al. 2013). Both studies have utilized the contingent negative variation (CNV), an evoked potential often used as an index of top-down anticipatory attention (e.g. Brunia and van Boxtel 2001; Gómez et al. 2007; Bidet-Caulet et al. 2014) and both have demonstrated a diminution in amplitude (or even a vanishing); i.e. reduced top-down anticipatory activity.

Taken together, these results suggest that patients could suffer from a deficit in intentionally orienting their attentional resources after a lPFC stroke, highlighting the potential role of the lPFC in top-down attention.

10.3.2 Impact of lPFC Lesions on Bottom-Up Mechanisms of Attention

Both groups displayed the reaction time (RT) pattern common to the CAT paradigm: participants were faster in trials with early distracting sounds rather than with late distracting sounds or with no distracting sounds. This pattern could be explained by the two opposite effects triggered by a distracting sound: (1) a persistent increase in arousal resulting in RT reduction (behavioral benefit) and (2) a stronger transient attentional capture (orienting) effect leading to RT augmentation (behavioral cost). The behavioral net effect of distracting sound varies according to the time interval between the distracting and the target sounds (Bidet-Caulet et al. 2014; Masson and Bidet-Caulet 2018). The difference in reaction time to targets between trials with late distracting sounds (DIS2) and trials with early distracting

sounds (DIS1) provides a good approximation of the attentional capture effect, while the difference in reaction time to targets between trials with early distracting sounds (DIS1) and trials with no distracting sounds (NoDIS) provides a good approximation of the arousal effect.

Preliminary statistical testing demonstrated similar attentional capture effect in both groups. However, visually, a difference (close to significance) between the two groups could be observed notably on the attentional capture effect of the distracting sounds which seems more exacerbated in the lPFC group (see **Figure** and **Figure** 5**B**). This observation goes in line with previous studies demonstrating that behaviorally, lesions to the lPFC are accompanied by increased distractibility where lPFC patient performances deteriorate in presence of distracting stimuli (Chao and Knight 1995; Gehring and Knight 2002). This increased distractibility could be due to an increased activation of the bottom-up ventral network or a reduced activation of inhibitory frontal areas. Analyses of the brain activities in response to distracting sounds should shed light on the origin of these attention difficulties.

Finally, there preliminary statistical testing demonstrated an arousal effect that is more pronounced in the patient group. However, we believe that such effect is mainly due to the low sample size and greater variability across control participants.

10.3.3 Future Analysis

Once we reach the recruitment of a minimum of twelve patients and their healthy matched controls, we shall investigate the impact of lPFC lesions on (1) top-down attentional mechanisms as indexed by oscillatory activity in the alpha band, (2) bottom-up attentional mechanisms as indexed by oscillatory activity in the gamma band, and (3) the balance between top-down and bottom-up mechanisms. In addition, we shall investigate how the connectivity patterns, highlighted in previous chapters would be modified following a lesion to the lPFC.

Part IV: General Discussion

11 Discussion and Perspectives

"Truth is found neither in the thesis nor the antithesis,
but in an emergent synthesis which reconciles the two."
— Hegel

Over the past fifty years, countless endeavors have been undertaken to dissect the neural correlates underlying mechanisms of attention using more and more sophisticated and precise methods of analysis. One of the recent methods is investigating oscillatory activity. In the present work, we aimed to improve our understanding of the role of oscillatory activity in the alpha and gamma bands in supporting top-down and bottom-up mechanisms of auditory attention and the interplay between them in the healthy, ageing and lesioned brain.

Within this general framework, four studies combining behavioral assessment and simultaneous MEG and EEG recording revealed how oscillatory activity in the alpha and gamma bands would reflect the dynamics of top-down and bottom-up mechanisms of attention, respectively, and how gamma oscillatory activity in the prefrontal cortex would orchestrate the balance between these two mechanisms. In addition, we highlighted how these mechanisms could be impaired in the ageing brain and how these impairments could explain attentional difficulties associated with healthy ageing. Finally, using data collected from patients with prefrontal damage, we provided preliminary evidence to the role of the lateral prefrontal cortex (lPFC) in supporting both top-down and bottom-up mechanisms of attention.

The discussion sections presented in chapters seven to ten of this thesis have already pointed out the major implications of each of these studies. The aim of the present section is to set this work into a broader context, by linking results together and presenting how our research could improve the understanding of the role of oscillatory activity in supporting the dynamics of attention, and more generally the communication within brain networks. Additionally, in each section, we will propose future lines of research that could be useful to further our understanding.

11.1 The Competitive Attention Test

11.1.1 Duplex Responses to Distracting Sounds

Throughout this thesis work, using different versions of the Competitive Attention Test (CAT), young participants displayed a similar pattern of behavioral responses to distracting sounds: In comparison to trials with no distracting sounds, participants responded faster to the following target in trials with early distracting sounds while they responded slower to targets in trials with late distracting sounds (see Figure 30).

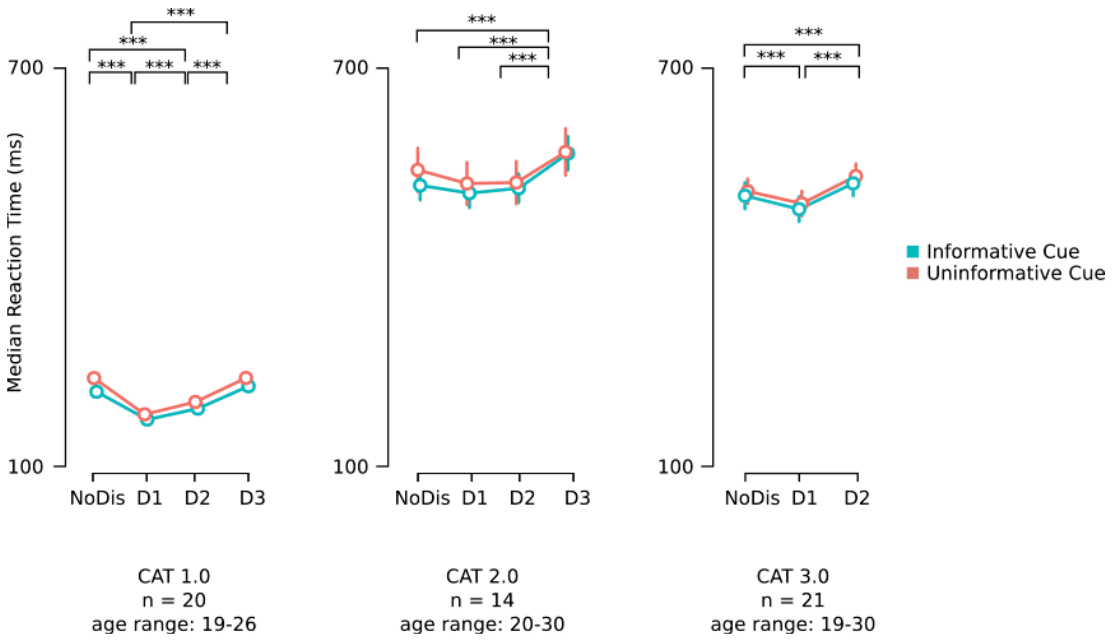


*Figure 30. Median Reaction Times (RTs) according to cue and distractor conditions. *** P < 0.001. Error bars represent SEM. Please note overall longer RTs when a discrimination task was used (CAT 2.0 and 3.0) compared to a detection task (CAT 1.0). Please note that for CAT1.0, SEMs are too small to be visible.*

This pattern affirms a clear distinction between two phenomena (see Figure 31) that could be triggered by a distracting sound: (1) a persistent increase in arousal resulting in RT reduction (behavioral benefit) and (2) a strong transient attentional capture (exogenous orienting) leading to RT augmentation (behavioral cost); with the behavioral net effect of distracting sound varying according to the time interval between the distracting and the target sounds (Bidet-Caulet et al. 2014; Masson and Bidet-Caulet 2018). Therefore, these findings highlight the importance of considering the different responses that are elicited by a distracting stimulus when investigating the brain mechanisms of distraction in future studies. In addition, we believe that these replicable results add to the validity of the Competitive

Attention Test (CAT) as a suitable test to investigate the dynamics of both top-down and bottom-up mechanisms of attention and the balance between them in an ecological setting in both healthy and clinical populations.

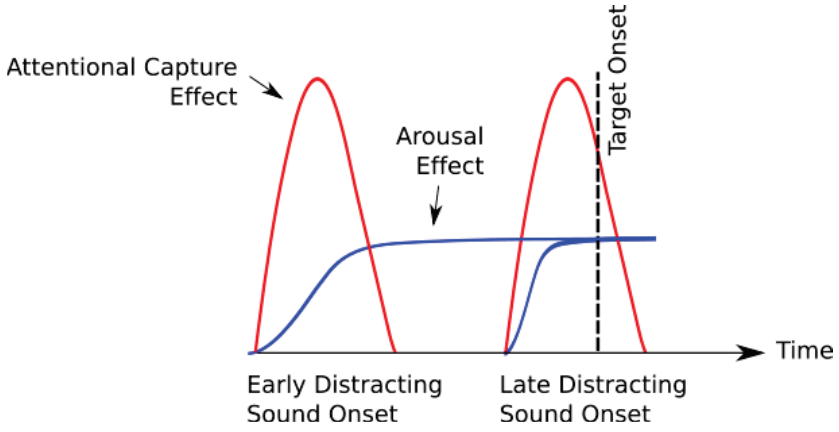


Figure 31. Schematic representation of the time-course of the two phenomena triggered by a distracting sound: increase in arousal (blue) and attentional capture (red).

11.1.2 CAT Wars: Differences Between CAT Iterations

In order to explore the differences between all versions of the CAT paradigm, we used three behavioral measures: the CUE BENEFIT (the differences in RTs Uninformative NoDIS – Informative NoDIS), the AROUSAL (RTs NoDIS – DIS1) and ATTENTION CAPTURE (Latest DIS – earliest DIS) (Bidet-Caulet et al., 2014; Masson and Bidet-Caulet, 2018).

As seen in Figure 32**A**, the cue benefit was highly reduced in CAT 3.0 in comparison to CAT1.0 and CAT2.0. This was expected as we have modified the ratio of informative to uninformative trials from 2:1 to 1:1. This was a necessary compromise in order to adapt the duration of the paradigm to elderly and patient populations while conserving a sufficient number of trials with a distracting sound. Nevertheless, participants in CAT3.0 seem to have utilized the cue information properly as evidenced by a significant effect of cue on RTs in the absence of distracting sound.

As for the distracting sound effects, we observed a marked decrease in their arousal effect (see Figure 32**C**) in both CAT2.0 and CAT3.0 in comparison to CAT1.0. We consider that this effect corroborates our aim to render the task more challenging by using a discrimination task. A slightly more difficult task is likely to increase the top-down attentional load as well as the tonic arousal level (Kahneman 1973; Sarter et al. 2006; Eysenck 2012). A larger tonic arousal level might have contributed to a ceiling effect of the phasic arousal burst to distracting sounds i.e. the arousal could not be indefinitely increased. Finally, in comparison

to the other effects, the attention capture effect seems to have varied the less (see Figure 32**B**). This shows that, in the CAT paradigm, the proportion of trials with distracting sounds to trials with no distracting sounds (1:3) is appropriate to trigger a strong transient bottom-up attentional capture towards these distracting sounds.

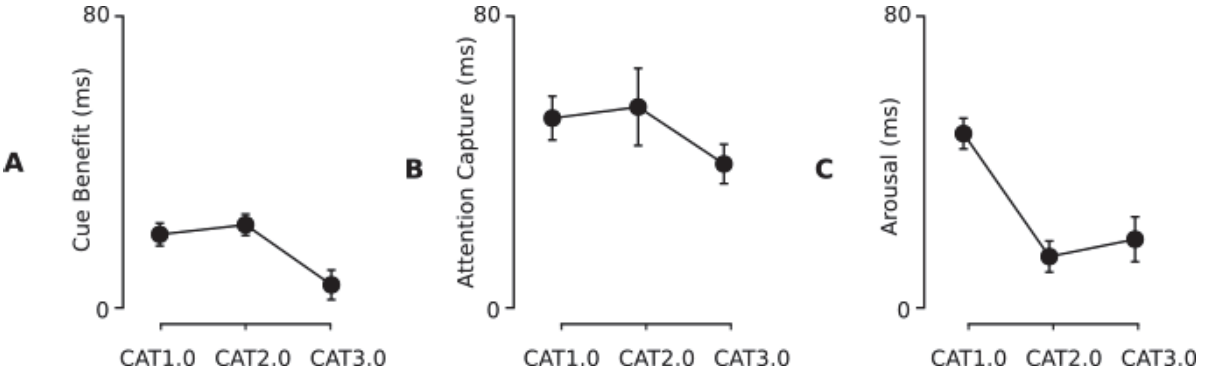


Figure 32. (A) the Cue benefit effect, (B) the Attention capture effect, and (C) the Arousal effect, according to groups. Error bars represent SEM.

11.2 Oscillatory Activity Orchestrating Mechanisms of Attention

11.2.1 Alpha Oscillations & Top-down Mechanisms of Attention

11.2.1.1 A Role for Power

We demonstrated that anticipation of an auditory target (**Study I**) modulated the power of alpha oscillations differently in both task-relevant auditory cortices (alpha power decrease: alpha desynchronization) and task-irrelevant occipital cortices (alpha power increase: alpha synchronization). We also showed that the occipital alpha synchronization correlated negatively with reaction times and that alpha power in the right auditory cortex was modulated by the visual cue. Finally, we displayed in **supplementary study III** that even after the presentation of a distracting sound, a similar pattern of auditory alpha modulation was re-established.

The auditory alpha literature is fairly recent with concerns that auditory oscillations might reflect spectral leakage from higher frequencies (e.g. beta) and/or neighboring cortical regions such as the motor cortex (Weisz et al. 2011). While it has not been presented, we found no evidence of power modulations by the cue in neither auditory beta activity, nor motor alpha activity. In addition, in the ageing study we showed that auditory and motor alpha(s) display distinct profiles and are differently impacted by ageing. We believe that our

findings confirm the existence of independent generators of alpha oscillations that are specific to the auditory cortex and that can be modulated by top-down endogenous attention (Muller and Weisz 2012; Frey et al. 2014; Weisz and Obleser 2014; Weisz et al. 2014).

In a wider context, the ensemble of these results, at least on a sensory level, are in accordance with the inhibition-timing (Klimesch et al. 2007) and the gating by inhibition (Jensen and Mazaheri 2010) hypotheses that reaffirm an "inhibitory role" of alpha oscillations. This however does not exclude a potential "active processing" role of alpha oscillations (Palva and Palva 2007, 2011). While we have focused our investigations on alpha activity in the auditory and visual cortices, we have observed feeble yet not negligible alpha synchronization in frontal regions, notably in the ventrolateral prefrontal cortex. While, the significance and the mechanisms underlying this alpha power synchronization remains a matter of debate (Palva et al. 2005; Palva and Palva 2007, 2011), we posit that this frontal alpha synchronization might reflect the deactivation of the task-irrelevant ventral BU attention network.

11.2.1.2 A Role for Peak Frequency

In addition, we demonstrated that alpha synchronization in the visual cortex (in anticipation of an auditory target) and in the right auditory cortex (in anticipation of an ipsilateral auditory target) were centered around 13Hz (high alpha). On the contrary, alpha synchronization in the auditory cortices (in anticipation of an auditory target) and in the right auditory cortex (in anticipation of a contralateral auditory target) were centered around 9Hz (low alpha). We have also replicated this pattern in the **ageing study (III)** where only young participants demonstrated such frequency differentiation. Taken together, these results not only confirm our hypothesis that alpha oscillations would support top-down mechanisms of attention but also add a fine detail on the dynamics of such support: different high and low alpha sub-bands would support suppressive and facilitatory mechanisms of anticipatory attention, respectively.

We discussed how alpha peak frequency could be considered as a "state" variable that would index performance fluctuations, cognitive demands and probably the functional task-relevance of cortical regions (Klimesch 1999; Başar 2012; Haegens et al. 2014) with very recent evidence that it could be dynamically controlled by top-down signals in order to alter information processing in the underlying cortical regions (Wutz et al. 2018). While our results fit well with such notion, we cannot overlook the "trait" or "characteristic" nature of alpha

peak frequency that could change across individuals and cortical regions (Klimesch 1999; Başar 2012; Haegens et al. 2014, 2015). Thus, we believe that in order to shed more light on the significance of alpha peak frequency, future studies should investigate more systematically the different alpha peak frequencies in different cortical regions using cross-modal paradigms where participants would be required to attend to a stimulus in a modality and ignore other stimuli in other modalities, i.e. attending to an auditory stimulus while ignoring concurrent visual and motor stimuli and vice versa.

Finally, in the ageing study, we observed that the differences between the alpha peak frequencies in the auditory and visual regions diminished with ageing; a phenomenon that was accompanied by a diminution of visual synchronization in older participants, relative to the younger ones. This raises the question of the functional (causal) link between alpha peak frequency and top-down attentional modulations: Is the successful allocation of different alpha-bands to distinct mechanisms of attention an imperative for these mechanisms to be functional? In this sense impaired top-down suppressive mechanisms could be the consequence of the diminished frequency peak differences. Or is the lack of alpha sub-band differentiation resulting from the ageing-related top-down impairments? Another possibility is that both phenomena: diminished peak differences and impaired suppressive top-down mechanisms are symptomatic of a third phenomenon e.g. reduced frontal alpha phase synchrony with auditory and visual cortices. Future investigations shall look into possible correlations between inter-regional alpha peak frequency differences and inter-regional alpha phase synchrony.

11.2.1.3 A Role for Phase

We have hypothesized that in anticipation of an auditory target, long-range communication between nodes of the dorsal top-down attention network, such as the Frontal eye fields (FEF) and/or the intraparietal sulcus (IPS), and the auditory cortex would be established through inter-areal phase synchrony in the alpha band. We have demonstrated that anticipating an ipsilateral right auditory target increased phase synchrony between the right auditory cortex and regions in the vicinity of the left Frontal eye fields (FEF) and the left dorsolateral prefrontal cortex. Please note that similar analyses have been undertaken in theta, beta and gamma bands with neither significant emergence of such connectivity nor modulations by the cue information.

This goes in line with our general oscillatory framework that long-range communication across the dorsal network of top-down attention would be preferentially indexed by alpha phase synchrony, rather than beta (or gamma) oscillations, as described by earlier studies (Bastos et al. 2015; Richter et al. 2017). This, however, does not exclude a role for other oscillations in supporting connections between other nodes of the dorsal network as proposed by Clayton and colleagues (2015). In their model of top-down sustained attention, communication between different nodes of the dorsal fronto-parietal network occur at different frequency bands i.e. frontal-frontal communication occurs in the theta band whereas frontal-sensory communication in the alpha band. Indeed, in our analysis, we have only used the auditory cortices as seed to investigate phase synchrony. Future analysis shall investigate synchrony with different seed regions within the dorsal network, such as the visual cortex, the Frontal Eye Fields or the lateral prefrontal cortex.

11.2.1.4 A Room for Gamma

We also demonstrated that in anticipation of an auditory target (**supplementary study II**), induced gamma activity in the auditory cortices was differentially modulated by the visual cue and negatively correlated with reaction times. Also, after the target presentation, auditory gamma activity was higher when preceded by an informative cue in comparison to an uninformative cue. This fits well with the notion that the power of gamma activity reflects local neuronal active processing (Fries 2005, 2009; Lachaux et al. 2005; Jensen et al. 2007) where in this context gamma activity would reflect (1) heightened cortical excitability (pre-activation) in the auditory cortices in order to optimally process the upcoming auditory target and (2) efficient processing of the auditory target.

Regarding to our framework, in a first step, we showed that both alpha phase-synchrony and gamma-amplitude are modulated by top-down attention (see Figure 33). However, the question remains whether this auditory gamma activity is coupled (nested) to auditory alpha oscillations i.e. whether the amplitude of gamma oscillations is related to the phase of alpha oscillations as it has been previously proposed (Canolty and Knight 2010; Bonnefond et al. 2017) and evidenced (Jensen and Colgin 2007; Lakatos et al. 2008; Bahramisharif et al. 2013; Szczepanski et al. 2014; Bonnefond and Jensen 2015; Esghaei et al. 2015; Chacko et al. 2018) in different cortical regions. Future investigation of phase amplitude

coupling has been planned in order to shed more light on how these frequency bands interact with each other.

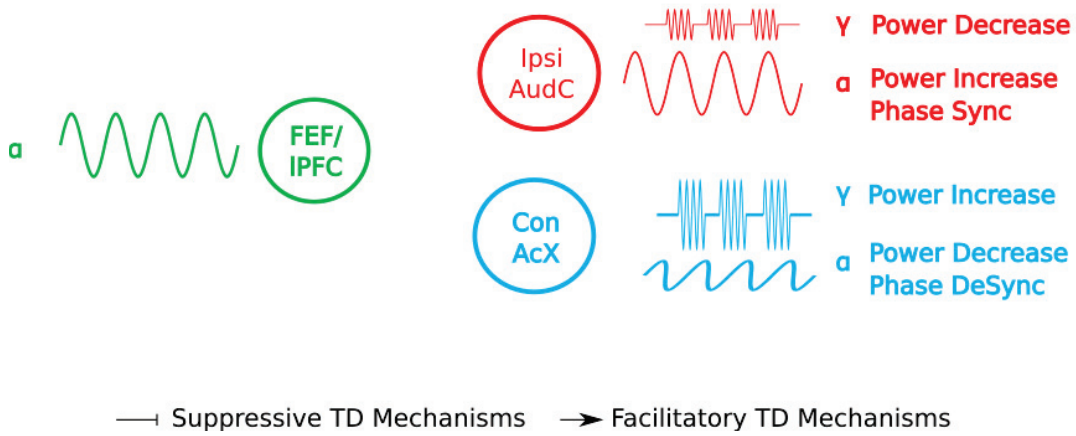


Figure 33. Schematic summary of the results investigating alpha (α) and gamma (γ) during top-down anticipation of an auditory target. FEF: Frontal eye fields, lPFC: lateral prefrontal cortex. AudC: auditory cortex. Ipsi: ipsilateral, Contra: contralateral, (de)Sync: (de)synchrony with FEF/lPFC.

11.2.2 Gamma Oscillations & Bottom-up Mechanisms of Attention

11.2.2.1 A Role for Power

We have demonstrated that in response to an unexpected salient distracting sound, gamma power increases in the auditory cortices and various nodes of the ventral network of bottom-up attention: bilateral temporo-parietal junctions and the right ventrolateral frontal cortex (**study II**). This pattern of activation is consistent with the architecture (Corbetta and Shulman 2002; Corbetta et al. 2008; Salmi et al. 2009; Ahveninen et al. 2013; Alho et al. 2014; Salo et al. 2017; Long and Kuhl 2018) of the auditory ventral fronto-parietal network. In addition, it accentuates previous evidence to the laterality differences between the bilateral auditory ventral fronto-parietal network and the right lateralized visual one (Kim 2014).

This finding is in accordance with our initial hypothesis that gamma oscillations would reflect the activation of the bottom-up network of attentional capture. This hypothesis was based upon the active processing role purported to be played by gamma oscillations where increase in gamma amplitude (and/or phase) reflects a facilitation of forward-transfer of information through the cortical populations (Fries 2005, 2009; Sedley and Cunningham 2013; Michalareas et al. 2016). This also fits in with the notion that bottom-up attentional capture is a rapid transient phenomenon. Thus, gamma activation would reflect the rapid "circuit-

breaking" effect of the distracting sound which causes a shift away from the focus of attention (DiQuattro et al. 2014).

11.2.2.2 A Role for Phase

We have also observed that during the presentation of a distracting sound, phase synchrony in the gamma band increased between the auditory cortices and several other brain regions, notably the lateral prefrontal cortices. This finding corroborates evidence that gamma oscillations could subtend inter-areal communication through phase synchrony (Communication through coherence hypothesis: Fries 2005, 2009). We suggest that gamma activity indexes not only the activation of the ventral the bottom-up network of attention but also the communication along this network. In the following we shall discuss how these oscillations could also reflect the interaction between bottom-up and top-down mechanisms of attention.

11.2.3 The Prefrontal Cortex: A Crossroad of Mechanisms of Attention

One of the main novelties of this thesis work is shedding new light on the role of the lateral prefrontal cortex in supporting top-down and bottom-up mechanisms of attention through phase synchrony in alpha and gamma bands, respectively (see Figure 34).

On one hand, the lateral prefrontal cortex was involved in top-down long-range synchrony in the alpha band with the right auditory cortex (**supplementary study I**). This corroborates growing evidence that the lateral prefrontal cortex (lPFC) could play a role in supporting top-down attentional by potentially inhibiting the task-irrelevant pathways (Caclin and Fonlupt 2006; Johnson et al. 2007; Miller, Vytlacil, et al. 2011; Zanto et al. 2011). Future investigations shall attempt to explore whether these synchrony patterns correlate with behavioral performances and activity in both auditory and visual cortices.

On the other hand, the lateral prefrontal cortex was involved in bottom-up gamma synchrony with both auditory cortices. Functional imaging studies demonstrated that the lateral prefrontal cortex is associated with (and correlates to) the inhibition of distraction responses (Dolcos et al. 2007; Suzuki and Gottlieb 2013; Yan et al. 2016). We suggest that this observed synchrony could be a means to regulate the distracting sound processing. Future investigations of top-down modulation of this bottom-up synchrony are planned.

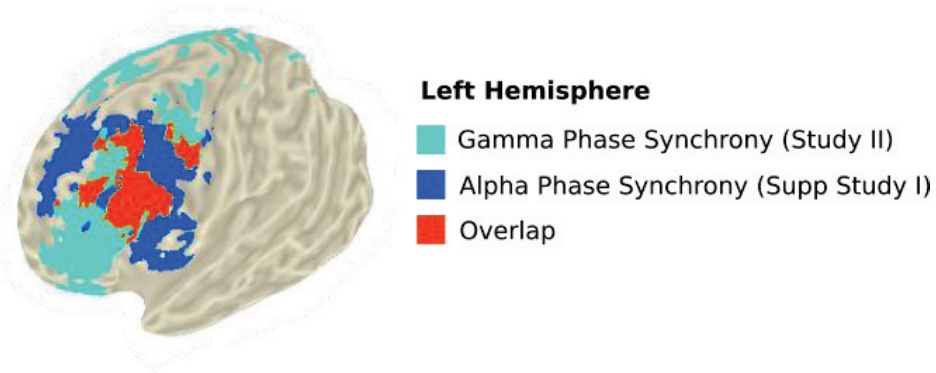


Figure 34. Brain regions that displayed increased synchrony with the auditory cortices in the alpha (dark blue) and the gamma (light blue) bands. Regions in red displayed increased in both oscillatory bands.

To the best of our knowledge, this is the first study, to utilize gamma activity (power) to investigate the potential role of the prefrontal cortex in subtending the balance (interaction) between top-down and bottom-up attentional mechanisms. While TD modulations of gamma activity did not occur in the lateral divisions of the prefrontal cortex, per se, we believe that such finding does not entirely invalidate our initial hypothesis. Gamma modulations occurred in neighboring regions: the dorso- and ventromedial prefrontal cortices and the anterior cingulate cortex. In these regions, gamma activity was more pronounced in response to distracting sounds preceded by an informative cue rather than an uninformative cue. On two accounts we believe that our hypothesis should withstand such contradictory results:

First, anatomically, both the lateral and medial prefrontal cortices have connections with the auditory cortices, and the anterior cingulate cortex and the lateral prefrontal cortex are highly interconnected (Barbas et al. 2012b). In addition, both the lateral and medial prefrontal cortices are highly interconnected (Miller and Cohen 2001) and display highly comparable functional connectivity to other brain regions (Cole et al. 2013).

Second, along with the lateral prefrontal cortex, these regions constitute the cognitive inhibitory control system (Salmi et al. 2009; Løvstad, Funderud, Meling, et al. 2012; Ossandon et al. 2012; Erika-Florence et al. 2014). Thus, they play more or less similar roles; for example, the ventromedial prefrontal cortex has also been found to be situated on the crossroads between top-down and bottom-up attention (Salmi et al. 2009; Chadick et al. 2014).

Thus, while top-down and bottom-up seem to interact via the medial prefrontal cortex (and the anterior cingulate gyrus), a role of the lateral prefrontal cortex cannot be excluded.

The lPFC could allow indirect communication between the mPFC and the ventral network through gamma phase synchrony between the lPFC and the auditory cortex (**study II**) on one hand, and between the lPFC and the mPFC on the other hand (to be investigated). Another mechanism for the lPFC to control the balance between top-down and bottom-up attention would be the coupling between alpha and gamma oscillations which shall be further investigated in future research.

11.2.4 An Oscillatory Model of Attention

Here, we propose an oscillatory model of auditory attention (see Figure 35). First aspect of this framework is that top-down anticipatory signals would modulate the amplitude of alpha oscillations in the auditory cortices (auditory alpha) either by synchronization (power increase) or desynchronization (alpha decrease) in order to regulate auditory cortical excitability down (anticipatory suppression) or up (anticipatory facilitation) according to the laterality of the upcoming target. These modulations seem to occur in distinct alpha bands (**study I**). Such modulations would be possible through alpha phase synchronization between fronto-parietal (FEF and/or IPS: **supplementary study I**) and ipsilateral auditory regions. In this top-down prepatory setting, auditory gamma could reflect increased cortical excitability, i.e. pre-activation, of the auditory cortices (**supplementary study II**).

Within our framework, it is plausible that auditory gamma could be nested upon auditory alpha, in accordance with the model proposed by Bonnefond and colleagues (2017). However, on the contrary to their model we have found no direct evidence of gamma activation in the dorsal network of TD attention (data not shown).

The second aspect is that the propagation of attentional capture-related bottom-up signals would be predominantly reflected in gamma activity in the ventral fronto-parietal network (plus the auditory cortex) of attention (**study II**). Whereas, the regulation of this these bottom-up signals would be predominantly reflected in gamma activity in medial subdivisions of the prefrontal network of cognitive control (**study II**). This of course marginalizes the role alpha oscillations in attentional capture, but we posit that given the rapid nature of the attentional capture, it would be more computationally (ecologically) efficient for the brain to rely on information transfer through fast gamma oscillations while alpha oscillations would be more suitable for communication over relatively longer periods of time.

These two aspects reconcile theoretical models of oscillatory communication (e.g. Bonnefond et al. 2017) and recent experimental findings in the attention domain (e.g. Buschman and Miller 2007; Richter et al. 2017) by taking into consideration the nature and timing of the (attentional) signal to be communicated. In other words, fast bottom-up signals would be communicated by high-frequency gamma oscillations while, relatively slower top-down signals would be communicated by low-frequency alpha oscillations.

Third aspect of this framework is the role of the lateral prefrontal cortex in subtending long-range (1) top-down alpha and bottom-up gamma synchrony, and (2) the interaction between the two mechanisms. We posit that the latter role could be subtended by fluctuations in the alpha-gamma coupling magnitude in the lPFC. While such role has been only partially validated, we believe that future analyses either in healthy subjects or patients with frontal damage would help reaffirm this role.

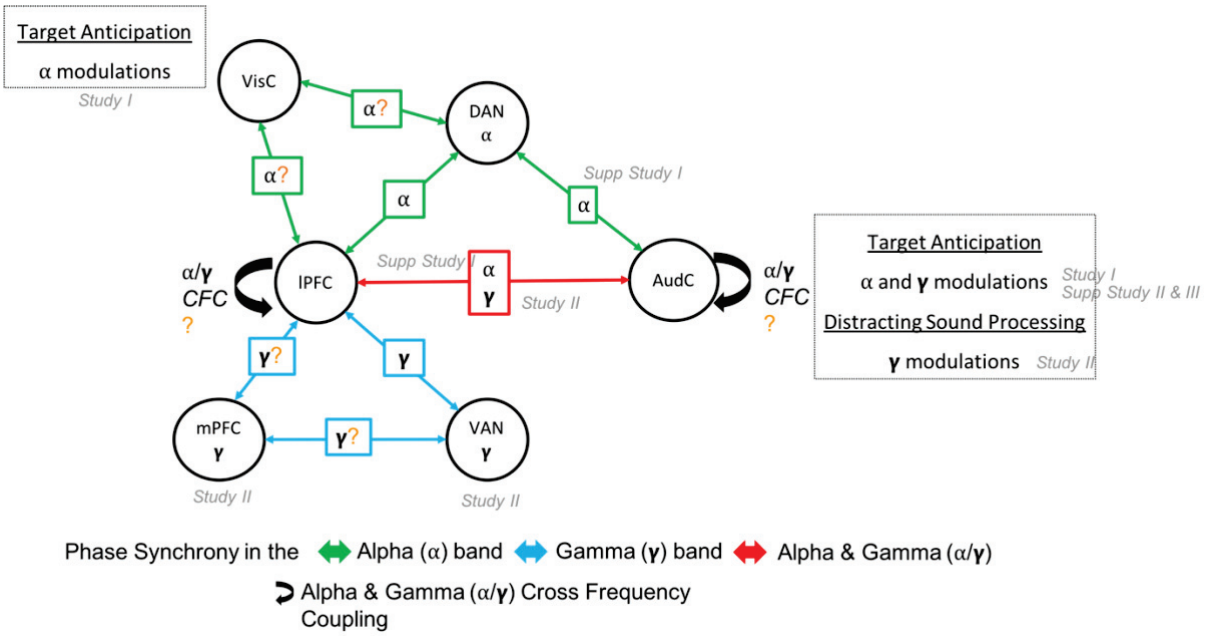


Figure 35. The Oscillatory model proposed in this thesis work. DAN: dorsal attentional network, VAN: ventral attentional network, lPFC: lateral prefrontal cortex, AudC: auditory cortex, mPFC: medial prefrontal cortex, VisC: visual cortex.

11.3 The Ageing Brain: A Top-Down Modulation Deficit

11.3.1 Ageing and Alpha Oscillations

Through the aforementioned oscillatory framework, we were able to disentangle the brain dynamics related to attentional difficulties often associated with ageing (see Figure 36). By investigating sensory (auditory/visual) and motor alpha activity, we were able to highlight a relatively intact facilitatory component of anticipatory attention (decrease in auditory alpha) and a deficit in the suppressive component (increase in visual alpha) and heightened motor preparation (decrease in motor alpha) with ageing. In healthy young adults, we demonstrated that suppression of visual alpha was linked to faster performances. Thus, would increased motor activity during ageing be compensatory to visual suppression deficits, in order to achieve similar behavioral performances?

In healthy young adults, we demonstrated that TD attentional orienting increases phase synchrony between the lPFC/FEF and the task-irrelevant ipsilateral auditory cortex. Given the negative inhibitory influence that could be exerted by the lateral and/or medial prefrontal cortex upon irrelevant sensory modality pathways (Caclin and Fonlupt 2006; Chadick et al. 2014), we predict an impaired synchrony between the lateral prefrontal cortex and the visual cortices during ageing, that would result in a deficit in inhibition of task-irrelevant visual information. Future investigations of the phase, rather than power, dynamics of alpha activity might uncover the origins of such deficit.

11.3.2 Ageing and Gamma Oscillations

As explained in section 11.1, using the CAT paradigm, we disentangled two responses to a distracting sound: a beneficial arousal effect and a detrimental attentional capture effect. Only the latter was exacerbated with ageing. This behavioral effect was accompanied by a reduced response to the distracting sounds in the medial prefrontal cortex and the anterior cingulate gyrus whose activity, as we have described above, seems to play an important role in top-down inhibition of distracting stimuli (Salmi et al., 2009; Ossandon et al., 2012; Zanto and Gazzaley, 2013; Erika-Florence et al., 2014). Interestingly, the BU attentional network remained intact, thus relating exacerbated behavioral attentional capture to a reduced activation of TD inhibitory processes.

This fits well with a growing hypothesis of top-down deficit in the ageing brain (Gazzaley and D'esposito 2007; Gazzaley 2013). This hypothesis reconciles the inhibitory

deficit hypothesis (Hasher and Zacks 1988) and the frontal ageing hypothesis (West 1996): the decrease in the functioning of the frontal control network might be the origin of the ageing-related deficit in inhibitory mechanisms. Thus, the exacerbated bottom-up behavioral distractibility might actually be of top-down origin.

Future investigations have two aims. First, we shall investigate the gamma phase synchrony within and between the prefrontal control and the bottom-up networks, in order to shed more light on the implication of these connectivity patterns in the ageing-related increased distractibility. Second, it has been proposed that auditory distraction is a three-stage phenomenon that involves the detection of the distracting stimulus followed by the orienting of attention processes towards it and finally these processes are reoriented back to the ongoing task (Wetzel and Schröger 2014). Thus, we believe that investigation of the evoked potentials that have been related to these processes during the Competitive Attention Test, shall provide complementary evidence to the results we already obtained in order to precisely outline facets of attentional capture that are inflicted by ageing.

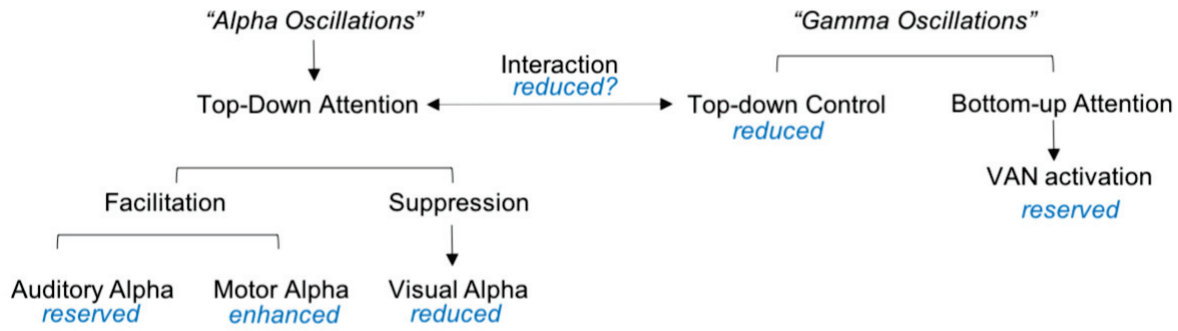


Figure 36. Summary of the impact of ageing on the oscillatory dynamics supporting mechanisms of top-down and bottom-up attention.

11.4 The Lesioned Brain

Finally, we provided preliminary behavioral results demonstrating two trending behavioral deficits for patients with frontal lesions: reduced capacity to utilize cue information to respond faster to target sounds and an exacerbated attentional capture by distracting sounds. In **study IV**, we provided possible explanations for these effects and below we shall discuss the implications of such preliminary results within the oscillatory framework we are proposing.

11.4.1 The Lesioned Brain & Alpha Oscillations

In supplementary study I, we highlighted a role of the lPFC in the top-down modulation of auditory alpha activity, i.e. increased synchrony with auditory cortex ipsilateral to the upcoming target which hints to a role of the lPFC in regulating activity in task-irrelevant regions in the alpha band. Thus, we expect deficits in signatures of the suppressive top-down anticipatory mechanisms: less alpha increase in visual areas with the CAT. In addition, based upon the failure to utilize the cue and the already existing literature pointing to an impaired top-down anticipatory attention system (Zappoli et al. 2000; Funderud et al. 2013), we also expect deficits in the signatures of facilitatory top-down anticipatory mechanisms: less auditory and motor alpha decreases. Relative to our framework, this shall add more details to the role the lPFC in supporting top-down mechanisms of attention through alpha oscillations.

11.4.2 The Lesioned Brain & Gamma Oscillations

In **study III** we demonstrated how healthy ageing affects the organization of the gamma hierarchy supporting bottom-up network of attention most probably due to a functionally impaired frontal cortex. lPFC lesions are associated with increased distractibility (Woods and Knight 1986; Knight et al. 1999; Gehring and Knight 2002) and given the trending exacerbated distractibility frontal patients demonstrated, this strengthens our original hypothesis that lPFC lesions would disrupt only the top-down control of auditory distraction while the architecture of the bottom-up network would remain intact. Relative to our framework, this shall add more details to the role of the lPFC in supporting bottom-up mechanisms of attention and the interaction with top-down mechanisms through gamma oscillations.

12 Conclusion

Taken together, this thesis work provides new insights on the oscillatory hierarchy supporting top-down and bottom-mechanisms of auditory attention. To our knowledge, this is the first attempt to simultaneously investigate the role of alpha and gamma oscillations in subtending communication within the dorsal and ventral networks of top-down and bottom-up auditory attention, respectively. Our results also shed new light on how the prefrontal cortex would support mechanisms of attention while its exact role in supporting the interaction between them remains to be investigated in future research in both healthy and clinical (frontal damage) populations. Several of our results have been barely reported in the literature and we believe it might be helpful as a guideline for future research. Finally, the oscillatory model that we have proposed also permits to scrutinize attentional difficulties in different populations i.e. while we have focused on healthy ageing and frontal damage, our protocol and working model could be applied to investigate attentional differences in other healthy or clinical populations such as children, migraine, schizophrenia or autism where the bottom-up/top-down balance is often affected.

“I don’t know where I’m going from here,
but I promise it won’t be boring.”
— David Bowie

Part V: References

13 Bibliography

Ahveninen J, Huang S, Belliveau JW, Chang W-T, Hämäläinen M. 2013. Dynamic oscillatory processes governing cued orienting and allocation of auditory attention. Psychologist. 26:194–198.

Akimoto Y, Kanno A, Kambara T, Nozawa T, Sugiura M, Okumura E, Kawashima R. 2013. Spatiotemporal Dynamics of High-Gamma Activities during a 3-Stimulus Visual Oddball Task. PLoS One. 8:1–12.

Akimoto Y, Nozawa T, Kanno A, Ihara M, Goto T, Ogawa T, Kambara T, Sugiura M, Okumura E, Kawashima R. 2014. High-gamma activity in an attention network predicts individual differences in elderly adults' behavioral performance. Neuroimage. 100:290–300.

Alain C, Woods DL. 1999. Age-related changes in processing auditory stimuli during visual attention: Evidence for deficits in inhibitory control and sensory memory. Psychol Aging. 14:507–519.

Alho K, Salmi J, Koistinen S, Salonen O, Rinne T. 2014. Top-down controlled and bottom-up triggered orienting of auditory attention to pitch activate overlapping brain networks. Brain Res. 1626:1–10.

Anderson SW, Damasio H, Tranel D, Damasio AR. 2000. Long-term sequelae of prefrontal cortex damage acquired in early childhood. Dev Neuropsychol. 18:281–296.

Andrés P, Parmentier FBR, Escera C. 2006. The effect of age on involuntary capture of attention by irrelevant sounds: A test of the frontal hypothesis of aging. Neuropsychologia. 44:2564–2568.

Arnal LH, Wyart V, Giraud A-LL. 2011. Transitions in neural oscillations reflect prediction errors generated in audiovisual speech. Nat Neurosci. 14:797–801.

Aston-Jones G, Cohen JD. 2005. An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. Annu Rev Neurosci. 28:403–450.

Badre D. 2008. Cognitive control, hierarchy, and the rostro-caudal organization of the frontal lobes. Trends Cogn Sci. 12:193–200.

Bahramisharif A, van Gerven MAJ, Aarnoutse EJ, Mercier MR, Schwartz TH, Foxe JJ, Ramsey NF, Jensen O. 2013. Propagating Neocortical Gamma Bursts Are Coordinated by Traveling Alpha Waves. J Neurosci. 33:18849–18854.

Baldauf D, Desimone R. 2014. Neural Mechanisms of object-based attention. Science (80-). 344:420–424.

Barbas H, Bunce JG, Medalla M. 2012a. Prefrontal pathways that control attention. Princ Front lobe Funct. 31–48.

Barbas H, Bunce JG, Medalla M. 2012b. Prefrontal pathways that control at tention. Princ Front lobe Funct. 31–48.

Barceló F, Suwazono S, Knight RT. 2000. Prefrontal modulation of visual processing in humans. Nat Neurosci. 3:399–403.

Başar E. 2012. A review of alpha activity in integrative brain function: Fundamental physiology, sensory coding, cognition and pathology. Int J Psychophysiol. 86:1–24.

Bastos AM, Schoffelen J-M. 2016. A Tutorial Review of Functional Connectivity Analysis Methods and Their Interpretational Pitfalls. Front Syst Neurosci. 9.

Bastos AM, Usrey WM, Adams RA, Mangun GR, Fries P, Friston KJ. 2012. Canonical microcircuits for predictive coding. Neuron. 76:695–711.

Bastos AM, Vezoli J, Bosman CA, Schoffelen J-MM, Oostenveld R, Dowdall JR, DeWeerd P, Kennedy H, Fries P, De Weerd P, Kennedy H, Fries P. 2015. Visual areas exert feedforward and feedback influences through distinct frequency channels. Neuron.

85:390–401.
Bates D, Mächler M, Bolker B, Walker S. 2014. Fitting linear mixed-effects models using lme4. arXiv Prepr arXiv14065823.
Beane M, Marrocco RT. 2004. Norepinephrine and acetylcholine mediation of the components of reflexive attention: implications for attention deficit disorders. Prog Neurobiol. 74:167–181.
Berger A, Henik A, Rafal R. 2005. Competition between endogenous and exogenous orienting of visual attention. J Exp Psychol Gen. 134:207–221.
Berger H. 1929. Über das Elektrenkephalogramm des Menschen. Arch Psychiatr Nervenkr. 87:527–570.
Berti S. 2008. Cognitive control after distraction: Event-related brain potentials (ERPs) dissociate between different processes of attentional allocation. Psychophysiology. 45:608–620.
Berti S. 2013. The role of auditory transient and deviance processing in distraction of task performance: a combined behavioral and event-related brain potential study. Front Hum Neurosci. 7:352.
Berti S, Grunwald M, Schröger E. 2013. Age dependent changes of distractibility and reorienting of attention revisited: An event-related potential study. Brain Res. 1491:156–166.
Bertrand O, Tallon-Baudry C. 2000. Oscillatory gamma activity in humans: A possible role for object representation. Int J Psychophysiol. 38:211–223.
Bidet-Caulet A. 2014. Brain oscillatory dynamics in the bottom-up / top-down balance of attention. ANR. 27–29.
Bidet-Caulet A, Barbe PG, Roux S, Viswanath H, Barthélémy C, Bruneau N, Knight RT, Bonnet-Brilhault F. 2012. Dynamics of anticipatory mechanisms during predictive context processing. Eur J Neurosci. 36:2996–3004.
Bidet-Caulet A, Bottemanne L, Fonteneau C, Giard M-H, Bertrand O. 2014. Brain Dynamics of Distractibility: Interaction Between Top-Down and Bottom-Up Mechanisms of Auditory Attention. Brain Topogr. 28:423–436.
Bidet-Caulet A, Buchanan KG, Viswanath H, Black J, Scabini D, Bonnet-Brilhault F, Knight RT. 2015. Impaired facilitatory mechanisms of auditory attention after damage of the lateral prefrontal cortex. Cereb Cortex. 25:4126–4134.
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. J Neurosci. 27:9252–9261.
Bidet-Caulet A, Mikyska C, Knight RT. 2010. Load effects in auditory selective attention: Evidence for distinct facilitation and inhibition mechanisms. Neuroimage. 50:277–284.
Bogousslavsky J. 1994. Frontal stroke syndromes. Eur Neurol.
Bolton DAE, Staines WR. 2014. Attention-based modulation of tactile stimuli: A comparison between prefrontal lesion patients and healthy age-matched controls. Neuropsychologia. 57:101–111.
Bonnefond M, Jensen O. 2012. Alpha oscillations serve to protect working memory maintenance against anticipated distracters. Curr Biol. 22:1969–1974.
Bonnefond M, Jensen O. 2015. Gamma activity coupled to alpha phase as a mechanism for top-down controlled gating. PLoS One. 10:1–11.
Bonnefond M, Kastner S, Jensen O. 2017. Communication between Brain Areas Based on Nested Oscillations. Eneuro. 4:ENEURO.0153-16.2017.
Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. 2001. Conflict Monitoring and Cognitive Control Despite the importance of these efforts to characterize the func- tion of cognitive control, most of them share an important limitation in scope. Most current

theories focus nearly exclusively on the. Psychol Rev. 108:624–652.
Bragin A, Jandó G, Nádasdy Z, Hetke J, Wise K, Buzsáki G. 1995. Gamma (40-100 Hz) oscillation in the hippocampus of the behaving rat. J Neurosci. 15:47–60.
Broadbent DE. 1958. The selective nature of learning. Percept Commun. 244–267.
Brunia CH, van Boxtel GJ. 2001. Wait and see. Int J Psychophysiol. 43:59–75.
Brunia CHM. 1999. Neural aspects of anticipatory behavior. Acta Psychol (Amst). 101:213–242.
Bueti D, Macaluso E. 2010. Auditory temporal expectations modulate activity in visual cortex. Neuroimage. 51:1168–1183.
Busch NA, Dubois J, VanRullen R. 2009. The Phase of Ongoing EEG Oscillations Predicts Visual Perception. J Neurosci. 29:7869–7876.
Buschman TJ, Kastner S. 2015. From Behavior to Neural Dynamics: An Integrated Theory of Attention. Neuron. 88:127–144.
Buschman TJ, Miller EK. 2007. Top-Down Versus Bottom-Up Control of Attention in the Prefrontal and Posterior Parietal Cortices. Science (80-). 8–11.
Bush G, Luu P, Posner MI. 2000. Cognitive and emotional influences in anterior cingulate cortex. TrendsCogn Sci. 4:215–222.
Bushara KO, Weeks RA, Ishii K, Catalan M-J, Tian B, Rauschecker JP, Hallett M. 1999. Modality-specific frontal and parietal areas for auditory and visualspatial localization in humans. Nat Neurosci. 2:759–766.
Buzsaki G. 2006. Rhythms of the Brain. Oxford University Press.
Buzsaki G, Draguhn A, Buzsáki G. 2004. Neuronal oscillations in cortical networks. Science (80-). 304:1926–1929.
Caclin A, Fonlupt P. 2006. Functional and effective connectivity in an fMRI study of an auditory-related task. Eur J Neurosci. 23:2531–2537.
Campbell KL, Grady CL, Ng C, Hasher L. 2012. Age differences in the frontoparietal cognitive control network: Implications for distractibility. Neuropsychologia. 50:2212–2223.
Canolty RT, Knight RT. 2010. The functional role of cross-frequency coupling. Trends Cogn Sci.
Caporello Bluvas E, Gentner TQ. 2013. Attention to natural auditory signals. Hear Res.
Capotosto P, Babiloni C, Romani GL, Corbetta M. 2009. Frontoparietal Cortex Controls Spatial Attention through Modulation of Anticipatory Alpha Rhythms. J Neurosci. 29:5863–5872.
Capotosto P, Babiloni C, Romani GL, Corbetta M. 2011. Differential contribution of right and left parietal cortex to the control of spatial attention: a simultaneous EEG–rTMS study. Cereb cortex. 22:446–454.
Capotosto P, Baldassarre A, Sestieri C, Spadone S, Romani GL, Corbetta M. 2016. Task and regions specific top-down modulation of alpha rhythms in parietal cortex. Cereb cortex. 27:4815–4822.
Capotosto P, Spadone S, Tosoni A, Sestieri C, Romani GL, Della Penna S, Corbetta M. 2015. Dynamics of EEG rhythms support distinct visual selection mechanisms in parietal cortex: a simultaneous transcranial magnetic stimulation and EEG study. J Neurosci. 35:721–730.
Carlen M. 2017. What constitutes the prefrontal cortex? Science (80-). 482:478–482.
Chacko R V., Kim B, Jung SW, Daitch AL, Roland JL, Metcalf N V., Corbetta M, Shulman GL, Leuthardt EC. 2018. Distinct phase-amplitude couplings distinguish cognitive processes in human attention. Neuroimage.
Chadick JZ, Zanto TP, Gazzaley A. 2014. Structural and functional differences in medial prefrontal cortex underlies distractibility and suppression deficits in aging. 69–81.

Chait M, Cheveigné A De, Poeppel D, Simon JZ. 2010. Neural dynamics of attending and ignoring in human auditory cortex. Neuropsychologia. 48:3262–3271.
Chao LL, Knight RT. 1995. Human prefrontal lesions increase distractibility to irrelevant sensory inputs. Neuroreport.
Chao LL, Knight RT. 1997. Prefrontal deficits in attention and inhibitory control with aging. Cereb Cortex. 7:63–69.
Chao LL, Knight RT. 1998. Contribution of human prefrontal cortex to delay performance. J Cogn Neurosci. 10:167–177.
Cherry EC. 1953. Some experiments on the recognition of speech, with one and with two ears. J Acoust Soc Am. 25:975–979.
Cheyne DO. 2013. MEG studies of sensorimotor rhythms: A review. Exp Neurol. 245:27–39.
Chica AB, Bartolomeo P, Lupiáñez J. 2013. Two cognitive and neural systems for endogenous and exogenous spatial attention. Behav Brain Res. 237:107–123.
Chrobak JJ, Buzsáki G. 1998. Gamma oscillations in the entorhinal cortex of the freely behaving rat. J Neurosci. 18:388–398.
Cid-Fernández S, Lindín M, Díaz F. 2014. Effects of aging and involuntary capture of attention on event-related potentials associated with the processing of and the response to a target stimulus. Front Hum Neurosci. 8:745.
Clapp WC, Rubens MT, Gazzaley A. 2010. Mechanisms of working memory disruption by external interference. Cereb Cortex. 20:859–872.
Clapp WC, Rubens MT, Sabharwal J, Gazzaley A. 2011. Deficit in switching between functional brain networks underlies the impact of multitasking on working memory in older adults. Proc Natl Acad Sci U S A. 108:7212–7217.
Clayton MS, Yeung N, Cohen Kadosh R. 2015. The roles of cortical oscillations in sustained attention. Trends Cogn Sci.
Cohen MX. 2014. Analyzing neural time series data: theory and practice. MIT press.
Cole MW, Reynolds JR, Power JD, Repovs G, Anticevic A, Braver TS. 2013. Multi-task connectivity reveals flexible hubs for adaptive task control. Nat Neurosci. 16:1348–1355.
Corbetta M, Kincade JM, Ollinger JM, McAvoy MP, Shulman GL. 2000. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nat Neurosci. 3:292.
Corbetta M, Kincade JM, Shulman GL. 2002. Neural systems for visual orienting and their relationships to spatial working memory. J Cogn Neurosci. 14:508–523.
Corbetta M, Miezin FM, Shulman GL, Petersen SE. 1993. A PET study of visuospatial attention. J Neurosci. 13:1202–1226.
Corbetta M, Patel G, Shulman G. 2008. The reorineting system of the human brain: From environment to theory of mind. Neuron. 58:306–324.
Corbetta M, Shulman GL. 2002. Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci. 3:201.
Cosman JD, Atreya P V, Woodman GF. 2015. Transient reduction of visual distraction following electrical stimulation of the prefrontal cortex. Cognition. 73–76.
Coull JT, Frith CD, Frackowiak RSJ, Grasby PM. 1996. A fronto-parietal network for rapid visual information processing: a PET study of sustained attention and working memory. Neuropsychologia. 34:1085–1095.
Coull JT, Nobre AC. 1998. Where and when to pay attention: the neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. J Neurosci. 18:7426–7435.
Crossman ER, Szafran J. 1956. Changes with age in the speed of information-intake and discrimination. Experientia. 128–134.
Dalton P, Hughes RW. 2014. Auditory attentional capture: Implicit and explicit approaches.

Psychol Res. 78:313–320.
Damasio AR, Sutherland S. 1994. Descartes' error: Emotion, reason and the human brain. Nature. 372:287.
Davis SW, Dennis NA, Daselaar SM, Fleck MS, Cabeza R. 2008. Que PASA? The Posterior-Anterior Shift in Aging. Cereb Cortex. 18:1201–1209.
Debener S, Herrmann CS, Kranczioch C, Gembris D, Engel AK. 2003. Top-down attentional processing enhances auditory evoked gamma band activity. Neuroreport. 14:683–686.
Degutis JM, Van Vleet TM. 2010. Tonic and phasic alertness training: a novel behavioral therapy to improve spatial and non-spatial attention in patients with hemispatial neglect. Front Hum Neurosci. 4.
Deiber MP, Ibañez V, Missonnier P, Rodriguez C, Giannakopoulos P. 2013. Age-associated modulations of cerebral oscillatory patterns related to attention control. Neuroimage. 82:531–546.
Desimone R, Duncan J. 1995. Neural mechanisms of selective visual attention. Annu Rev Neurosci. 18:193–222.
Desmedt JE, Tomberg C. 1994. Transient phase-locking of 40 Hz electrical oscillations in prefrontal and parietal human cortex reflects the process of conscious somatic perception. Neurosci Lett. 168:126–129.
DiQuattro NE, Sawaki R, Geng JJ. 2014. Effective Connectivity During Feature-Based Attentional Capture: Evidence Against the Attentional Reorienting Hypothesis of TPJ. Cereb Cortex. 24:3131–3141.
Doesburg SM, Bedo N, Ward LM. 2016. Top-down alpha oscillatory network interactions during visuospatial attention orienting. Neuroimage. 132:512–519.
Doesburg SM, Green JJ, McDonald JJ, Ward LM. 2009. From local inhibition to long-range integration: a functional dissociation of alpha-band synchronization across cortical scales in visuospatial attention. Brain Res. 1303:97–110.
Dolcos F, Miller B, Kragel P, Jha A, McCarthy G. 2007. Regional brain differences in the effect of distraction during the delay interval of a working memory task. Brain Res. 1152:171–181.
Downar J, Crawley AP, Mikulis DJ, Davis KD. 2000. A multimodal cortical network for the detection of changes in the sensory environment. Nat Neurosci. 3:277.
Downar J, Crawley AP, Mikulis DJ, Davis KD. 2001. The effect of task relevance on the cortical response to changes in visual and auditory stimuli: an event-related fMRI study. Neuroimage. 14:1256–1267.
Drag LL, Bieliauskas LA. 2010. Contemporary review 2009: Cognitive aging. J Geriatr Psychiatry Neurol. 23:75–93.
Duncan-Johnson CC, Donchin E. 1977. On Quantifying Surprise: The Variation of Event-Related Potentials With Subjective Probability. Psychophysiology.
Duncan J. 1980. The locus of interference in the perception of simultaneous stimuli. Psychol Rev. 87:272.
Eason RG, Harter MR, White CT. 1969. Effects of attention and arousal on visually evoked cortical potentials and reaction time in man. Physiol Behav. 4:283–289.
Eckhorn R, Bauer R, Jordan W, Brosch M, Kruse W, Munk M, Reitboeck HJ. 1988. Coherent oscillations: A mechanism of feature linking in the visual cortex? Biol Cybern. 60:121–130.
ElShafei HA, Bouet R, Bertrand O, Bidet-Caulet A. 2018. Two Sides of the Same Coin: Distinct Sub-Bands in the Alpha Rhythm Reflect Facilitation and Suppression Mechanisms during Auditory Anticipatory Attention. Eneuro. ENEURO.0141-18.2018.
Erika-Florence M, Leech R, Hampshire A. 2014. A functional network perspective on response inhibition and attentional control. Nat Commun. 5:1–12.

Eriksen CW, Hoffman JE. 1972. Temporal and spatial characteristics of selective encoding from visual displays. Percept Psychophys. 12:201–204.
Escera C, Alho K, Schröger E, Winkler IW. 2000. Involuntary attention and distractibility as evaluated with event-related brain potentials. Audiol Neurootol. 5:151–166.
Escera C, Alho K, Winkler I, Näätänen R. 1998. Neural mechanisms of involuntary attention to acoustic novelty and change. J Cogn Neurosci. 10:590–604.
Escera C, Corral MJ. 2007. Role of mismatch negativity and novelty-P3 in involuntary auditory attention. J Psychophysiol. 21:251–264.
Escera C, Yago E, Corral M-J, Corbera S, Nunez MI. 2003. Attention capture by auditory significant stimuli: semantic analysis follows attention switching. Eur J Neurosci. 18:2408–2412.
Esghaei M, Daliri MR, Treue S. 2015. Attention Decreases Phase-Amplitude Coupling, Enhancing Stimulus Discriminability in Cortical Area MT. Front Neural Circuits. 9.
Esterman M, Yantis S. 2010. Perceptual expectation evokes category-selective cortical activity. Cereb Cortex. 20:1245–1253.
Eysenck M. 2012. Attention and arousal: Cognition and performance. Springer Science & Business Media.
Fabiani M, Gratton G. 2012. Aging, working memory, and at tention control. 582–592.
Fabiani M, Low KA, Wee E, Sable JJ, Gratton G. 2006. Reduced suppression or labile memory? Mechanisms of inefficient filtering of irrelevant information in older adults. J Cogn Neurosci. 18:637–650.
Fan J, Gub X, Guisea KG, Liua X, Fossellaa J, Wang H, Posner MI. 2009. Testing the behavioral interaction and integration of attentional networks. Brain Cogn. 70:209–220.
Fontolan L, Morillon B, Liegeois-Chauvel C, Giraud A-L. 2014. The contribution of frequency-specific activity to hierarchical information processing in the human auditory cortex. Nat Commun. 5:4694.
Fox MD, Corbetta M, Snyder AZ, Vincent JL, Raichle ME. 2006. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proc Natl Acad Sci. 103:9381–9386.
Foxe JJ, Simpson G V, Ahlfors SP. 1998. Parieto-occipital ~10 Hz activity reflects anticipatory state of visual attention mechanisms. Neuroreport. 9:3929–3933.
Frey JN, Mainy N, Lachaux J-P, Muller N, Bertrand O, Weisz N. 2014. Selective Modulation of Auditory Cortical Alpha Activity in an Audiovisual Spatial Attention Task. J Neurosci. 34:6634–6639.
Friedman NP, Miyake A. 2004. The Relations Among Inhibition and Interference Control Functions: A Latent-Variable Analysis. J Exp Psychol Gen. 133:101–135.
Fries P. 2005. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends Cogn Sci. 9:474–480.
Fries P. 2009. Neuronal Gamma-Band Synchronization as a Fundamental Process in Cortical Computation. Annu Rev Neurosci. 32:209–224.
Fries P. 2015. Rhythm for Cognition: Communication Through Coherence. Neuron. 88:220–235.
Fries P, Reynolds JH, Rorie AE, Desimone R. 2001. Modulation of oscillatory neuronal synchronization by selective visual attention. Science (80-). 291:1560–1563.
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. J Neurosci. 28:4823–4835.
Fründ I, Busch NA, Körner U, Schadow J, Herrmann CS. 2007. EEG oscillations in the gamma and alpha range respond differently to spatial frequency. Vision Res. 47:2086–2098.

Fu KMG, Foxe JJ, Murray MM, Higgins BA, Javitt DC, Schroeder CE. 2001. Attention-dependent suppression of distracter visual input can be cross-modally cued as indexed by anticipatory parieto-occipital alpha-band oscillations. Cogn Brain Res. 12:145–152.

Funderud I, Løvstad M, Lindgren M, Endestad T, Due-Tønnessen P, Meling TR, Knight RT, Solbakk AK. 2013. Preparatory attention after lesions to the lateral or orbital prefrontal cortex - An event-related potentials study. Brain Res. 1527:174–188.

Gaebler AJ, Mathiak K, Koten JW, König AA, Koush Y, Weyer D, Depner C, Matentzoglu S, Edgar JC, Willmes K, Zvyagintsev M. 2015. Auditory mismatch impairments are characterized by core neural dysfunctions in schizophrenia. Brain. 138:1410–1423.

Galambos R. 1992. A Comparison of Certain Gamma Band (40-HZ) Brain Rhythms in Cat and Man. In: Induced Rhythms in the Brain. Boston, MA: Birkhäuser Boston. p. 201–216.

Gazzaley A. 2013. Top-Down Modulation Deficit in the Aging Brain an Emerging Theory of Cognitive Aging. Princ Front Lobe Funct. 593–608.

Gazzaley A, Cooney JW, Rissman J, D'Esposito M, McEvoy K, Knight RT, D'Esposito M. 2005. Top-down Enhancement and Suppression of the Magnitude and Speed of Neural Activity. Nat Neurosci. 8:507–517.

Gazzaley A, D'esposito M. 2007. Top-down modulation and normal aging. Ann N Y Acad Sci. 1097:67–83.

Geerligs L, Saliasi E, Maurits NM, Lorist MM. 2012. Compensation through Increased Functional Connectivity: Neural Correlates of Inhibition in Old and Young. J Cogn Neurosci. 24:2057–2069.

Gehring WJ, Knight RT. 2002. Lateral prefrontal damage affects processing selection but not attention switching. Cogn Brain Res. 13:267–279.

Getzmann S, Gajewski PD, Falkenstein M. 2013. Does age increase auditory distraction? Electrophysiological correlates of high and low performance in seniors. Neurobiol Aging. 34:1952–1962.

Ghatan PH, Hsieh JC, Petersson KM, Stone-Elander S, Ingvar M. 1998. Coexistence of attention-based facilitation and inhibition in the human cortex. Neuroimage. 7:23–29.

Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Kim Y-H, Meyer JR, Mesulam M-M. 1999. A large-scale distributed network for covert spatial attention: further anatomical delineation based on stringent behavioural and cognitive controls. Brain. 122:1093–1106.

Godefroy O, Rousseaux M. 1996. Divided and focused attention in patients with lesion of the prefrontal cortex. Brain Cogn. 30:155–174.

Golob EJ, Pratt H, Starr A. 2002. Preparatory slow potentials and event-related potentials in an auditory cued attention task. Clin Neurophysiol. 113:1544–1557.

Gomez-Ramirez M, Kelly SP, Molholm S, Sehatpour P, Schwartz TH, Foxe JJ. 2011. Oscillatory sensory selection mechanisms during intersensory attention to rhythmic auditory and visual inputs: a human electrocorticographic investigation. J Neurosci. 31:18556–18567.

Gómez CM, Fernández A, Maestú F, Amo C, González-Rosa JJ, Vaquero E, Ortiz T. 2004. Task-specific sensory and motor preparatory activation revealed by contingent magnetic variation. Cogn Brain Res. 21:59–68.

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

Gonzalez Andino SL, Michel CM, Thut G, Landis T, De Peralta RG. 2005. Prediction of response speed by anticipatory high-frequency (gamma band) oscillations in the human brain. Hum Brain Mapp. 24:50–58.

Gottlob LR, Madden DJ. 1998. Time course of allocation of visual attention after equating for

sensory differences: An age-related perspective. Psychol Aging. 13:138–149.
Gregoriou GG, Gotts SJ, Zhou H, Desimone R. 2009. High-Frequency, long-range coupling between prefrontal and visual cortex during attention. Science (80-). 324:1207–1210.
Gross J, Kujala J, Hämäläinen M, Timmermann L, Schnitzler A, Salmelin R. 2001. Dynamic imaging of coherent sources: studying neural interactions in the human brain. Proc Natl Acad Sci. 98:694–699.
Guerreiro MJS, Anguera JA, Mishra J, Gerven PWM Van, Gazzaley A. 2013. Age-equivalent Top–Down Modulation during Cross-modal Selective Attention. Psychologist. 26:194–198.
Guerreiro MJS, Eck J, Moerel M, Evers EAT, Gerven PWM Van. 2015. Top-down modulation of visual and auditory cortical processing in aging. Behav Brain Res. 278:226–234.
Guerreiro MJS, Murphy DR, Van Gerven PWM. 2013. Making sense of age-related distractibility: The critical role of sensory modality. Acta Psychol (Amst). 142:184–194.
Guerreiro MJS, Van Gerven PWM. 2011. Now you see it, now you don't: Evidence for age-dependent and age-independent cross-modal distraction. Psychol Aging. 26:415–426.
Guerreiro MJSS, Murphy DR, Van Gerven PWMM. 2010. The Role of Sensory Modality in Age-Related Distraction: A Critical Review and a Renewed View. Psychol Bull. 136:975–1022.
Haegens S, Barczak A, Musacchia G, Lipton ML, Mehta AD, Lakatos P, Schroeder CE. 2015. Laminar profile and physiology of the α rhythm in primary visual, auditory, and somatosensory regions of neocortex. J Neurosci. 35:14341–14352.
Haegens S, Cousijn H, Wallis G, Harrison PJ, Nobre AC. 2014. Inter- and intra-individual variability in alpha peak frequency. Neuroimage. 92:46–55.
Haegens S, Händel BF, Jensen O. 2011. Top-down controlled alpha band activity in somatosensory areas determines behavioral performance in a discrimination task. J Neurosci. 31:5197–5204.
Haegens S, Luther L, Jensen O. 2012. Somatosensory Anticipatory Alpha Activity Increases to Suppress Distracting Input. J Cogn Neurosci. 24:677–685.
Haegens S, Osipova D, Oostenveld R, Jensen O. 2010. Somatosensory working memory performance in humans depends on both engagement and disengagement of regions in a distributed network. Hum Brain Mapp. 31:26–35.
Han SW, Marois R. 2014. Functional Fractionation of the Stimulus-Driven Attention Network. J Neurosci. 34:6958–6969.
Händel BF, Haarmeier T, Jensen O. 2011. Alpha Oscillations Correlate with the Successful Inhibition of Unattended Stimuli. J Cogn Neurosci. 23:2494–2502.
Hansen JC, Hillyard SA. 1980. Endogeneous brain potentials associated with selective auditory attention. Electroencephalogr Clin Neurophysiol. 49:277–290.
Harmony T, Bernal J, Fernández T, Silva-Pereyra J, Fernández-Bouzas A, Marosi E, Rodríguez M, Reyes A. 2000. Primary task demands modulate P3a amplitude. Brain Res Cogn Brain Res. 9:53–60.
Hart SJ, Lucena N, Cleary KM, Belger A, Donkers FCL. 2012. Modulation of early and late event-related potentials by emotion. Front Integr Neurosci. 6:102.
Hartley AA, Kieley JM, Slabach EH. 1990. Age Differences and Similarities in the Effects of Cues and Prompts. J Exp Psychol Hum Percept Perform. 16:523–537.
Hasher L, Zacks RT. 1988. Working memory, comprehension, and aging: A review and a new view. In: Psychology of learning and motivation. Elsevier. p. 193–225.
Hawkins HL, Shafto MG, Richardson K. 1988. Effects of target luminance and cue validity on the latency of visual detection. Percept Psychophys. 44:484–492.
Hayward DA, Ristic J. 2013. Measuring attention using the Posner cuing paradigm: the role

of across and within trial target probabilities. Front Hum Neurosci. 7:1–11.
He BJ, Snyder AZ, Vincent JL, Epstein A, Shulman GL, Corbetta M. 2007. Breakdown of Functional Connectivity in Frontoparietal Networks Underlies Behavioral Deficits in Spatial Neglect. Neuron. 53:905–918.
Heideman SG, Rohenkohl G, Chauvin JJ, Palmer CE, Ede F van, Nobre AC. 2018. Anticipatory neural dynamics of spatial-temporal orienting of attention in younger and older adults. Neuroimage.
Hillyard SA, Hink RF, Schwent VL, Picton TW. 1973. Electrical signs of selective attention in the human brain. Science (80-). 182:177–180.
Hillyard SA, Vogel EK, Luck SJ. 1998. Sensory gain control (amplification) as a mechanism of selective attention: electrophysiological and neuroimaging evidence. Philos Trans R Soc London B Biol Sci. 353:1257–1270.
Hirel C, Nighoghossian N, Lévêque Y, Hannoun S, Fornoni L, Daligault S, Bouchet P, Jung J, Tillmann B, Caclin A. 2017. Verbal and musical short-term memory: Variety of auditory disorders after stroke. Brain Cogn. 113:10–22.
Hong X, Sun J, Bengson JJ, Mangun GR, Tong S. 2015. Normal aging selectively diminishes alpha lateralization in visual spatial attention. Neuroimage. 106:353–363.
Hopfinger JB, Buonocore MH, Mangun GR. 2000. The neural mechanisms of top-down attentional control. Nat Neurosci. 3:284–291.
Horváth J, Winkler I, Bendixen A. 2008. Do N1/MMN, P3a, and RON form a strongly coupled chain reflecting the three stages of auditory distraction? Biol Psychol. 79:139–147.
Huang S, Belliveau JW, Tengshe C, Ahveninen J. 2012. Brain networks of novelty-driven involuntary and cued voluntary auditory attention shifting. PLoS One. 7:e44062.
Huang S, Chang WT, Belliveau JW, Hämäläinen M, Ahveninen J. 2014. Lateralized parietotemporal oscillatory phase synchronization during auditory selective attention. Neuroimage. 86:461–469.
Hugdahl K, Nordby H. 1994. Electrophysiological correlates to cued attentional shifts in the visual and auditory modalities. Behav Neural Biol. 62:21–32.
Hughes JR. 2008. Gamma, fast, and ultrafast waves of the brain: Their relationships with epilepsy and behavior. Epilepsy Behav. 13:25–31.
Hughes RW. 2014. Auditory distraction: A duplex-mechanism account. PsyCh J. 3:30–41.
Hülsdünker T, Mierau A, Strüder HK. 2015. Higher Balance Task Demands are Associated with an Increase in Individual Alpha Peak Frequency. Front Hum Neurosci. 9:695.
Hung J, Driver J, Walsh V. 2005. Visual selection and posterior parietal cortex: effects of repetitive transcranial magnetic stimulation on partial report analyzed by Bundesen's theory of visual attention. J Neurosci. 25:9602–9612.
Hung J, Driver J, Walsh V. 2011. Visual Selection and the Human Frontal Eye Fields: Effects of Frontal Transcranial Magnetic Stimulation on Partial Report Analyzed by Bundesen's Theory of Visual Attention. J Neurosci. 31:15904–15913.
Hyde KL, Peretz I, Zatorre RJ. 2008. Evidence for the role of the right auditory cortex in fine pitch resolution. Neuropsychologia. 46:632–639.
Jacobsen T, Horenkamp T, Schröger E. 2003. Preattentive memory-based comparison of sound intensity. Audiol Neurotol. 8:338–346.
James W. 1890. The Principles of Psychology. 2:94.
Jensen O, Colgin LL. 2007. Cross-frequency coupling between neuronal oscillations. Trends Cogn Sci. 11:267–269.
Jensen O, Gelfand J, Kounios J, Lisman JE. 2002. Oscillations in the alpha band (9-12 Hz) increase with memory load during retention in a short-term memory task. Cereb Cortex. 12:877–882.

Jensen O, Kaiser J, Lachaux J. 2007. Human gamma-frequency oscillations associated with attention and memory. 30.
Jensen O, Mazaheri A. 2010. Shaping Functional Architecture by Oscillatory Alpha Activity: Gating by Inhibition. Front Hum Neurosci. 4:1–8.
Jia X, Smith MA, Kohn A. 2011. Stimulus Selectivity and Spatial Coherence of Gamma Components of the Local Field Potential. J Neurosci. 31:9390–9403.
Jiang H, Bahramisharif A, van Gerven MAJ, Jensen O. 2015. Measuring directionality between neuronal oscillations of different frequencies. Neuroimage. 118:359–367.
Johnson JA, Strafella AP, Zatorre RJ. 2007. The Role of the Dorsolateral Prefrontal Cortex in Bimodal Divided Attention: Two Transcranial Magnetic Stimulation Studies. J Cogn Neurosci. 19:907–920.
Johnson JA, Zatorre RJ. 2006. Neural substrates for dividing and focusing attention between simultaneous auditory and visual events. Neuroimage. 31:1673–1681.
Jokeit H, Makeig S. 1994. Different event-related patterns of gamma-band power in brain waves of fast-and slow-reacting subjects. Proc Natl Acad Sci. 91:6339–6343.
Jones D, Madden C, Miles C. 1992. Privileged access by irrelevant speech to short-term memory: The role of changing state. Q J Exp Psychol. 44:645–669.
Jones DM, Macken WJ. 1993. Irrelevant tones produce an irrelevant speech effect: Implications for phonological coding in working memory. J Exp Psychol Learn Mem Cogn. 19:369.
Jonides J. 1981. Voluntary versus automatic control over the mind's eye's movement. Atten Perform. 187–203.
Jung J, Mainy N, Kahane P, Minotti L, Hoffmann D, Bertrand O, Lachaux JP. 2008. The neural bases of attentive reading. Hum Brain Mapp. 29:1193–1206.
Kahkonen S, Ahveninen J. 2002. Combination of magneto-and electroencephalography in studies of monoamine modulation on attention. Methods Find Exp Clin Pharmacol. 24:27–34.
Kahneman D. 1973. Attention and effort. Prentice-Hall Englewood Cliffs, NJ.
Kaiser J, Heidegger T, Lutzenberger W. 2008. Behavioral relevance of gamma-band activity for short-term memory-based auditory decision-making. Eur J Neurosci. 27:3322–3328.
Kaiser J, Heidegger T, Wibral M, Altmann CF, Lutzenberger W. 2008. Distinct Gamma-Band Components Reflect the Short-Term Memory Maintenance of Different Sound Lateralization Angles. Cereb Cortex. 18:2286–2295.
Kaiser J, Hertrich I, Ackermann H, Lutzenberger W. 2006. Gamma-band activity over early sensory areas predicts detection of changes in audiovisual speech stimuli. Neuroimage. 30:1376–1382.
Kaiser J, Lutzenberger W. 2005. Human gamma-band activity: a window to cognitive processing. Neuroreport. 16:207–211.
Kaiser J, Rahm B, Lutzenberger W. 2009. Temporal dynamics of stimulus-specific gamma-band activity components during auditory short-term memory. Neuroimage. 44:257–264.
Kastner S, Pinsk MA, De Weerd P, Desimone R, Ungerleider LG. 1999. Increased activity in human visual cortex during directed attention in the absence of visual stimulation. In: Helsinki University of Technology. Citeseer. p. 751–761.
Kastner S, Ungerleider L. 2000. Mechanisms of visual attention in the human cortex. Annu Rev Neurosci. 23:315–341.
Katsuki F, Constantinidis C. 2014. Bottom-up and top-down attention: Different processes and overlapping neural systems. Neuroscientist. 20:509–521.
Kawasaki M, Kitajo K, Yamaguchi Y. 2010. Dynamic links between theta executive functions and alpha storage buffers in auditory and visual working memory. Eur J Neurosci. 31:1683–1689.

Kelly SP, Lalor EC, Reilly RB, Foxe JJ. 2006. Increases in alpha oscillatory power reflect an active retinotopic mechanism for distracter suppression during sustained visuospatial attention. J Neurophysiol. 95:3844–3851.
Kim H. 2014. Involvement of the dorsal and ventral attention networks in oddball stimulus processing: A meta-analysis. Hum Brain Mapp. 35:2265–2284.
Kim YH, Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Mesulam MM. 1999. The large-scale neural network for spatial attention displays multifunctional overlap but differential asymmetry. Neuroimage. 9:269–277.
Kirino E, Belger A, Goldman-Rakic P, McCarthy G. 2000. Prefrontal activation evoked by infrequent target and novel stimuli in a visual target detection task: an event-related functional magnetic resonance imaging study. J Neurosci. 20:6612–6618.
Klimesch W. 1999. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res Brain Res Rev. 29:169–195.
Klimesch W. 2012. Alpha-band oscillations, attention, and controlled access to stored information. Cell. 16:606–617.
Klimesch W, Doppelmayr M, Russegger H, Pachinger T, Schwaiger J. 1998. Induced alpha band power changes in the human EEG and attention. Neurosci Lett. 244:73–76.
Klimesch W, Sauseng P, Hanslmayr S. 2007. EEG alpha oscillations: The inhibition–timing hypothesis. Brain Res Rev. 53:63–88.
Klimesch W, Schimke H, Pfurtscheller G. 1993. Alpha frequency, cognitive load and memory performance. Brain Topogr. 5:241–251.
Knight RT, Hillyard SA, Woods DL, Neville HJ. 1981. The effects of frontal cortex lesions on event-related potentials during auditory selective attention. Electroencephalogr Clin Neurophysiol. 52:571–582.
Knight RT, Scabini D. 1998. Anatomic bases of event-related potentials and their relationship to novelty detection in humans. J Clin Neurophysiol.
Knight RT, Scabini D, Woods DL. 1989. Prefrontal cortex gating of auditory transmission in humans. Brain Res. 504:338–342.
Knight RT, Staines WR, Swick D, Chao LL. 1999. Prefrontal cortex regulates inhibition and excitation in distributed neural networks. Acta Psychol (Amst). 101:159–178.
Kok A. 2000. Age-related changes in involuntary and voluntary attention as reflected in components of the event-related potential (ERP). Biol Psychol. 54:107–143.
Kong L, Michalka SW, Rosen ML, Sheremata SL, Swisher JD, Shinn-Cunningham BG, Somers DC. 2012. Auditory spatial attention representations in the human cerebral cortex. Cereb Cortex. 24:773–784.
Kornblith S, Buschman TJ, Miller EK. 2016. Stimulus load and oscillatory activity in higher cortex. Cereb Cortex. 26:3772–3784.
Kristeva-Feige R, Feige B, Makeig S, Ross B, Elbert T. 1993. Oscillatory brain activity during a motor task. Neuroreport. 4:1291–1294.
Lachaux JP, George N, Tallon-Baudry C, Martinerie J, Hugueville L, Minotti L, Kahane P, Renault B. 2005. The many faces of the gamma band response to complex visual stimuli. Neuroimage. 25:491–501.
Lachaux JP, Rodriguez E, Martinerie J, Varela FJ. 1999. Measuring phase synchrony in brain signals. Hum Brain Mapp. 8:194–208.
Lakatos P, Karmos G, Mehta AD, Ulbert I, Schroeder CE. 2008. Entrainment of neuronal oscillations as a mechanism of attentional selection. Science (80-). 320:110–113.
Lakatos P, Shah AS, Knuth KH, Ulbert I, Karmos G, Schroeder CE. 2005. An Oscillatory Hierarchy Controlling Neuronal Excitability and Stimulus Processing in the Auditory Cortex. J Neurophysiol. 94:1904–1911.
Langner R, Kellermann T, Boers F, Sturm W, Willmes K, Eickhoff SB. 2011. Modality-

Specific Perceptual Expectations Selectively Modulate Baseline Activity in Auditory, Somatosensory, and Visual Cortices. Cereb Cortex. 21:2850–2862.
Larson E, Lee AKC. 2013a. Influence of preparation time and pitch separation in switching of auditory attention between streams. J Acoust Soc Am. 134:EL165-71.
Larson E, Lee AKCC. 2013b. The cortical dynamics underlying effective switching of auditory spatial attention. Neuroimage. 64:365–370.
Larson E, Lee AKCC. 2014. Switching auditory attention using spatial and non-spatial features recruits different cortical networks. Neuroimage. 84:681–687.
Lattner S, Meyer ME, Friederici AD. 2005. Voice perception: sex, pitch, and the right hemisphere. Hum Brain Mapp. 24:11–20.
Laurienti PJ, Burdette JH, Wallace MT, Yen Y-F, Field AS, Stein BE. 2002. Deactivation of sensory-specific cortex by cross-modal stimuli. J Cogn Neurosci. 14:420–429.
Lecoffre C, de Peretti C, Gabet A, Grimaud O, Woimant F, Giroud M, Béjot Y, Olié V. 2017. National Trends in Patients Hospitalized for Stroke and Stroke Mortality in France, 2008 to 2014. Stroke. 48:2939–2945.
Lee AKC, Rajaram S, Xia J, Bharadwaj H, Larson E, Hämäläinen M, Shinn-Cunningham BG. 2013. Auditory selective attention reveals preparatory activity in different cortical regions for selection based on source location and source pitch. Front Neurosci. 6:190.
Lee B, Park KS, Kang D-H, Kang KW, Kim YY, Kwon JS. 2007. Generators of the gamma-band activities in response to rare and novel stimuli during the auditory oddball paradigm. Neurosci Lett. 413:210–215.
Leenders MP, Lozano-Soldevilla D, Roberts MJ, Jensen O, De Weerd P. 2018. Diminished Alpha Lateralization During Working Memory but Not During Attentional Cueing in Older Adults. Cereb Cortex. 28:21–32.
Lewis JW, Beauchamp MS, DeYoe EA. 2000. A comparison of visual and auditory motion processing in human cerebral cortex. Cereb Cortex. 10:873–888.
Li L, Zhao D. 2015. Age-related inter-region EEG coupling changes during the control of bottom-Up and top-Down attention. Front Aging Neurosci. 7:1–14.
Liu Y, Bengson J, Huang H, Mangun GR, Ding M. 2014. Top-down Modulation of Neural Activity in Anticipatory Visual Attention: Control Mechanisms Revealed by Simultaneous EEG-fMRI. Cereb Cortex.
Lobier M, Palva JM, Palva S. 2018. High-alpha band synchronization across frontal, parietal and visual cortex mediates behavioral and neuronal effects of visuospatial attention. Neuroimage. 165:222–237.
Long NM, Kuhl BA. 2018. Bottom-up and top-down factors differentially influence stimulus representations across large-scale attentional networks. J Neurosci. 2724–17.
Løvstad M, Funderud I, Lindgren M, Endestad T, Due-Tønnessen P, Meling T, Voytek B, Knight RT, Solbakk A-KK. 2012. Contribution of Subregions of Human Frontal Cortex to Novelty Processing. J Cogn Neurosci. 24:378–395.
Løvstad M, Funderud I, Meling T, Krämer UM, Voytek B, Due-Tønnessen P, Endestad T, Lindgren M, Knight RT, Solbakk AK. 2012. Anterior cingulate cortex and cognitive control: Neuropsychological and electrophysiological findings in two patients with lesions to dorsomedial prefrontal cortex. Brain Cogn. 80:237–249.
Lustig C, Hasher L. 2001. Implicit memory is not immune to interference. Psychol Bull. 127:618–628.
Lustig C, Hasher L, Zacks RT. 2007. Inhibitory deficit theory: Recent developments in a "new view." Inhib Cogn. 145–162.
Lv J-Y, Wang T, Qiu J, Feng S-H, Tu S, Wei D-T. 2010. The electrophysiological effect of working memory load on involuntary attention in an auditory–visual distraction paradigm: an ERP study. Exp Brain Res. 205:81–86.

Macaluso E. 2010. Orienting of spatial attention and the interplay between the senses. cortex. 46:282–297.
Macaluso E, Driver J. 2005. Multisensory spatial interactions: a window onto functional integration in the human brain. Trends Neurosci. 28:264–271.
Macaluso E, Eimer M, Frith CD, Driver J. 2003. Preparatory states in crossmodal spatial attention: spatial specificity and possible control mechanisms. Exp brain Res. 149:62–74.
Mangun GR, Hillyard SA. 1991. Modulations of sensory-evoked brain potentials indicate changes in perceptual processing during visual-spatial priming. J Exp Psychol Hum Percept Perform. 17:1057.
Maris E, Oostenveld R. 2007. Nonparametric statistical testing of EEG- and MEG-data. J Neurosci Methods. 164:177–190.
Marois R, Leung H-C, Gore JC. 2000. A stimulus-driven approach to object identity and location processing in the human brain. Neuron. 25:717–728.
Marrocco RT, Davidson MC. 1998. Neurochemistry of attention.
Marrocco RT, Witte EA, Davidson MC. 1994. Arousal systems. Curr Opin Neurobiol. 4:166–170.
Mars RB, Debener S, Gladwin TE, Harrison LM, Haggard P, Rothwell JC, Bestmann S. 2008. Trial-by-trial fluctuations in the event-related electroencephalogram reflect dynamic changes in the degree of surprise. J Neurosci. 28:12539–12545.
Marshall TR, Bergmann TO, Jensen O. 2015. Frontoparietal Structural Connectivity Mediates the Top-Down Control of Neuronal Synchronization Associated with Selective Attention. PLoS Biol. 13:1–17.
Marshall TR, O'Shea J, Jensen O, Bergmann TO. 2015. Frontal Eye Fields Control Attentional Modulation of Alpha and Gamma Oscillations in Contralateral Occipitoparietal Cortex. J Neurosci. 35:1638–1647.
Martinovic J, Gruber T, Hantsch A, Müller MM. 2008. Induced gamma-band activity is related to the time point of object identification. Brain Res. 1198:93–106.
Martinovic J, Gruber T, Müller MM. 2007. Induced Gamma Band Responses Predict Recognition Delays during Object Identification. J Cogn Neurosci. 19:921–934.
Masson R, Bidet-Caulet A. 2018. Fronto-central P3a to distracting sounds: an index of their arousing properties. bioRxiv. 333419.
Mathewson KE, Fabiani M, Gratton G, Beck DM, Lleras A. 2010. Rescuing stimuli from invisibility: Inducing a momentary release from visual masking with pre-target entrainment. Cognition. 115:186–191.
Mayer AR, Franco AR, Harrington DL. 2009. Neuronal modulation of auditory attention by informative and uninformative spatial cues. Hum Brain Mapp. 30:1652–1666.
Mayer AR, Harrington D, Adair JC, Lee R. 2006. The neural networks underlying endogenous auditory covert orienting and reorienting. Neuroimage. 30:938–949.
Maylor EA, Lavie N. 1998. The influence of perceptual load on age differences in selective attention. Psychol Aging. 13:563.
Mazaheri A, van Schouwenburg MR, Dimitrijevic A, Denys D, Cools R, Jensen O. 2013. Region-specific modulations in oscillatory alpha activity serve to facilitate processing in the visual and auditory modalities. Neuroimage. 87:356–362.
McGinnis D. 2012. Susceptibility to distraction during reading in young, young-old, and old-old adults. Exp Aging Res. 38:370–393.
Michalareas G, Vezoli J, Van Pelt S, Schoffelen J-M, Kennedy H, Fries P. 2016. Alpha-beta and gamma rhythms subserve feedback and feedforward influences among human visual cortical areas. Neuron. 89:384–397.
Michels L, Bucher K, Lüchinger R, Klaver P, Martin E, Jeanmonod D, Brandeis D. 2010. Simultaneous EEG-fMRI during a working memory task: Modulations in low and high

frequency bands. PLoS One. 5.
Mierau A, Klimesch W, Lefebvre J. 2017. State-dependent alpha peak frequency shifts: Experimental evidence, potential mechanisms and functional implications. Neuroscience. 360:146–154.
Miller BT, Vytlacil J, Fegen D, Pradhan S, D'Esposito M. 2011. The Prefrontal Cortex Modulates Category Selectivity in Human Extrastriate Cortex. J Cogn Neurosci. 23:1–10.
Miller E, Cohen J. 2001. An integrative theory of prefrontal cortex function. Annu Rev Neurosci. 167–202.
Miller LM, D'Esposito M. 2005. Perceptual Fusion and Stimulus Coincidence in the Cross-Modal Integration of Speech. J Neurosci. 25:5884–5893.
Miller MW, Rietschel JC, McDonald CG, Hatfield BD. 2011. A novel approach to the physiological measurement of mental workload. Int J Psychophysiol. 80:75–78.
Milner B. 1962. Laterality effects in audition. Interhemispheric relations Cereb Domin.
Mittag M, Inauri K, Huovilainen T, Leminen M, Salo E, Rinne T, Kujala T, Alho K. 2013. Attention effects on the processing of task-relevant and task-irrelevant speech sounds and letters. Front Neurosci. 7:231.
Müller HJ, Findlay JM. 1988. The effect of visual attention of peripheral discrimination thresholds in single and multiple element displays. Acta Psychol (Amst). 69:129–155.
Müller HJ, Rabbitt PM. 1989. Reflexive and voluntary orienting of visual attention: time course of activation and resistance to interruption. J Exp Psychol Hum Percept Perform. 15:315.
Muller N, Weisz N. 2012. Lateralized auditory cortical alpha band activity and interregional connectivity pattern reflect anticipation of target sounds. Cereb Cortex. 22:1604–1613.
Mund I, Bell R, Buchner A. 2010. Age differences in reading with distraction: Sensory or inhibitory deficits? Psychol Aging. 25:886–897.
Myers NE, Stokes MG, Walther L, Nobre AC. 2014. Oscillatory Brain State Predicts Variability in Working Memory. J Neurosci. 34:7735–7743.
Näätänen R, Picton T. 1987. The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. Psychophysiology. 24:375–425.
Neath I. 2000. Modeling the effects of irrelevant speech on memory. Psychon Bull Rev. 7:403–423.
Neelon MF, Williams J, Garell PC. 2006. The effects of auditory attention measured from human electrocorticograms. Clin Neurophysiol. 117:504–521.
Nir R-R, Sinai A, Raz E, Sprecher E, Yarnitsky D. 2010. Pain assessment by continuous EEG: Association between subjective perception of tonic pain and peak frequency of alpha oscillations during stimulation and at rest. Brain Res. 1344:77–86.
Nissen MJ, Corkin S. 1985. Effectiveness of attentional cueing in older and younger adults. Journals Gerontol. 40:185–191.
Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RS, Frith CD. 1997. Functional localization of the system for visuospatial attention using positron emission tomography. Brain a J Neurol. 120:515–533.
Nolte G. 2003. The magnetic lead field theorem in the quasi-static approximation and its use for magnetoencephalography forward calculation in realistic volume conductors. Phys Med Biol. 48:3637.
Ochsner KN, Kosslyn SM, Cosgrove GR, Cassem EH, Price BH, Nierenberg AA, Rauch SL. 2001. Deficits in visual cognition and attention following bilateral anterior cingulotomy. Neuropsychologia. 39:219–230.
Oehrn CR, Hanslmayr S, Fell J, Deuker L, Kremers NA, Do Lam AT, Elger CE, Axmacher

N. 2014. Neural Communication Patterns Underlying Conflict Detection, Resolution, and Adaptation. J Neurosci. 34:10438–10452.
Ofek E, Pratt H. 2004. Ear advantage and attention: An ERP study of auditory cued attention. Hear Res. 189:107–118.
Oken BS, Salinsky MC, Elsas SM. 2006. Vigilance, alertness, or sustained attention: physiological basis and measurement. Clin Neurophysiol. 117:1885–1901.
Onofrj M, Thomas A, Iacono D, D'Andreamatteo G, Paci C. 2001. Age-related changes of evoked potentials. Neurophysiol Clin. 31:83–103.
Onslow ACE, Bogacz R, Jones MW. 2011. Quantifying phase-amplitude coupling in neuronal network oscillations. Prog Biophys Mol Biol. 105:49–57.
Ossandon T, Vidal JR, Ciumas C, Jerbi K, Hamame CM, Dalal SS, Bertrand O, Minotti L, Kahane P, Lachaux J-P. 2012. Efficient "Pop-Out" Visual Search Elicits Sustained Broadband Gamma Activity in the Dorsal Attention Network. J Neurosci. 32:3414–3421.
Palva JM, Palva S, Kaila K. 2005. Phase Synchrony among Neuronal Oscillations in the Human Cortex. J Neurosci. 25:3962–3972.
Palva S, Kulashekhar S, Hämäläinen M, Palva JM. 2011. Localization of cortical phase and amplitude dynamics during visual working memory encoding and retention. J Neurosci. 31:5013–5025.
Palva S, Palva JM. 2007. New vistas for α-frequency band oscillations. Trends Neurosci. 30:150–158.
Palva S, Palva JM. 2011. Functional roles of alpha-band phase synchronization in local and large-scale cortical networks. Front Psychol.
Park DC, Reuter-Lorenz P. 2009. The adaptive brain: aging and neurocognitive scaffolding. Annu Rev Psychol. 60:173–196.
Parmentier FBR. 2008. Towards a cognitive model of distraction by auditory novelty: The role of involuntary attention capture and semantic processing. Cognition. 109:345–362.
Parmentier FBR, Elsley J V, Ljungberg JK. 2010. Behavioral distraction by auditory novelty is not only about novelty: The role of the distracter's informational value. Cognition. 115:504–511.
Parmentier FBR, Hebrero M. 2013. Cognitive control of involuntary distraction by deviant sounds. J Exp Psychol Learn Mem Cogn. 39:1635.
Parmentier FBRR, Elford G, Escera C, Andrés P, Miguel IS, San Miguel I. 2008. The cognitive locus of distraction by acoustic novelty in the cross-modal oddball task. Cognition. 106:408–432.
Payne L, Guillory S, Sekuler R. 2013. Attention-modulated Alpha-band Oscillations Protect against Intrusion of Irrelevant Information. J Cogn Neurosci. 25:1463–1476.
Peiffer AM, Hugenschmidt CE, Maldjian JA, Casanova R, Srikanth R, Hayasaka S, Burdette JH, Kraft RA, Laurienti PJ. 2009. Aging and the interaction of sensory cortical function and structure. Hum Brain Mapp. 30:228–240.
Petersen S., Posner M. 2012. The attention system of the human brain: 20 years after. Annu Rev Neurosci. 21:73–89.
Pfurtscheller G, Stancak A, Neuper C. 1996. Event-related synchronization (ERS) in the alpha band—an electrophysiological correlate of cortical idling: a review. Int J Psychophysiol. 24:39–46.
Picton TW, Hillyard SA. 1974. Human auditory evoked potentials. II: Effects of attention. Clin Neurophysiol. 36:191–200.
Pinsk M a, Doniger GM, Kastner S. 2004. Push-pull mechanism of selective attention in human extrastriate cortex. J Neurophysiol. 92:622–629.
Popov T, Kastner S, Jensen O. 2017. FEF-Controlled Alpha Delay Activity Precedes Stimulus-Induced Gamma-Band Activity in Visual Cortex. J Neurosci. 37:4117–4127.

Posner MI. 1980. Orienting of attention. Q J Exp Psychol. 32:3–25.
Posner MI, Fan J. 2008. Attention as an organ system, Topics in Integrative Neuroscience: From Cells to Cognition.
Posner MI, Petersen S. 1990. The attention system of the human brain. Annu Rev Neurosci. 13:25–42.
Ramot M, Fisch L, Harel M, Kipervasser S, Andelman F, Neufeld MY, Kramer U, Fried I, Malach R. 2012. A Widely Distributed Spectral Signature of Task-Negative Electrocorticography Responses Revealed during a Visuomotor Task in the Human Cortex. J Neurosci. 32:10458–10469.
Raz A, Buhle J. 2006. Typologies of attentional networks. Nat Rev Neurosci. 7:367–379.
Reuter-Lorenz PA, Lustig C. 2005. Brain aging: reorganizing discoveries about the aging mind. Curr Opin Neurobiol. 15:245–251.
Reynolds JH, Heeger DJ. 2009. The Normalization Model of Attention. Neuron.
Richter CG, Thompson WH, Bosman CA, Fries P. 2017. Top-Down Beta Enhances Bottom-Up Gamma. J Neurosci. 37:6698–6711.
Rihs TA, Michel CM, Thut G. 2007. Mechanisms of selective inhibition in visual spatial attention are indexed by alpha-band EEG synchronization. Eur J Neurosci. 25:603–610.
Rihs TA, Michel CM, Thut G. 2009. A bias for posterior alpha-band power suppression versus enhancement during shifting versus maintenance of spatial attention. Neuroimage. 44:190–199.
Robin DA, Rizzo M. 1992. Orienting attention in audition and between audition and vision: young and elderly subjects. J Speech Hear Res. 35:701–707.
Robinson DL, Bowman EM, Kertzman C. 1995. Covert orienting of attention in macaques. II. Contributions of parietal cortex. J Neurophysiol. 74:698–712.
Rosahl SK, Knight RT. 1995. Role of prefrontal cortex in generation of the contingent negative variation. Cereb Cortex. 5:123–134.
Rosano C, Krisky CM, Welling JS, Eddy WF, Luna B, Thulborn KR, Sweeney JA. 2002. Pursuit and saccadic eye movement subregions in human frontal eye field: a high-resolution fMRI investigation. Cereb Cortex. 12:107–115.
Rosenberg JR, Amjad AM, Breeze P, Brillinger DR, Halliday DM. 1989. The Fourier approach to the identification of functional coupling between neuronal spike trains. Prog Biophys Mol Biol. 53:1–31.
Rossi AF, Bichot NP, Desimone R, Ungerleider LG. 2007. Top Down Attentional Deficits in Macaques with Lesions of Lateral Prefrontal Cortex. J Neurosci. 27:11306–11314.
Rouhinen S, Panula J, Palva JM, Palva S. 2013. Load Dependence of β and γ Oscillations Predicts Individual Capacity of Visual Attention. J Neurosci. 33:19023–19033.
Ruff CC. 2013. Sensory processing: Who's in (top-down) control? Ann N Y Acad Sci. 1296:88–107.
Rule RR, Shimamura AP, Knight RT. 2002. Orbitofrontal cortex and dynamic filtering of emotional stimuli. Cogn Affect Behav Neurosci. 2:264–270.
Sacchet MD, LaPlante RA, Wan Q, Pritchett DL, Lee AKC, Hamalainen M, Moore CI, Kerr CE, Jones SR. 2015. Attention Drives Synchronization of Alpha and Beta Rhythms between Right Inferior Frontal and Primary Sensory Neocortex. J Neurosci. 35:2074–2082.
Saleem AB, Lien AD, Krumin M, Haider B, Rosón MR, Ayaz A, Reinhold K, Busse L, Carandini M, Harris KD. 2017. Subcortical Source and Modulation of the Narrowband Gamma Oscillation in Mouse Visual Cortex. Neuron. 93:315–322.
Salmi J, Rinne T, Degerman A, Salonen O, Alho K. 2007. Orienting and maintenance of spatial attention in audition and vision: Multimodal and modality-specific brain activations. Brain Struct Funct. 212:181–194.

Salmi J, Rinne T, Koistinen S, Salonen O, Alho K. 2009. Brain networks of bottom-up triggered and top-down controlled shifting of auditory attention. Brain Res. 1286:155–164.
Salo E, Rinne T, Salonen O, Alho K. 2013. Brain activity during auditory and visual phonological, spatial and simple discrimination tasks. Brain Res. 1496:55–69.
Salo E, Salmela V, Salmi J, Numminen J, Alho K. 2017. Brain activity associated with selective attention, divided attention and distraction. Brain Res. 1664:25–36.
Salthouse TA. 1996. The processing-speed theory of adult age differences in cognition. Psychol Rev. 103:403.
SanMiguel I, Corral M-J, Escera C. 2008. When loading working memory reduces distraction: behavioral and electrophysiological evidence from an auditory-visual distraction paradigm. J Cogn Neurosci. 20:1131–1145.
Sara SJ, Bouret S. 2012. Orienting and Reorienting: The Locus Coeruleus Mediates Cognition through Arousal. Neuron.
Sarter M, Gehring WJ, Kozak R. 2006. More attention must be paid: the neurobiology of attentional effort. Brain Res Rev. 51:145–160.
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. Eur J Neurosci. 22:2917–2926.
Schadow J, Lenz D, Dettler N, Fründ I, Herrmann CS. 2009. Early gamma-band responses reflect anticipatory top-down modulation in the auditory cortex. Neuroimage. 47:651–658.
Schröger E. 1996. A Neural Mechanism for Involuntary Attention Shifts to Changes in Auditory Stimulation. J Cogn Neurosci. 8:527–539.
Schröger E. 1997. On the detection of auditory deviations: A pre-attentive activation model. Psychophysiology. 34:245–257.
Schröger E. 2005. The mismatch negativity as a tool to study auditory processing. Acta Acust United with Acust. 91:490–501.
Schröger E, Bendixen A, Denham SL, Mill RW, Bőhm TM, Winkler I. 2014. Predictive Regularity Representations in Violation Detection and Auditory Stream Segregation: From Conceptual to Computational Models. Brain Topogr. 27:565–577.
Searle SR, Speed FM, Milliken GA. 1980. Population marginal means in the linear model: an alternative to least squares means. Am Stat. 34:216–221.
Sedley W, Cunningham MO. 2013. Do cortical gamma oscillations promote or suppress perception? An under-asked question with an over-assumed answer. Front Hum Neurosci. 7:595.
Serences J, Shomstein S, Leber A, Egeth H, Yantis S. 2002. Neural mechanisms of goal-directed and stimulus-driven attentional control. In: JOURNAL OF COGNITIVE NEUROSCIENCE. MIT PRESS FIVE CAMBRIDGE CENTER, CAMBRIDGE, MA 02142 USA. p. 45.
Serences JT, Yantis S. 2007. Spatially selective representations of voluntary and stimulus-driven attentional priority in human occipital, parietal, and frontal cortex. Cereb Cortex. 17:284–293.
Shinichiro Koga, Rothermel R, Juhász C, Nagasawa T, Sood S, Asano E. 2012. Electrocorticographic correlates of cognitive control in a Stroop task: Intracranial recording in epileptic patients. 40:1301–1315.
Shomstein S, Yantis S. 2004. Control of attention shifts between vision and audition in human cortex. J Neurosci. 24:10702–10706.
Shulman GL, Ollinger JM, Akbudak E, Conturo TE, Snyder AZ, Petersen SE, Corbetta M. 1999. Areas involved in encoding and applying directional expectations to moving

objects. J Neurosci. 19:9480–9496.
Siegel M, Donner TH, Oostenveld R, Fries P, Engel AK. 2008. Neuronal Synchronization along the Dorsal Visual Pathway Reflects the Focus of Spatial Attention. Neuron. 60:709–719.
Singer W. 2001. Consciousness and the binding problem. Ann N Y Acad Sci. 929:123–146.
Sinnett S, Snyder JJ, Kingstone A. 2009. Role of the lateral prefrontal cortex in visual object-based selective attention. Exp Brain Res. 194:191–196.
Slagter HA, Prinssen S, Reteig LC, Mazaheri A. 2016. Facilitation and inhibition in attention: Functional dissociation of pre-stimulus alpha activity, P1, and N1 components. Neuroimage. 125:25–35.
Smith D V, Davis B, Niu K, Healy EW, Bonilha L, Fridriksson J, Morgan PS, Rorden C. 2010. Spatial attention evokes similar activation patterns for visual and auditory stimuli. J Cogn Neurosci. 22:347–361.
Snyder AC, Foxe JJ. 2010. Anticipatory Attentional Suppression of Visual Features Indexed by Oscillatory Alpha-Band Power Increases:A High-Density Electrical Mapping Study. J Neurosci. 30:4024–4032.
Solbakk A-K, Fuhrmann Alpert G, Furst AJ, Hale LA, Oga T, Chetty S, Pickard N, Knight RT. 2008. Altered prefrontal function with aging: insights into age-associated performance decline. Brain Res. 1232:30–47.
Solbakk AK, Løvstad M. 2014. Effects of focal prefrontal cortex lesions on electrophysiological indices of executive attention and action control. Scand J Psychol. 55:233–243.
Spierer L, Bellmann-Thiran A, Maeder P, Murray MM, Clarke S. 2009. Hemispheric competence for auditory spatial representation. Brain. 132:1953–1966.
Steinmetz MA, Constantinidis C. 1995. Neurophysiological evidence for a role of posterior parietal cortex in redirecting visual attention. Cereb Cortex. 5:448–456.
Stern Y. 2002. What is cognitive reserve? Theory and research application of the reserve concept. J Int Neuropsychol Soc. 8:448–460.
Stothart G, Kazanina N. 2016. Auditory perception in the aging brain: the role of inhibition and facilitation in early processing. Neurobiol Aging. 47:23–34.
Stroop JR. 1935. Studies of interference in serial verbal reactions. J Exp Psychol. 18:643.
Sturm W, De Simone A, Krause BJ, Specht K, Hesselmann V, Radermacher I, Herzog H, Tellmann L, Müller-Gärtner HW, Willmes K. 1999. Functional anatomy of intrinsic alertness: Evidence for a fronto-parietal-thalamic-brainstem network in the right hemisphere. Neuropsychologia. 37:797–805.
Stuss DT. 2011. Functions of the frontal lobes: relation to executive functions. J Int Neuropsychol Soc. 17:759–765.
Suwazono S, MacHado L, Knight RT. 2000. Predictive value of novel stimuli modifies visual event-related potentials and behavior. Clin Neurophysiol. 111:29–39.
Suzuki M, Gottlieb J. 2013. Distinct neural mechanisms of distractor suppression in the frontal and parietal lobe. Nat Neurosci. 16:98–104.
Swann NC, Tandon N, Pieters TA, Aron AR. 2013. Intracranial electroencephalography reveals different temporal profiles for dorsal- and ventro-lateral prefrontal cortex in preparing to stop action. Cereb Cortex. 23:2479–2488.
Szczepanski SM, Crone NE, Kuperman RA, Auguste KI, Parvizi J, Knight RT. 2014. Dynamic Changes in Phase-Amplitude Coupling Facilitate Spatial Attention Control in Fronto-Parietal Cortex. PLoS Biol. 12.
Szczepanski SM, Kastner S. 2013. Shifting attentional priorities: control of spatial attention through hemispheric competition. J Neurosci. 33:5411–5421.
Szczepanski SM, Konen CS, Kastner S. 2010. Mechanisms of spatial attention control in

frontal and parietal cortex. J Neurosci. 30:148–160.
Takeuchi H, Taki Y, Nouchi R, Sekiguchi A, Hashizume H, Sassa Y, Kotozaki Y, Miyauchi CM, Yokoyama R, Iizuka K, Nakagawa S, Nagase T, Kunitoki K, Kawashima R. 2015. Degree centrality and fractional amplitude of low-frequency oscillations associated with Stroop interference. Neuroimage. 119:197–209.
Tallon-Baudry, Bertrand. 1999. Oscillatory gamma activity in humans and its role in object representation. Trends Cogn Sci. 3:151–162.
Tallon-Baudry C, Bertrand O, Delpuech C, Permier J. 1997. Oscillatory gamma-band (30-70 Hz) activity induced by a visual search task in humans. J Neurosci Off J Soc Neurosci. 17:722–734.
Tallon-Baudry C, Bertrand O, Delpuech C, Pernier J. 1996. Stimulus specificity of phase-locked and non-phase-locked 40 Hz visual responses in human. J Neurosci. 16:4240–4249.
Tallon-Baudry C, Kreiter AG, Bertrand O. 1999. Sustained and transient oscillatory responses in the gamma and beta bands in a visual short-term memory task in humans. Vis Neurosci. 16:449–459.
Tallon C, Bertrand O, Bouchet P, Pernier J. 1995. Gamma-range activity evoked by coherent visual stimuli in humans. Eur J Neurosci. 7:1285–1291.
Talsma D, Kok A, Ridderinkhof KR. 2006. Selective attention to spatial and non-spatial visual stimuli is affected differentially by age: Effects on event-related brain potentials and performance data. Int J Psychophysiol. 62:249–261.
Taylor K, Mandon S, Freiwald WA, Kreiter AK. 2005. Coherent oscillatory activity in monkey area v4 predicts successful allocation of attention. Cereb Cortex. 15:1424–1437.
Team RC. 2014. R: A Language and Environment for Statistical Computing. Vienna: R Foundation for Statistical Computing. Available online at: h ttp. www R-project org.
Thut G. 2006. alpha-Band Electroencephalographic Activity over Occipital Cortex Indexes Visuospatial Attention Bias and Predicts Visual Target Detection. J Neurosci. 26:9494–9502.
Treisman A. 1988. Features and objects: The fourteenth Bartlett memorial lecture. Q J Exp Psychol. 40:201–237.
Treisman AM. 1964. Selective attention in man. Br Med Bull.
Treisman AM, Gelade G. 1980. A feature-integration theory of attention. Cogn Psychol. 12:97–136.
Tune S, Wöstmann M, Obleser J. 2018. Probing the limits of alpha power lateralisation as a neural marker of selective attention in middle-aged and older listeners. Eur J Neurosci. 1–14.
Vaden RJ, Hutchesona NL, McColluma LA, Kentrosa JG, M. VK. 2012. Older adults, unlike younger adults, do not modulate alpha power to suppress irrelevant information. North. 29:1883–1889.
van der Waal M, Farquhar J, Fasotti L, Desain P. 2017. Preserved and attenuated electrophysiological correlates of visual spatial attention in elderly subjects. Behav Brain Res. 317:415–423.
van Diepen RM, Mazaheri A. 2017. Cross-sensory modulation of alpha oscillatory activity: suppression, idling, and default resource allocation. Eur J Neurosci. 45:1431–1438.
Van Gerven PWM, Guerreiro MJS. 2016. Selective Attention and Sensory Modality in Aging: Curses and Blessings. Front Hum Neurosci. 10:1–7.
van Kerkoerle T, Self MW, Dagnino B, Gariel-Mathis M-A, Poort J, van der Togt C, Roelfsema PR. 2014. Alpha and gamma oscillations characterize feedback and feedforward processing in monkey visual cortex. Proc Natl Acad Sci. 111:14332–14341.
Van Veen BD, van Drongelen W, Yuchtman M, Suzuki A. 1997. Localization of brain

electrical activity via linearly constrained minimum variance spatial filtering. Biomed Eng IEEE Trans. 44:867–880.
Vandenberghe R, Duncan J, Dupont P, Ward R, Poline J-B, Bormans G, Michiels J, Mortelmans L, Orban GA. 1997. Attention to one or two features in left or right visual field: a positron emission tomography study. J Neurosci. 17:3739–3750.
Voisin J, Bidet-Caulet A, Bertrand O, Fonlupt P. 2006. Listening in Silence Activates Auditory Areas: A Functional Magnetic Resonance Imaging Study. J Neurosci. 26:273–278.
Von Békésy G, Wever EG. 1960. Experiments in hearing. McGraw-Hill New York.
von Stein A, Chiang C, Konig P. 2000. Top-down processing mediated by interareal synchronization. Proc Natl Acad Sci. 97:14748–14753.
Vossel S, Geng JJ, Fink GR. 2014. Dorsal and ventral attention systems: Distinct neural circuits but collaborative roles. Neuroscientist. 20:150–159.
Vossel S, Weidner R, Driver J, Friston KJ, Fink GR. 2012. Deconstructing the architecture of dorsal and ventral attention systems with dynamic causal modelling. J Neurosci. 32:10637–10648.
Wais PE, Martin GM, Gazzaley A. 2012. The impact of visual distraction on episodic retrieval in older adults. Brain Res. 1430:78–85.
Wardak C, Ibos G, Duhamel J-R, Olivier E. 2006. Contribution of the monkey frontal eye field to covert visual attention. J Neurosci. 26:4228–4235.
Watkins S, Dalton P, Lavie N, Rees G. 2007. Brain Mechanisms Mediating Auditory Attentional Capture in Humans. Cereb Cortex.
Weise A, Hartmann T, Schröger E, Weisz N, Ruhnau P. 2016. Cross-modal distractors modulate oscillatory alpha power: the neural basis of impaired task performance. Psychophysiology. 53:1651–1659.
Weisz N, Hartmann T, Müller N, Lorenz I, Obleser J. 2011. Alpha rhythms in audition: Cognitive and clinical perspectives. Front Psychol. 2:1–15.
Weisz N, Muller N, Jatzev S, Bertrand O. 2014. Oscillatory alpha modulations in right auditory regions reflect the validity of acoustic cues in an auditory spatial attention task. Cereb Cortex. 24:2579–2590.
Weisz N, Obleser J. 2014. Synchronisation signatures in the listening brain: A perspective from non-invasive neuroelectrophysiology. Hear Res.
Welford AT. 1981. Signal, noise, performance, and age. Hum Factors. 23:97–109.
West RL. 1996. An application of prefrontal cortex function theory to cognitive aging. Psychol Bull. 120:272.
Wetzel N, Schröger E. 2014. On the development of auditory distraction: A review. PsyCh J. 3:72–91.
Winkler I. 2007. Interpreting the mismatch negativity. J Psychophysiol. 21:147–163.
Wojciulik E, Kanwisher N. 1999. The generality of parietal involvement in visual attention. Neuron. 23:747–764.
Womelsdorf T, Fries P. 2007. The role of neuronal synchronization in selective attention. 154–160.
Woods DL, Knight RT. 1986. Electrophysiologic evidence of increased distractibility after dorsolateral prefrontal lesions. Neurology.
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. J Neurosci. 20:RC63.
Wu C-T, Weissman DH, Roberts KC, Woldorff MG. 2007. The neural circuitry underlying the executive control of auditory spatial attention. Brain Res. 1134:187–198.
Wutz A, Melcher D, Samaha J. 2018. Frequency modulation of neural oscillations according

to visual task demands. Proc Natl Acad Sci U S A. 115:1346–1351.
Xiao-Jing Wang. 2013. Neurophysiological and Computational Principles of Cortical Rhythms in Cognition. Neuron. 15:1195–1268.
Yago E, Duarte A, Wong T, Barceló F, Knight RT. 2004. Temporal kinetics of prefrontal modulation of the extrastriate cortex during visual attention. Cogn Affect Behav Neurosci. 4:609–617.
Yan Y, Wei R, Zhang Q, Jin Z, Li L. 2016. Differential roles of the dorsal prefrontal and posterior parietal cortices in visual search: A TMS study. Sci Rep. 6:1–9.
Zanto TP, Gazzaley A. 2013. Fronto-parietal network: flexible hub of cognitive control. Trends Cogn Sci. 14:384–399.
Zanto TP, Gazzaley A. 2014. Attention and ageing. Oxford Handb Atten. 927–971.
Zanto TP, Rubens MT, Thangavel A, Gazzaley A. 2011. Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. Nat Neurosci. 14:656–663.
Zappoli R, Versari A, Paganini M, Arnetoli G, Gangemi PF, Muscas GC, Arneodo MG, Battaglia A. 1992. Changes in bit-mapped contingent negative variation (CNV) activity due to initial normal involutional processes of the human brain. Int J Psychophysiol. 12:101–121.
Zappoli R, Versari A, Paganini M, Arnetoli G, Roma V, Battaglia A, Porcù S. 1988. Age differences in contingent negative variation activity of healthy young adults and presenile subjects. Ital J Neurol Sci. 9:219–230.
Zappoli R, Versari A, Zappoli F, Chiaramonti R, Zappoli Thyrion GD, Grazia Arneodo M, Zerauschek V. 2000. The effects on auditory neurocognitive evoked responses and contingent negative variation activity of frontal cortex lesions or ablations in man: Three new case studies. Int J Psychophysiol.
Zatorre RJ, Belin P. 2001. Spectral and temporal processing in human auditory cortex. Cereb cortex. 11:946–953.
Zatorre RJ, Belin P, Penhune VB. 2002. Structure and function of auditory cortex: music and speech. Trends Cogn Sci. 6:37–46.
Zatorre RJ, Mondor TA, Evans AC. 1999. Auditory Attention to Space and Frequency Activates Similar Cerebral Systems. Neuroimage. 10:544–554.
Zatorre RJ, Penhune VB. 2001. Spatial localization after excision of human auditory cortex. J Neurosci. 21:6321–6328.
Zhang P, Chen X, Yuan P, Zhang D, He S. 2006. The effect of visuospatial attentional load on the processing of irrelevant acoustic distractors. Neuroimage. 33:715–724.
Zumer JM, Scheeringa R, Schoffelen JM, Norris DG, Jensen O. 2014. Occipital Alpha Activity during Stimulus Processing Gates the Information Flow to Object-Selective Cortex. PLoS Biol. 12.