The functional mechanisms of top-down attentional control

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The functional mechanisms of top-down attentional control

De functionele mechanismes van top-down controle van de aandacht

(met een samenvatting in het Nederlands)

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Attention

One day a man of the people said to Zen master Ikkyu,
"Master, will you please write for me some maxims of the highest wisdom?"
Ikkyu immediately took his brush and wrote the word: "Attention."

"Is that all?" asked the man. "Will you not add something more?"
Ikkyu then wrote twice running: "Attention. Attention."
"Well," remarked the man rather irritably, "I really don't see much depth or subtlety in what you have just written."
Then Ikkyu wrote the same word three times running:
"Attention. Attention. Attention."
Half-angered, the man demanded,
"What does that word 'attention' mean anyway?"
Ikkyu answered gently, "Attention means attention."

From *"The Three Pillars of Zen"* by Philip Kapleau

Attention

our selective filter
our weapon against distraction
our memory assistant
our performance streamliner
and our experience booster
Shouldn't it deserve all our attention?

Tineke Grent - 't Jong

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Chapter 1

Introduction

1. Introduction

"The average PhD thesis is nothing but a transference of bones
from one grave-yard to another"

J. Frank Dobie (1888-1964)
US folklorist and raconteur (storyteller),
who rebelled against convention
and refused to earn a doctoral degree

According to Frank Dobie, PhD theses often lack meaning and significant purpose. So let me first briefly summarize what you can expect to find on the remaining pages in terms of meaning and significant purpose. In this Introduction, some relevant background on the concept of attention in general will be discussed first (section 1.1), including a brief history on the study of mental functions, and an introduction of the concept of preparatory (top-down) attentional control. Second, an overview of the main findings concerning the effects of selective attention on brain activity and behavior will be provided in section 1.2, including an overview of the different methods used to study cognitive brain functions in general. Third, a review is provided in section 1.3 of the existing knowledge on top-down attentional control activity in the brain, focusing particularly (but not exclusively) on the findings that existed prior to the onset of this thesis work. Fourth, relevant theories on selective attention and attentional control mechanisms will be discussed in section 1.4. And finally, in the sections 1.5 and 1.6, the specific research questions central to this thesis will be introduced, followed by an outline of the subsequent chapters, including those that contain the studies executed during this thesis work in order to answer those specific questions. On a final note, the sections 1.1, 1.2, 1.5 and 1.6 of this introduction are written with non-expect readers in mind, whereas sections 1.3 and 1.4 have a stronger scientific language focus.

1.1 The concept of attention in cognitive neuroscience research

The concept of attention in cognitive psychology and cognitive neuroscience is not always used in the same way as it is used outside the scientific community. Most people typically think of attention as a form of concentration, but as we will see below, the scientific concept of attention contains much more than our ability to concentrate. Another more general and slightly different view -- typically held by people who meditate or clinicians who provide stress reduction training -- is that attention equals mindfulness. Mindfulness, however, involves self-regulated attention with the goal to be consciously aware of one's own thoughts, feelings and surroundings, which differs from the use of attention in this thesis in that it is much more internalized, passive, less goal/task-driven with respect to external stimuli. So let's go over some more details first on what cognitive neuroscientist mean by "attention" and which type of attention exactly is studied in this current thesis.

1.1.1 A bit of history regarding scientific research on attention

Attention research has a long history and is still regarded as one of the main topics of interest within the study of human cognition. Cognition is an umbrella term that includes things like thinking, planning, remembering, decision making, and of course attention, and it is used to refer to those mental processes that contribute to or underlie human behavior. The study of cognitive processes (in ancient times called "mental faculties") dates back to at least ancient Greek times, for example to the work of Aristotle (384-322 BC). In those days it already included the development of models speculating the existence of covert cognitive processes, including the focusing of attention. Interestingly, however, Aristotle's concepts of mental faculties (including attention) had them not in the brain, but in the heart, which in those days was regarded by many as the origin of the mind. In those early days, only the Italian born writer and philosopher-scientist Alcmaeon of Croton (~530-470 BC) is known to explicitly have believed in the brain as the origin of intellectual activity. Generally speaking though, the idea that the brain, and not the heart, is the origin of mental faculties did not became mainstream earlier than in the 16th and 17th century. A good example is the 17th century French philosopher René Descartes (1596-1650) who observed that attention could be voluntarily directed, but also involuntarily captured by objects of interest. He argued that consciousness (including attention), was produced by the soul, which operated independently from the body. He hypothesized that the soul interacted with reflex pathways and the rest of body in the pineal gland, a small structure that is located just below the center of the bottom of the brain and that produces melatonin, a hormone that affects the modulation of wake/sleep cycles and photoperiodic (seasonal) functions. No one before Descartes had ever seriously proposed that phenomena as complex as human behavior could be viewed as the product of purely physical interactions in physiological systems (Glimcher, 2003, pg. 7).

Attention, however, wasn't really studied in those days, at least not in the sense of being studied by means of experimental investigations. Most theories were merely observational and/or introspective in nature. It took another couple of centuries for the instantiation of experimental psychology as a scientific field in order for attention to begin to be studied more rigorously and with more sound scientific methods. The most relevant early experimental research on attention (for our current focus) is probably the work by the German physician and physicist Hermann von Helmholtz (1821-1894), who experimentally studied covert visual-spatial attention. Covert attention is a form of attention that is hidden from observation by someone else (hence the term "covert", which means hidden or concealed), because when we use covert attention, we may attend to another location than the one to which our are senses are directed. Hermann von Helmholtz was the first to provide scientific evidence for this type of attention. Examples of this type of attention will also be presented in the studies reported in Chapters 3 and 4. Chapters 2 and 5, in contrast, contain studies in which attention is more "overt", more unconcealed and openly visible, because in these studies participants attended to the same location as their eyes were directed.

Another individual that should be mentioned in this brief historical overview, because of his important contributions to the field of cognitive psychology, is the Dutch ophthalmologist and medical scientist Franciscus Cornelis Donders (1818-1889). F.C. Donders is mostly known for his inventions of the now famous subtraction logic, particularly of reaction time measures for the decomposition of cognitive processes. His method forms the core of what is referred to as "mental chronometry", the study of content, duration and temporal sequencing of cognitive operations. From him stems the idea that sensory stimuli that enter the brain go through a number of information processing stages, including sensory registration, perceptual identification, and a more central set of discrimination and task evaluation stages, after which a response decision can be made, prepared, and executed. Some references to these information processing stages will be discussed in the later chapters of this work.

1.1.2 Defining attention

Although "attention" is a commonly used word, defining attention isn't easy. The most often cited definition of attention stems from the work of the late 19th century, Professor of Psychology at Harvard University, William James. He published two volumes on "The Principles of Psychology" (James, 1890a; James, 1890b), reviewing many of the same topics that are still the focus of cognitive research today, such as sensation and perception, stimulus discrimination, memory, the production of movement (action), habitual behaviors, emotions, consciousness, and of course attention. He described attention with the following famous quote:

> *"Everyone knows what attention is. It is the taking possession of the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatterbrained state which in French is called "distraction" and "Zerstreutheit" in German".*
>
> *William James (1890), Principles of Psychology, Volume I, pages 403-404*

This quote captures many of the properties of attention that are still addressed in today's research, such as the selectivity of attention and its beneficial effect on behavior, particularly that which is task or goal oriented. This selectivity of attention was also noted by the American psychologist Walter B. Pillsbury -- author of the first official book on the topic of attention (Pillsbury, 1908) -- summarizing the essence of attention as *"an increase in the clearness of an idea or group of ideas at the expense of others"* (Pillsbury, 1908, page 11). Nowadays, cognitive neuroscience textbooks typically distinguish several basic types of attention. The first one is the type James and Pillsbury were referring to, namely our ability to focus on certain sources of information and ignore others. For example, in situations in which more than one person is talking at the same time (e.g., a cocktail party) you can only effectively listen to one person at the time. This phenomenon is known as *"selective attention"* and it includes mechanisms such as our ability to orient and shift attention to focus on what is important or relevant at that time and to filter out what is not important and might distract us. Another type of attention, not mentioned in this quote of James, involves our ability to divide attention among multiple tasks, such as driving a car while carrying a conversation on the phone. This is called *"divided attention"* because we divide our limited central attentional resources across multiple sources of interest, often by rapidly shifting attention from one task to the other in order to ensure sufficient performance on both tasks (e.g., Cave et al., 2010; Jans et al., 2010). Still another type of attention relates to our capacity to sustain the focus of attention on one object for a prolonged period of time. This is refered to as *"sustained attention"*.

1.1.3 Top-down preparatory attentional control

Another way to characterize attention is to describe the way it is triggered. Imagine waiting in your car for a red traffic light. You are focusing on the lower light that you expect to turn green within the next minute or so, which will indicate permission for you to step on the gas and continue your way to your destination. In such a situation, you have selected one object out of many in your environment and remain focused on that object for a certain amount of time before responding to the expected, and very specific, change in that object of focus. This type of attention clearly has characteristics of both selective and sustained attention, but is not purely either. First, it is distinguishable from sustained attention by its relatively short time span. Preparatory attention, the type of attention studied in this dissertation, usually last only seconds to a few minutes, whereas we use sustained attention more in situations of prolonged attention that might last for 15 minutes to an hour or so, sometimes even longer. Second, it differs slightly from the more general use of the concept of selective attention in that preparatory attention is the part of selective attention that is more concerned with attention directed to a future event, in contrast to selective attention used to guide stimulus processing and respond to an already perceived behaviorally relevant event. We typically refer to such a relatively brief future-driven, selective attentional state as *"preparatory or anticipatory attention"*. Another term that is often used for this state is *"top-down attention"*, or *"top-down attentional control"*, because you, as the owner of attention, have determined to *voluntarily* and selectively direct your attention in a controlled way to the object of interest. This sort of attention is sometimes also called *"endogenous attention"*, meaning “from within”, rather than having your attention being pulled *involuntarily* to various events occurring unexpectedly in the environment, such as the sudden sound of a siren from an approaching ambulance or a sudden clap of thunder. Attention that is triggered by such an external event is referred to as *"bottom-up attention"* or *"exogenous attention"* and the triggering of the reflexive attentional shift is sometimes referred to as *"attentional capture"*.

1.2 The effects of selective attention on brain activity and behavior

1.2.1 Behavioral effects of selective attention

Selectively paying attention to what is of interest to us obviously has many beneficial behavioral effects. We would have many more accidents if we wouldn't have been taught to always keep our eyes on the road and also pay attention to important traffic signs along the way. We also would hardly learn anything if we wouldn't pay attention in the classroom to the relevant information provided. On the other hand, selectively paying attention to only some information provided in our environment also comes at a cost. One of the most intriguing examples of this fact probably stems from research on *"inattentional blindness"* -- a term coined by Arien Mack and Irvin Rock in 1992 -- describing the phenomenon of missing something that is in plain view, because you are selectively paying attention to something else. In the famous "gorilla test video" experiment (see e.g., Simons and Chabris, 1999), participants were asked to watch a short video in which two groups of people - some wearing black, others wearing white T-shirts - passed a basketball around. The participants were asked to either count the number of passes made by one of the teams or to keep count of bouncing passes vs. aerial passes. In some of the several versions of the experiment, somewhere halfway into the video a woman walks through the scene wearing a full black gorilla suit, stopping halfway to turn her head to the observer for a frantic series of beats on her chest. After watching the video, the participants were asked if they saw anything out of the ordinary. Across all task conditions, on average ~58% of the participants did not report seeing the obviously present gorilla. All participants did very well on the counting task, which can be taken as evidence of the benefits of selective attention. But the fact that many missed the obvious gorilla shows that this comes at a cost, a problem most aptly described as "the dark side of visual attention" by Marvin M. Chun & René Marois in their 2002 review (Chun and Marois, 2002). We remember mostly what we have chosen to attend to.

Another intriguing effect of selective attention is that a selective expectation for an expected event to occur in one particular location can delay our response if that event actually ends up occurring at a different location. Such effects of selective attention on behavioral performance have been consistently found in studies using the classic “Posner cueing paradigm” (e.g., Posner et al., 1980). In such a paradigm, directional, most often arrow, cues are presented shortly before the appearance of a target stimulus. Typically, these cues predict the location of the upcoming target stimulus with some degree of validity (e.g., 75% correctly, or validly cued, and 25% incorrectly, or invalidly, cued), resulting in participants being faster to respond to the targets appearing at the validly cued (and thus most expected) location compared to when targets are presented elsewhere (i.e., at invalidly cued location(s)). The studies reported in Chapters 3 and 4 in this thesis contain experiments in which cues are used to initiate expectations of the most probable location of a target stimulus, in a way comparable to the classical Posner cueing paradigm. The difference with the classical cueing paradigm, however, is that in those studies more symbolic letter cues were used, rather than the perhaps more automatic arrow cues, and that cue validity was increased to fully 100% predictability. This way the participants in those studies were presumed to maximize to use the information provided in the cue in order to direct their attention to the cued location, so we could look in those studies at what exactly happens in the brain during such periods of specific expectation. For example, we wanted to know which brain areas were recruited and in what order during preparatory attention toward a specific spatial location, information that could provide some clues as to the specific functional roles of these brain areas and how they are doing it.

But before getting into the details of the included studies, let's briefly look at the methods cognitive neuroscientists use to study brain activity related to such cognitive functions. For selective attention, such a discussion needs to include what kind of brain responses typically are recorded to study this cognitive function, the effects selective attention has on the processing of stimuli, and the brain activity patterns that have been related to the initiation and maintenance of a particular attentional expectation.

1.2.2 Methods used to study selective attention

In order to study brain activity related to the effects and control of selective attention, cognitive neuroscientist use a number of different recording techniques, such as electroencephalography (EEG), magnetoencephalography (MEG), functional Magnetic Resonance Imaging (fMRI), Positron Emission Tomography (PET), Event Related Optical Signals (EROS), and event-related electrical signals recorded directly from single neurons or groups of neurons (typically this research includes monkey brain neurons). Below, the focus is mostly on EEG and fMRI, the methods of choice in the studies presented in this thesis.

1.2.2.1 Measuring electrical signals from the scalp with EEG (or MEG) sensors

EEG signals are electrical signals, typically recorded from across multiple locations at the scalp, whereas MEG signals are their magnetic counterparts recorded with magnetometer machines. The signals are thought to be generated primarily by neurons located in the cortical layers of the brain. One type of stimulus and task-related activity that can be extracted from these EEG signals is what is known as event-related potentials (ERPs). As the name suggests, ERPs are those brain potentials that are related to the presence and processing of certain events. By assuming that the same type of event, presented over and over again under the same experimental condition, is processed approximately the same every time it occurred, we can average together pieces of EEG surrounding these events in order to extract what they have in common and remove all other random brain and environmental activity that is also being picked up but not related to the processing of that particular event type. Typically, one needs on average 50-200 events in order to have a high enough "signal-to-noise ratio" to reliably interpret the extracted ERPs.

Extracted ERPs show a characteristic pattern of peaks and troughs, representing time-varying electrical polarity current (positive or negative). These recordings are typically differential in nature (that is, recorded in reference to a reference signal). ERP waves or components are labeled in terms of their polarity and the length of time that has expired since the initiating event: a P300 (also called P3), for example, is a positive component that occurs approximately 300 milliseconds after the onset of an event. Experimental manipulations of stimuli and cognitive demands show how the component might be linked to particular types of processing. For example, early components (e.g. N100, or simplified, the N1) are most sensitive to physical stimulus characteristics, and can often be localized to sensory cortex, implying that they index early-stage perceptual processes. Conversely, later components such as the P300 are sensitive to more cognitive factors such as expectations and task demands. You can find many references to such ERP components in the current thesis.

Another type of activity that can be extracted from EEG data is rhythmic activity, also known as oscillatory activity. Human scalp-recorded brain activity that is related to cognitive processing has oscillatory power across a frequency range between approximately 0.1 and 50 Hz. The best known rhythm is the alpha frequency rhythm, occurring around 10 Hz (8-12 Hz). This rhythm is typically more pronounced (has higher power) when participants are either not involved in a specific task, getting sleepy, closing their eyes, directing their attention to auditory input, or experiencing a lapse in attention. In addition, a decrease in alpha power arising from a certain brain region has been found to be associated with an increased strength of activity in that brain area (see also Chapter 5). Accordingly, such an effect seen over visual sensory brain areas contralateral to the direction of attention has been associated with a shift of covert visual spatial attention to the contralateral visual space (see especially Chapter 4). Other well-known brain rhythms are the delta rhythm (0.5-4 Hz), the theta rhythm (4-8 Hz), the beta rhythm (12-30 Hz) and the gamma rhythm (30-50 Hz). Delta rhythms, if they dominate the EEG and have high amplitudes, are characteristic of slow-wave sleep (Contreras and Steriade, 1995), whereas this low frequency slow-wave activity derived from EEG shortly before an expected event or planned movement has been related to anticipatory brain activity, including both motor and non-motor aspects (e.g., Brunia and van Boxtel, 2001). Event-related theta rhythms have mostly been linked to working memory and effort, as well as to attention, especially auditory attention (see, for example, reviews by Basar-Eroglu et al., 1992; Klimesch, 1999; Knyazev, 2007). The higher-frequency beta and gamma rhythms are related in general to a higher state of alert and focused attention, and have been argued to also be related to motor- or working-memory and to perceptual binding processes (e.g., Herrmann et al., 2010).

As a final note, ERP responses and oscillatory activity changes overlap but are not identical. ERPs reflect the time-locked and phase-locked activity, averaged across all frequencies, whereas oscillatory activity represents time-locked but not necessarily phase-locked activity within one frequency band. Higher-frequency and non-phase-locked oscillatory activity especially tends to be averaged out in ERP averages.

1.2.2.2 Hemodynamic brain imaging techniques; PET and fMRI

Hemodynamic brain imaging refers to a family of techniques, including PET (Positron Emission Tomography) and fMRI (Functional Magnetic Resonance Imaging), that monitor activity of different regions of the brain, typically mostly gray matter. PET and fMRI have in common that they use detectors circling around a participant's head, while the participant is laying inside a machine. With PET, after the participant is positioned in the machine, the experimenter injects into a vein in the participant's arm a small amount of water labeled with the positron-emitting radioactive isotope oxygen-15. Over the next minute or so following the injection, the radioactive water accumulates in the brain in direct proportions to the local blood flow. The greater the blood flow (active area), the more the radiation is recorded by PET, and thus the greater activity is imaged.

In contrast to PET, the fMRI technique is more non-invasive -- nothing gets injected -- but the technique still requires the participants to be positioned inside a narrow tube of a large machine (which sometimes is problematic with participants who are claustrophobic [fearful of narrow places]). MRI uses magnetic fields, induced by strong magnets circling around the participant's head, in combination with radio waves of different frequencies to produce high quality two- or three-dimensional images of brain structures, either focusing on structure alone (structural MRI) or on activity changes across and within different brain areas in time (functional or fMRI). In the case of fMRI, the dependent variable most often used in attention research is the blood-oxygen-level-dependent (BOLD) changes, which are closely related to neural-activity-induced variations in blood flow. Like PET, images of task selective activity are displayed with the use of color scales (typically a red-yellow-blue scale in which red means higher activity and blue signals lower activity).

Useful experimental fMRI activations are almost always extracted relative to another condition, either rest or a control condition. In contrast to the hemodynamic PET or fMRI measures, EEG and MEG signals reflect more directly the electrical (neuronal) brain activity, typically of the dendritic fields of large cortical pyramidal cells. Although the raw ERP responses can be visualized, researchers still typically need to contrast an experimental condition with a control condition to obtain useful information.

One of the difficulties with PET and fMRI is their low temporal resolution. With PET, due to the nature of its approach, the image of one type of activity requires a full minute of acquisition (followed by a waiting time of 1 minutes before the next can be acquired). Although fMRI can be acquired much more quickly (1-3 seconds for the whole brain, the signal that is measures is rather slow (relative to the speed of human information processing) due to its dependence on blood-flow changes. Accordingly, even fMRI is not well suited to investigate the time-course of cognition. It takes for example only 200-500 ms in a simple reaction time task to press a button to record having seen the target stimulus. It has to be said though that the temporal resolution of fMRI recordings has improved over time, now being able to reliably extract changes in the range of 1-2 seconds, an improvement mostly resulting from advances in experimental paradigms that are for example better able to deal with temporal overlap from adjacent stimuli (see also Chapter 3), and also large improvements in the quality of the recording equipment itself. With respect to temporal resolution (how fine-grained in time one can look at recorded signals), ERPs are capable of providing information with the millisecond resolution needed to study the temporal cascade of human cognition. However, the generators of scalp recorded ERP activity are much harder to localize in the brain due to a number of factors, including its need to infer locations in a volume based on activity on its surface, as well the strong attenuation of the signals and smearing caused by the different tissues in the brain, skull and scalp. Thus, each of the cognitive neuroscience techniques that can examine brain activity has limitations along at least one of these dimensions (time or location). For this reason, recent empirical investigations often combine a technique that is capable of fine-grained localization with one that can achieve high temporal resolution. An example can be found in Chapter 3, a study in which information from fMRI and EEG is combined.

1.2.3 Brain activity markers of selective attention to visual events

Visual events enter our brain through light receptors in our eyes that transform the received signals into patterns of electrical current that are then send to other areas in the brain for further processing. In the case of visual stimuli, the next station is the lateral geniculate nucleus (LGN) of the thalamus, which in turn relays the signals to primary and secondary visual cortices in the back of the brain. There they give rise to the typical sensory-evoked (stimulus-modality specific) ERP signals to visual events, such as the first positive component over occipital-parietal areas (the P1: ~70-120 ms) -- sometimes preceded by another smaller component over mid-parietal-occipital areas (C1: ~50-70 ms) -- and the first, slightly later negative component (N1: ~140-200 ms) over the same areas. The P1/N1 complex is typically followed by a posterior N2 (~200-250 ms) and P2 (~200-300 ms) component, and a parietal P3 (~300-500 ms), that are all less sensitive to stimulus features and more sensitive to higher-level cognitive (endogenous) processes such as those related to stimulus evaluation and decision making.

A typical finding in visual-spatial attention studies -- studies in which participants use covert attention to a particular spatial location in order to perform a task there -- is that the same stimulus when attended produces larger amplitudes of these early sensory-evoked P1 and N1 components than when unattended (e.g., Eason et al., 1969; Hillyard and Munte, 1984). In addition, this difference is most pronounced in the visual cortical areas contralateral to the location of attentional focus. This makes sense, because the connections to visual cortex are organized such that, for example, signals received from the left visual field are mostly relayed to the right visual cortex and those from the right to the left (contralateral means contra or opposite to the stimulated, laterally located, visual field). Accordingly, if one attends to the left side of space and attention increases the sensory responses to stimuli from there, then the enhanced sensory responses should be also contralateral to the attended stimulus location. The location of origin of these P1 and N1 components has been reliably reported as extrastriate, or secondary, visual cortex (see e.g., Di Russo F. et al., 2002). In addition, studies using fMRI and/or PET in combination with ERPs have also reported evidence for a specific relationship between the P1 attention effect and increased brain activation in extrastriate cortical areas (Heinze et al., 1994; Mangun et al., 1997; Mangun et al., 1998; Woldorff et al., 1997). Finally, following these early amplifications of the stimulus-driven P1 and N1 potentials, visual-spatial attention studies also often report experimental changes in amplitude (usually amplifications) of the later N2, P2, and P3 components.

On the other hand, when participants are asked to attend to a non-spatial feature, such as for example color or form, the ERP effects of attention (i.e., the difference between the same stimulus attended versus unattended) look quite different. Typically, rather than enhancing the amplitude of the early sensory P1 and N1 components, these attention effects are characterized by a negative ERP component overlapping the exogenous (P1/N1) components, beginning around 150 ms after stimulus onset. This component was called Selection Negativity (SN) by Harter and colleagues (Harter et al., 1984; Previc and Harter, 1982) and Occipital Selection Negativity (OSN) by others (e.g., Kenemans et al., 1993). Selection Negativities have been found for selective attention to color (e.g., Anllo-Vento et al., 1998; Hillyard and Munte, 1984; Wijers et al., 1989b), to orientation (e.g., Harter and Guido, 1980; Kenemans et al., 1993; Previc and Harter, 1982), and to spatial frequency (e.g., Baas et al., 2002; Kenemans et al., 1995; Zani and Proverbio, 1995). In addition to this more posterior cortical component, a more anterior component has also been described, refered to as the Frontal Selection Positivity (FSP), both for color selection (e.g., Lange et al., 1998) and spatial frequency selection (Baas et al., 2002; Kenemans et al., 1993). The FSP typically has a slightly earlier onset (around 120 ms) compared to the OSN (around 150 ms). Interestingly, however, this earliest effect of non-spatial attention (the FSP) is still relatively late compared to the earliest effect of spatial attention (P1 effect) that starts at about 70 ms poststimulus. Researchers don't know yet why this is the case. An often proposed mechanism is that location always has to be selected first, and then features such as color or form, a reasoning that would indeed fit these findings. Finally, following the earlier FSP and OSN effects, later selective attention effects for non-spatial features typically include a frontocentral N2b and a parietal P3b component that are associated with target detection and categorization.

1.2.4 Brain activity markers of selective attention to auditory events

Auditory stimuli enter our brain through receptors in our inner ears. Like visual input, the received sound waves are first transformed into patterns of electrical currents that are then send to subcortical structures. In the case of auditory stimuli these structures include ventral and dorsal cochlear nuclei, the superior olive, and the inferior colliculi, all located in the brainstem, and the medial geniculate nucleus of the thalamus. From the medial geniculate, the signals propagate to parts of the temporal cortex (over the sides of the brain, approximately around and behind the ears) called the primary and secondary auditory projection areas. Thus, comparable to what we have seen with the reception of visual stimuli, auditory stimuli also travel through lower parts of the brain first, after which they are projected to sensory-input specific cortical areas.

Scalp recorded auditory ERP components can be separated into (1) early brainstem evoked responses, very small potentials recorded between 2-10 ms following the onset of the stimulus, (2) somewhat larger midlatency components recorded between 10 and 50 ms post-stimulus onset, originating from low-level auditory cortex, and (3) much larger late waves, including the midfrontal scalp recorded N1 (~80-100 ms), the P2 (~130-180 ms), and the processing negativity (130-250 ms), which derive from secondary and association auditory cortices. With respect to early effects of attention on the processing of auditory stimuli, the most reliably and therefore most reported early attention effect is the amplification of the midfrontally recorded N1 component, peaking around 100 ms post-stimulus onset (Hillyard et al., 1973; Hillyard and Picton, 1987; Woldorff et al., 1993). Despite its frontal distribution, the N1 component has its generators in the supratemporal plane mainly in early auditory cortex on the bottom bank of the Sylvian fissure (see e.g., Giard et al., 1994; Hillyard et al., 1973; Pantev et al., 1995). It is recorded over frontal cortex only because of the folding of the auditory cortices, which happen to be such that the electrical currents produced in those regions project most strongly towards the frontal scalp areas.

The auditory N1 attention effect is typically followed by amplification of the later P2 and processing negativity waves. Occasionally, under very restricted task situations (highly focused selective attention to rapid streams of auditory stimuli) an attention effect earlier than the N1 effect can be recorded in the form of an enhanced positive difference between 20 and 50 ms post-stimulus onset in response to the same stimulus when attended versus when unattended, which has been termed the "P20-50" attention effect electrically (Woldorff et al., 1987) or the “M20-50” effect magnetically (Woldorff et al., 1993). Finally, whereas in the visual modality clear effects of attention to spatial location are found in the contralaterality of the P1/N1 attention effects, such lateralization effects of attention have rarely been reported for spatial auditory attention (although see Woldorff and Hillyard, 1991).

1.3 Brain activity reflecting top-down attentional control activity

At the onset of this dissertation work the dominant view on top-down preparatory attention was that preparatory attention was controlled by a network of frontal and parietal brain areas that in turn controlled the initiation and maintenance of biasing activity in sensory cortical areas selective for the attended stimulus feature (see review by Corbetta and Shulman, 2002). In the following three subsections, I will summarize the findings that are consistent with this view, focusing most strongly (but not entirely) on the evidence existing at the onset of this dissertation work. Evidence for the involvement of a frontal-parietal network will be discussed first (1.3.1), followed by evidence for sensory cortex biasing activity (1.3.2) and the possible additional involvement of subcortical structures in top-down attentional control (1.3.3).

Evidence for the involvement of a particular set of brain areas in attentional control stems from different lines of research, including 1) human brain imaging studies, 2) brain lesion studies, 3) single-cell recordings in non-human primates, (4) ERP studies, and stimulation techniques such as (5) micro stimulation of neurons in monkey brains and 6) Transcranial Magnetic Stimulation (TMS) applied to the scalp of human participants. The evidence discussed below will be organized according to the technique used to investigate such attentional control activity.

1.3.1 Evidence for the involvement of frontal and parietal cortical areas

There is an overwhelming amount of evidence that particular regions of the dorsal frontal and parietal cortex are involved in top-down attentional control. In the frontal cortex, for example, areas most often associated with voluntary shifts of attention are the lateral frontal areas known as the frontal eye fields (FEF), the adjacent supplementary eye fields (SEF) and the slightly more lateral and anteriorly located dorsolateral prefrontal cortex (DLPFC). In addition, more medial (and superior) frontal areas have been implicated in control processes, such as the anterior cingulate cortex (ACC) and the supplementary motor area (SMA). Also, some evidence points toward a possible role of the posterior cingulate in attentional orienting. Finally, in the parietal cortex, most evidence points toward the involvement of the intra-parietal sulcus (IPS) and the superior parietal lobule (SPL).

1.3.1.1. Human brain imaging studies, including PET and fMRI studies, have found quite some evidence for sustained activation of FEF and IPS (the dorsal fronto-parietal network), and often the DLPFC, during a cue-target delay period when participants directed attention toward a peripheral location in the absence of overt eye or motor movements (Corbetta et al., 1993; Corbetta, 1998; Corbetta et al., 2000; Gitelman et al., 1996; Hopfinger et al., 2000; Kastner et al., 1999; Kato et al., 2001; Kim et al., 1999; Nobre et al., 1997; Nobre et al., 2000a; Peelen et al., 2004; Rosen et al., 1999; Small et al., 2003; Vandenberghe et al., 2000; Woldorff et al., 2004). In addition, this dorsal frontal parietal network has been found in studies in which participants were asked to direct attention to non-spatial visual features such as color, motion, or another sensory modality (Giesbrecht et al., 2003; Le et al., 1998; Macaluso et al., 2002; Shulman et al., 1999; Shulman et al., 2002; Weissman et al., 2004), or were asked to switch from attending to the global or to the local level letters presented in the target-letter object (Weissman et al., 2002). The involvement of the SPL has been argued to be the source of attention shift signals itself, rather than the maintenance of the focus of attention on the expected target location, because this area was found to be more transiently activated when participants voluntarily shifted their attention from one stream to another stream during a Rapid Visual Serial Presentation (RSVP) task (Yantis et al., 2002), whereas frontal areas were activated in a more sustained way (not shift specific). This transient SPL activity appeared to be largely modality non-specific, because it was found also for shifts between motion and color (Liu et al., 2003), shifts between superimposed objects (Serences et al., 2004), and shifts between sensory modalities (Shomstein and Yantis, 2004). The involvement of ACC/SMA regions has been shown for shifts towards different peripheral locations (e.g., Kim et al., 1999; Woldorff et al., 2004) as well as for shifts across modalities (Macaluso et al., 2003; Weissman et al., 2004). The frontal-parietal attentional control network has even been implicated in attention to temporal aspects of the task, such as attending to the expected onset of the target stimulus (Coull et al., 2000; Coull and Nobre, 1998). Finally, a possible role for the posterior cingulate cortex in visual-spatial attentional orienting has been suggested (e.g, Small et al., 2003).

1.3.1.2. Brain lesion studies have pointed to a possible crucial role of the parietal cortex in attentional control, mainly by the effects parietal lesions have on attention-related behavior. For example, right parietal cortex lesions often cause a problem called "hemispatial neglect" in which the patient ignores stimuli presented at the side of the body opposite (i.e., contralateral) to the lesioned hemisphere of the brain (Mesulam, 1981; Petersen et al., 1989; Posner et al., 1982; Posner et al., 1984; Posner et al., 1987; Rafal, 1994). This deficit was also reported to be more pronounced after lesions to the right than left parietal cortex. When lesions are centered primarily in the IPS, one of the regions strongly implicated in attentional control, the ability to voluntarily shift attention is clearly impaired (Friedrich et al., 1998). Hemispatial neglect symptoms have also been successfully created through experimentally induced lesions of parietal or parietal-occipital regions in monkeys (Lynch and McLaren, 1989).

In general, the effects of parietal lesions have often been explained as a problem with disengaging of attention from an attended location, rather than a problem with shifting of attention itself. This could, however, also strongly depend on the location of the lesion. A dorsal-medial frontal-parietal network is believed to be involved in the control of top-down attention orienting (Corbetta and Shulman, 2002), thus lesions in those areas can directly explain the problems with shifting of visual-spatial attention. In contrast, a more ventral-lateral (mostly right-sided) frontal-parietal-temporal (including the right temporal-parietal junction) attentional control system has been implicated in triggering attention shifts more exogenously, signaling the dorsal-medial attentional orienting system to control the further shifting of attention (more on this so-called "Circuit Breaker System" in section 1.4.3), so lesions in those areas might more indirectly cause neglect symptoms.

In contrast to parietal lesions, reports of hemispatial neglect symptoms due to frontal lesions have been relatively absent. The only clear more general attentional impairments after frontal lesions have been reported by Knight and colleagues. They found that ERP correlates of auditory selective attention were enhanced after left DLPFC lesions (Knight et al., 1981), whereas after right DLPFC lesions, patients showed an absence of attention effects for auditory stimuli presented on the left, and an impaired response for auditory stimuli on the right (Woods and Knight, 1986). In addition, Funahashi and colleagues (Funahashi et al., 1993; Funahashi et al., 2004) found evidence for memory deficits of visual field locations of expected targets following DLPFC lesions in monkeys.

1.3.1.3. Single-cell recordings in non-human primates also have argued for the involvement of both frontal and parietal cortices in attentional orienting. In matching-to-sample tasks, for example, several researchers have found sample-related signals during the delay period in prefrontal regions (Miller et al., 1996; Takeda and Funahashi, 2002). Activation of monkey LIP (comparable to human IPS) has been found to be increased when attention was directed to locations associated with the receptive fields of the recorded neurons (Bisley and Goldberg, 2003; Colby et al., 1996; Goldberg et al., 2002; Snyder et al., 2000). In a more recent study by Buschman and Miller (2007), simultaneous recordings from cells in both frontal and parietal cortices in monkeys particularly clearly showed evidence for crucial roles of these areas in top-down (as well as bottom-up) attention.

1.3.1.4. ERP studies, published before the early years of this thesis work, have mostly investigated shifting of visual-spatial attention, starting with the groundbreaking work of Harter and colleagues (Harter et al., 1989; Harter and Anllo-Vento, 1991), which was soon followed by work from other researchers (Eimer, 1993; Eimer et al., 2002; Hopf and Mangun, 2000; Nobre et al., 2000b; van Velzen and Eimer, 2003; Yamaguchi et al., 1994b; Yamaguchi et al., 1995). As a group, these studies reported three ERP components of preparatory visual-spatial attention shift activity that can be evoked contralateral to the direction of attention: 1) the Early-Directing-Attention-Negativity (EDAN) over posterior parietal-occipital scalp sites (200-400 ms postcue onset), 2) the Anterior-Directing-Attention-Negativity (ADAN) over lateral frontal and central scalp sites (300-500 ms postcue onset), and 3) the Late-Directing-Attention-Positivity (LDAP) over lateral ventral-occipital-temporal scalp sites (>500 ms post-cue onset). Interestingly, these components were not consistently found in all studies. The EDAN for example, was often absent in the studies from Eimer's group and was argued in one of their studies (van Velzen and Eimer, 2003) to be related to attention drawn to assymetrical aspects of the instructional cue stimulus itself (such as the arrow head of an arrow cue), rather than indicating attention shifts for future target locations. The ADAN was not found in the initial studies from Harter and colleagues, but later appeared in a number of studies (e.g., Eimer and van Velzen, 2002; Hopf and Mangun, 2000; Yamaguchi et al., 1994b). The LDAP component, found originally by Harter and colleagues, proved initially hard to replicate in subsequent studies. The most clear early replication was reported by Hopf & Mangun (2000). However, this component is more consistently described in more recent research (e.g., Green and McDonald, 2006; Jongen et al., 2007; McDonald and Green, 2008; Seiss et al., 2007; van der Lubbe et al., 2006).

Finally, few of the early studies (before 2004) looked at directing attention to non-spatial visual features. One was a study by Yamaguchi and colleagues, using a paradigm that cued for global or local features of an hierarchical letter, which induced both early and late cue-induced activity over temporal-parietal areas (Yamaguchi et al., 2000). Some more recently published studies also looked at preparatory attention shifts to color (Slagter et al., 2005b; Slagter et al., 2005a), and, for example, preparatory attention shifts to different sensory modalities (Green and McDonald, 2006; Talsma et al., 2008), but the majority of the studies still tend to focus on visual-spatial attentional control. As a result, no specific preparatory ERP components -- such as the visual-spatial attention shift related EDAN, ADAN, or LDAP components -- have ever been clearly described for non-spatial visual attention shifts.

1.3.1.5. Microstimulation of FEF neurons was already known for decades to produce contralateral saccades when threshold electrical currents were used (Robinson and Fuchs, 1969). However, even with subthreshold microstimulation of the same regions (i.e. with currents that were below the threshold required to evoke a saccade), shifts of attention to the locations corresponding to the stimulated neurons' receptive fields were induced, which was interpreted as a strong indication that this area is not only involved in initiating the motor aspects of this shift but also the attentional aspects of it (Moore and Fallah, 2001; Moore and Fallah, 2004). Microstimulation of monkey LIP (and a medial parietal region) also was reported to evoke memory activity, which includes attentional orienting activity, for saccadic eye movement (Thier and Andersen, 1998).

1.3.1.6. TMS (Transcranial Magnetic Stimulation) is a technique that can be used to temporarily disrupt or enhance the function of stimulated areas in humans. Using this technique, one can, for example, investigate the role of a brain area by studying the effects that a "virtual lesion" of this area has on performance (and other brain activity) in healthy participants. Although TMS was still a very recently discovered technique in those early days, some intriguing results had already been found with respect to the involvement of frontal and parietal areas in top-down attentional control. For example, TMS applied directly to the right posterior parietal cortex in healthy participants induced impairments in the ability to disengage attention from the ipsi-lesional side, very similar to effects seen in patients with real lesions in those areas (Fierro et al., 2000; Hilgetag et al., 2001). Also, TMS applied to left frontal areas in patients with unilateral right brain lesions was capable of reducing the contralesional neglect symptoms in those patients (Oliveri et al., 1999). TMS applied to the left FEF in a study by Grosbras and Paus resulted in a facilitation of detection of targets in the right hemifield only, whereas TMS applied to the right FEF region in this study resulted in increased slowing of responses to invalidly cued targets (Grosbras and Paus, 2002). Furthermore, by inducing contralateral saccade delays, TMS was shown to be capable of locating the FEFs in humans (Ro et al., 2002). Finally, a more recent TMS/ERP study by Taylor and colleagues (Taylor et al., 2007) showed a clear modulation of visual cortex, target-processing related, activity as a direct result of applying TMS pulses to the FEFs during the cue-target delay.

1.3.2 Evidence for target-stimulus specific biasing of sensory cortices

1.3.2.1. Human brain imaging studies have, besides strong evidence for the involvement of a frontal-parietal network of attention control areas, also very consistently reported increases in activity prior to the presentation of an attended target stimulus in areas in visual cortex that represented the attended location (Giesbrecht et al., 2003; Hopfinger et al., 2000; Kastner et al., 1999; Woldorff et al., 2004) or the attended feature (Chawla et al., 1999; Giesbrecht et al., 2003; Slagter et al., 2007). Such changes in those areas were also found to correlate with the outcome of perceptual decisions in highly trained observers, subjected to a near threshold detection task (Ress et al., 2000; Ress and Heeger, 2003).

1.3.2.2. Brain lesion studies are not specifically relevant as evidence for the idea of preparatory biasing signals present in sensory cortices before the presentation of the expected target stimulus. Lesions in visual (or auditory) cortex itself severely impairs detection of visual (or auditory) stimuli -- patients with such lesions are functionally blind or deaf, despite having properly functioning eyes or ears -- and thus selective attention effects to visual (or auditory) stimuli are also severely impaired. Which is not to say that these patients would, theoretically speaking, not be capable of directing attention to a cued location in visual space for example. Especially if the lesions are unilateral, their intact sensory cortex can be expected to show normal spatial attention effects (as well as preparatory attention effects).

1.3.2.3. Single-cell recordings in monkeys have found that cells in inferior temporal cortex, that are sensitive to a given stimulus, exhibit elevated pre-stimulus baseline firing rates when a stimulus is to be fixated in an upcoming visual search display (Chelazzi et al., 1993; Chelazzi et al., 1998). Similarly, Luck and colleagues (Luck et al., 1997) found that cells in visual cortex increase pre-stimulus baseline firing rates when the visual field locations that the cells represent are covertly attended. A very recent review by Bisley and Goldberg (2010) reports ample evidence for pre-stimulus visual-spatial attention (and action) based modulation of baseline firing-rates in monkey lateral intraparietal areas. Comparable results have been described for directing attention to non-spatial visual features such as color, orientation, and the direction of motion, in feature-specific visual cortical areas (see, for example, a review by Maunsell and Treue, 2006).

1.3.2.4. ERP studies showing evidence for pretarget location specific biasing have been reported in the previous subsection on evidence for the involvement of frontal and parietal areas in top-down attentional control. Especially the late LDAP component has been argued to represent such biasing activity. In addition to the studies reporting LDAP activity, an early study by Worden and colleagues showed evidence for increases in alpha-band (8-14 Hz) activity over occipital areas contralateral to the ignored visual-spatial location, in other words, ipsilateral to the direction of attention (Worden et al., 2000). More recently, many studies have been published showing consistent and strong evidence for spatially specific preparatory changes in pre-stimulus alpha-band oscillatory activity (Green and McDonald, 2010; Kelly et al., 2009; Rihs et al., 2007; Rihs et al., 2009; Snyder and Foxe, 2010; Thut et al., 2006; van Dijk H. et al., 2008; Yamagishi et al., 2008).

1.3.2.5. Microstimulation studies, revealing evidence for preparatory biasing, have been rather limited. The study mentioned above on stimulating monkey LIP and medial parietal areas (Thier and Andersen, 1998) is one example. Other examples from the early 2000s include primarily studies from Moore and colleagues (Moore and Armstrong, 2003; Moore and Fallah, 2004), showing modulation of spatial attention effects in visual areas such as area V4 as a result of microstimulation of retinotopically corresponding areas in the FEFs.

1.3.2.6. TMS applied to both striate and extrastriate areas has been shown to impair the detection of central and peripheral targets respectively (Kastner et al., 1998b). In addition, 20 minutes of repeated TMS pulses over parietal, but not occipital cortex, prior to a visuospatial mental imagery task had been reported to be successful in impairing behavioral performance (Aleman et al., 2002). However, clear evidence of TMS impaired visual-spatial *biasing* activity is not present in the literature. Most studies report the effect of frontal and/or parietal cortex applied TMS pulses on later visual cortex processing activity of targets, or only on behavioral performance (Brighina et al., 2002; Fierro et al., 2006; Hamidi et al., 2009; Hilgetag et al., 2001; Ruff et al., 2008; Thut et al., 2005).

1.3.3 Evidence for the involvement of subcortical structures

In addition to a substantial amount of evidence for cortical control of attention, some evidence points to additional involvement of subcortical structures. Most clearly this includes the superior colliculi for the control of visual-spatial attention, but some evidence also points to areas such as the pulvinar, the putamen, and a number of thalamic subregions.

1.3.3.1. Human brain imaging studies have mostly contrasted two active conditions (e.g., attend left versus attend right), which cancels out activity that is common to both conditions. Interestingly, the few studies that have used a more passive control condition all reported some evidence for the involvement of subcortical structures in preparatory attention such as the right and left thalamic regions, the basal ganglia, including the putamen, in attentional control (Coull et al., 2000; Gitelman et al., 1999; Kim et al., 1999; Woldorff et al., 2004; Wu et al., 2007).

1.3.3.2. Brain lesion studies from the early nineteen-eighties already reported symptoms very similar to hemispatial neglect in a patient with right medial thalamic lesions (Watson et al., 1981). A better controlled study published by Karnath and colleagues in 2002 confirmed that hemispatial neglect can indeed also be induced by subcortical lesions, in particular by lesions in the putamen and pulvinar, and to a lesser extent by lesions in the caudate nucleus (Karnath et al., 2002).

1.3.3.3. Single-cell recording data showing the involvement of subcortical brain regions in preparatory states mostly involve macaque or monkey recordings in the superior colliculus (SC). Although many studies concluded that the SC is more involved in saccade than attention related preparation, some studies have reported prestimulus activity in SC that appeared to be more attentional in nature, because it correlated with successful suppression of subsequently, reflexively, triggered saccades (Everling et al., 1998; Everling et al., 1999). Also of interest for our current focus are the findings of elevated tonic levels of activity in the locus coeruleus nucleus of the brainstem, activity which correlated with increased sustained attentiveness (e.g., Aston-Jones et al., 1999). This finding is relevant, because a state of preparatory top-down attentional control is dominated by a state of heightened cortical arousal, and the locus coeruleus is thought to serve an important role in the regulation of cortical arousal.

1.3.3.4. ERP studies can not generally provide evidence for the involvement of subcortical structures, due to their general insensitivity to activity in these structure. Activity generated in deeper brain structures is simply too weak to be picked up at the scalp, either because of too strong attenuation of the potentials by intervening tissues or because of the neurons producing a "closed" potential field. A closed field is created by neurons with more random (or circular) orientations, which results in potentials in all directions that more easily cancel each other out. EEG recording are known to be primarily sensitive to activity generated by cortical pyramidal cells. They are organized in parallel columns, so their potentials more easily summate and are then strong enough to reach the scalp.

1.3.3.5. Microstimulation of superior colliculus (SC) neurons has shown evidence favoring Everling's conclusions of a possible contribution not only to saccade generation, but also to attention shifts. For example, Muller and colleagues found that microstimulation of SC neurons enhanced visual performance by decreasing detection thresholds at the location in visual space represented by the stimulated SC site, but not at a control location in the opposite hemifield (Muller et al., 2005).

1.3.3.6. TMS evidence for the involvement of subcortical structures is not available, because TMS pulses to the scalp are necessarily fairly shallow, reaching only cortical regions in the range of about one to three centimeters underneath the coil.

1.4 Models of selective attention and top-down attentional control

In section 1.2 we have looked at the *effects* of selective attention on brain activity and behavior, whereas in section 1.3 we have focused more on evidence favoring the view that these selective attention effects on stimulus processing are brought about by prestimulus *top-down preparatory* changes in activity in certain brain areas, including a frontal-parietal network, sensory cortices, and some subcortical brain structures. In the current section, we will look at *models of selective attention*.

Over the years, numerous models have been proposed for the different aspects of both selective and top-down aspects of attention. The subsections below summarizes the most relevant models for this thesis, organized by which basic aspect of attentional control and attentional selectivity is most strongly highlighted: 1) When, in the processing hierarchy, does selection of task relevant information occur and what determines this timing of selection (section 1.4.1); 2) How is selection implemented at the neuronal / cellular level (section 1.4.2); and 3) Where in the brain (in which areas) is attentional control orchestrated; which region or regions are the main controllers (section 1.4.3)?

1.4.1 Models focusing primarily on timing and on factors influencing the latency of attentional selection

Models focusing primarily on the timing of selection of task-relevant information and the factors influencing this timing were predominantly active during the decades prior to the introduction of modern brain-imaging techniques (such as fMRI and PET). Thus these models were developed in an era when most knowledge had to be gathered through behavioral experiments or inferred from the effects of brain lesion on human and animal behavior. Such models included, for example, the "Filter Theory of Selective Attention" (Broadbent, 1958), the "Filter Attenuation Model" (Treisman, 1964), the "Late Selection Model" (Deutsch and Deutsch, 1963), the "Load Theory of Selective Attention" (Lavie, 1995), and the idea of a "Supervisory Attention System" (Norman and Shallice, 1986).

When the contribution of F.C. Donders to attention research was discussed in section 1.1.1 of this introduction, the idea of different stages of information processing was briefly introduced, including early sensory reception and perceptual identification stages, followed by a limited capacity central processing stage, and ending with decisional and execution stages. The five models discussed here all have something to say about the specific stage in which task-relevant and task-irrelevant input is identified and treated in terms of their subsequent access to selective processing modules. Some models also indicate situational factors that might play a role in the timing of selection.

To start with the earliest influential model, Broadbent's (1958) "Filter Theory of Selective Attention" proposed that selection of task-relevant information is early, before identification takes place (thus at the sensory level), and the selective input filter used for this selection has all-or-none properties; unwanted information is blocked completely. The sensory filter was proposed to be capable of being adjusted on the basis of relatively gross physical characteristics, such as spatial location or vocal pitch, to allow information from only one source of input to enter the limited capacity identification stage. Because some findings were inconsistent with this model (especially the "break-through-of-unattended" information such as your own name), an updated version was proposed by Treisman's (1964), known as the "Filter Attenuation Model". In this model, the early selective filter served to attenuate, rather than block, the signal of an unattended message. Thus, irrelevant auditory information is heard with a dull ear, not a deaf ear. In this model, stimulus properties and their relevance, stored in short-term and long-term memory, was proposed to be the causal agent for the tuning of the filter. In contrast to these "Early Selection" models, the "Late Selection" model proposed by Deutsch and Deutsch (1963), placed selection after the sensory and perceptual stages. According to this model, everything entering our senses is meaningfully processed, and therefore selection is said to operate at a later, response stage. We select information not because of limited processing capacity, but of limitations in our capacity to respond to all received input. What is of importance for a response gets selected, everything else rapidly decays.

In contrast to selection being either "early" or "late", the "Load Theory of Selective Attention" proposed by N. Lavie (1995) provided some needed flexibility: selection can be early in one situation and late in another. The crucial factor is perceptual load. All depends on the degree to which the task already exhausts available capacity. If perceptual discrimination is hard and overloads available capacity, irrelevant stimuli will not be perceived, and thus selection is early. In the earlier discussed basketball-gorilla study (Simon and Chabris, 1999), for example, the obviously present gorilla was more often missed in the condition with the harder task of counting bounces vs. aerial passes than in the much more easy condition of counting the passes within one team. However, if perceptual discrimination is easy (low processing load), attention will inevitably spill over to the processing of irrelevant stimuli, which would lead to making selection at a later stage. Later research (Lavie et al., 2004) showed that when cognitive load (e.g., working memory), rather than perceptual load, is high, the opposite pattern occurs. Increases in cognitive load (exhausting more the anterior, rather than posterior, brain areas) result in an increase, rather than a decrease, in distractor interference.

A conceptually rather different idea is the concept of a "Supervisory Attention System", introduced by Norman and Shallice (1986), a system proposed to regulate stored schemas that include information such as the importance of the stimulus and its associated response. This model has different levels that effect how much extra control over activation of schemas is needed in a given situation in order to deal with the task demands. For familiar tasks, the output from the perceptual systems automatically triggers the appropriate schemas actions without interference from the Supervisory Attention System (SAS). However, for tasks requiring planning or trouble-shooting (e.g., conflicting input/output situations), including novelty, or a high degree of difficulty, the SAS is called into operation, with the major task being that of a controller biasing activation of relevant schemas upwards and irrelevant schemas downwards. What is limited in this model is not input or output selection, but the process of biasing of the activation level of the lower level schemas, presumably during the central processing stage. In terms of the early-versus-late selection dichotomy, this model does not explicitly address the timing of selection, but based on the predictions of this model, familiar situations are more likely to result in earlier selection, whereas more challenging situations would require later selection. This would be consistent with the idea of high (frontal cortex activating) cognitive load resulting in increased distractor processing, discussed previously in the context of the "Load Theory of Selective Attention". As we will see below, the idea of a frontal SAS controller module also overlaps with the ideas of Miller & Cohen (2001), in that frontal control is not so needed in familiar situations, but is much more required in novel or challenging situations.

1.4.2 Models focusing more on neuronal mechanisms of selective attention

Whereas the previously discussed models dealt more with the timing of selection, the models discussed in this section are more concerned with the mechanisms of selection at the neuronal level. We will look more closely at models such as the "Neural Specificity Model" (Harter and Aine, 1984), the "Biased Competition Model" (Desimone and Duncan, 1995), the "Sensory Gain Control Model" (e.g., Hillyard and Mangun, 1987), the "Effective Contrast Modulation Model" (Reynolds et al., 1999), and a "Frontal Executive Control Model" (e.g., Miller and Cohen, 2001).

Based on primarily human ERP studies of selective (visual) attention, Harter and Aine (1984) proposed a model that includes a principle that is still incorporated today in many other models of selective attention, namely the idea of "neural specificity". Neural specificity refers to the idea that specific neuronal populations can code for different stimulus properties such as, for example, location, color or orientation. The resulting stimulus-feature specific patterns of activation can be modulated by attention, presumably under control of higher-order mechanisms, leading to enhanced responsiveness of neurons coding the relevant information and suppressed responsiveness of neurons coding for the irrelevant information.

This idea is clearly present in, for example, the "Sensory Gain Control Model" (e.g., Hillyard and Mangun, 1987). The neural specificity principle is basically what explains the specific pattern of visual-spatial attention effects seen on the early P1/N1 sensory ERP components generated in extrastriate cortex; generally speaking, only the amplitudes are modulated, not the distribution of potentials across the scalp. In other words, the response is neural population (generator) specific. In this model, such "sensory gain control" is thought to be a result of a filtering process in which unattended information gets blocked or suppressed and attended information gets boosted. The resulting pattern of sensory cortex ERP responses was taken as evidence for "early selection" at a low sensory level in the processing hierarchy.

The neural specificity principle, as implemented in the "Biased Competition Model" (Desimone and Duncan, 1995) and the "Effective Contrast Modulation Model" (Reynolds et al., 1999), takes a somewhat different form in that the modulatory effect has a more tonic, sustained profile, rather than a brief, transient one such as proposed by the "Sensory Gain Control" model. The core idea expressed in the "Biased Competition Model" is that enhancing effects of attention in sensory neurons can be best understood in the context of competitive interactions among neurons representing all of the stimuli present in the visual field. Such interactions can be "biased" in favor of the behaviorally relevant stimuli by both bottom-up and top-down mechanisms, including those underlying working memory in, for example, the prefrontal cortex. The activity in favored neurons will then dominate the response patterns. Reynolds' "Effective Contrast Modulation Model" (1999) can be seen as a formalization of the "Biased Competition Model", in that it is more specific about the underlying mechanisms of these attentional modulations. According to this model, all neurons have specific contrast-response functions that can be shifted to the left by attention. For example, without attention a faint stimulus can have too low contrast to elicit a neuronal response, but this same stimulus could well elicit a neuronal response when its corresponding visual field is attended, without any changes in the physical contrast aspects of the attended stimulus.

Taken together, the last three models show that there are at least two, conceptually quite different mechanisms of attentional modulation that can occur in visual sensory cortices: 1) a sensory gain mechanism that improves signal-to-noise of attended input in a transient way, and 2) a more tonic sensory biasing mechanism that incorporates the establishment and implementation of an attentional template, favoring responses of neurons to attended locations or features.

One more model can be discussed here though, a model that doesn't specify neuronal mechanisms of attentional modulation in sensory cortices, but has clearly something to say about the relationship between biasing and template matching mechanisms, particularly as implemented by higher-order control mechanisms. This is the "Frontal Executive Control" model, proposed by Miller and Cohen (2001). The core idea in this model is that the prefrontal cortex stores and maintains abstract task rules (as part of an attentional template or task set) that are then available for processing in situations that require top-down attentional (executive) control (novel and/or challenging situations). Such control is especially needed to select, presumably at a later stage of processing, a weaker relevant stimulus amongst stronger distractors. The core difference with the "Biased Competition Model" is that this model is not only more specific about the prefrontal top-down control mechanisms, but also places the attentional template more in frontal areas, rather than in sensory areas. Frontally stored attentional templates are argued to be better maintained in the face of distraction than sensory ones, which in turn more easily decay as a result of processing of intervening stimuli.

1.4.3 Models focusing primarily on network representations of selective attentional control

Finally, a number of models have focused on outlining a network of brain areas involved in top-down selective attentional control. These models include the most famous and highly influential "Attention Networks Model" (originally proposed in Posner and Petersen, 1990), the somewhat related model of two interacting frontal-parietal networks, one acting as a "Circuit Breaker System" for the other (Corbetta and Shulman, 2002), the "Triangular Model of Attention" (LaBerge, 1995), the

"Premotor Theory of Attention" (Rizzolatti et al., 1987), the "Thalamo-Cortical Gating Model" (e.g., Skinner and Yingling, 1976; Yingling and Skinner, 1976), and later updates of the last model by C. Brunia (e.g., Brunia, 1993).

According to the "Attention Networks Model" (Posner and colleagues), three interrelated mechanisms operate, semi-autonomously, in human (visual-spatial) attention: 1) orienting, 2) selection (in later updates of the model referred to as executive attention), and 3) alerting and sustaining of attention. These three attentional mechanisms are linked to specific brain networks. "Orienting" is controlled by a "Posterior Attention System" that includes the posterior parietal lobe (PPL), the superior colliculus (SC) and the lateral pulvinar nucleus (PN) of the thalamus. The PPL is proposed to control the disengagement of attention from its current location, the SC to control the movement of attention to a new location, and the PN to amplify the activity at the new location. "Selection" (executive control), involves an "Anterior Attention System" that is based in more anterior regions including the Anterior Cingulate Cortex and the Supplementary Motor Areas. This network controls target selection and recognition, and works closely together with the Posterior Attention Network. "Alerting and sustained attention" is controlled by a mostly right hemisphere system of prefrontal and parietal areas, likely under control of arousal-regulating subcortical structures, that are activated automatically by salient or novel stimuli and remain activated during preparation intervals in the absence of such external triggering stimuli.

The idea of two interacting frontal-parietal attentional control networks, proposed by Corbetta and Shulman (2002), is tightly linked to the "Attention Network Model" idea of separate networks controlling different aspects of attentional control. In Corbetta and Shulman's model, a more dorsal-medial fronto-parietal network (including the Intra-Parietal Sulcus and the Frontal-Eye-Fields) is engaged in top-down attentional preparation and goal-directed selection of task-relevant information, whereas a more ventral-lateral fronto-parietal network (including the right Temporal Parietal Junction and the right Inferior Frontal Cortex) is specialized more in the detection of salient and unexpected behaviorally relevant stimuli. This right-hemisphere ventral network works as a "Circuit Breaker" for the dorsal system, directing attention to salient events. It may well be comparable to Posner's Alerting system, conceptually in that it is about detecting rare stimuli (as one source of salience), and neuroanatomically, in that includes a mostly right-sided network of brain areas. As such, one could also argue that it provides the neural sources for the observed "break-through-of-the-unattended" problem indicated in the early nineteen-sixties, resolved theoretically in those days by the development of Treisman's "Filter Attenuation Model". Another idea from Corbetta and Shulman's model (2002) is that the dorsal system is both activated by the shift of covert visual-spatial attention as well as by actual overt shifts that are accompanied by eye movements to the to-be-attended location. An earlier "Premotor Theory of Attention" proposed by Rizzolatti and colleagues (1987) is consistent with this idea in that it proposed that spatial attention is driven by the same mechanisms responsible for movement in space.

The proposed role of the Pulvinar Nuclei in Posner's Posterior Attention Network in boosting activity at the attended location was also embraced by the "Triangular Model of Attention" proposed by LaBerge (1995), based on a review of the literature as well as results from his own study (LaBerge and Buchsbaum, 1990). Also somewhat overlapping with the previous two models is LaBerge's idea of "expressing of attention" subserved by clusters of neurons in posterior and anterior cortex that are involved in planning and executive functions. In contrast, the "control of attention" in LaBerge's model is much more a frontal cortex function, realized by clusters of neurons in dorso- and ventrolateral frontal cortex, than a function controlled by a posterior network. LaBerge's model has received a lot of critics, however, mostly related to its lack of depth and the lack of experimental data to back up the claims made by the model.

A part of LaBerge's model that should also be discussed is a mechanism that was already proposed in the much older "Thalamo-Cortical Gating Model" by Skinner and Yingling (1976); namely the idea of a subcortical switch for opening and closing of a thalamo-cortical gate. Briefly, the idea here was that different subcortical structures such as the reticular nucleus (RN) of the thalamus, the sensory-specific thalamo-cortical relay (TCR) nuclei and the brainstem reticular formation (RF) work together as a whole. They facilitate and/or inhibit each other in such a way that the relevant sensory cortex can be activated by allowing the information received by the TCR neurons to be relayed to the sensory-specific projection areas in the neocortex, whereas at the same time the relay of information to other sensory cortices can be blocked. This principle works in a bottom-up as well as in a top-down way. In a bottom-up way it is supposedly activated by the saliency or novelty of the stimulus, activating the brainstem's RF arousal regulating neurons, which influence the TCR nuclei through its connections to the RN of the thalamus. In a top-down way, the PFC provides the input to the RN and TCR nodes in the system. In both cases, the modulation of cortical activation is a more tonic one, rather than a transient one, such as proposed by the "Sensory Gain Control" model discussed earlier, and appears to be relatively aspecific for stimulus features within a sensory modality. Preparatory cortical activity in the "Thalamo-Cortical Gating Model" takes the form of sustained negative slow wave ERP potentials, also known as the Contingent Negative Variations (CNV), typically found over fronto-central and central-parietal scalp sites during preparatory intervals, and that are proposed to be linked to increases in cortical excitation levels. The extension of this model proposed by C. Brunia (1997) includes the idea that this same thalamo-cortical gating principle also works in the domain of motor preparation, giving rise to motor-related CNV components such as the Readiness Potential (RP).

1.5 Summary and conclusions

Summarizing the previous sections, we have seen that selective attention is clearly beneficial for appropriate and successful behavior; it helps us to respond faster and more accurately and to filter out distraction. We have also seen that selective attention causes increased stimulus-feature selective and sensory-input specific brain activity. This often occurs very early in time, in vision at approximately between 70-150 ms following the onset of a visual stimulus at the attended location, and in audition as early as 20 msec following the onset of a sound in an attended location or ear. Furthermore, we have learned that, in situations where we can anticipate a certain event, the effects attention has on the processing of that event is likely controlled already before the event occurs, because the same areas that show early attention effects also are often activated in advance, when the stimulus is not yet presented. The dominant view, backed up by much evidence, is that this so-called sensory cortex biasing activity is brought about by preparatory (top-down) attentional control activity in a network of frontal and parietal areas, maybe with some help from subcortical structures.

Despite these various advances and findings, there are still numerous aspects of these attentional systems and their mechanisms that we do not yet understand, and/or various inconsistencies between findings that need to be resolved. For example:

- Although the dominant view is that top-down attentional control is orchestrated by the FEF and IPS, other brain areas such as the DLPFC, the ACC/SMA region, the SPL, the posterior cingulate, and some subcortical structures have also been indicated as being involved. Accordingly, it's not at all clear what the real "control system" is, let alone what all these areas that are assumed to represent the control system are exactly doing, what their functional role is in attentional control, and why we find between-study differences in exact areas involved in top-down attentional control. Moreover, the association of activity in these areas with attentional control have been derived mainly from hemodynamically based imaging, such as fMRI and PET, neither of which has the temporal resolution to delineate the temporal cascade of the activity of these regions to accomplish attentional control or whatever other cognitive functions they may contribute to. Without understanding this temporal cascade of functional activity, our understanding of the underlying mechanisms will be intrinsically limited in depth and scope.
- Another inconsistency is that this dominant view basically argues for one, supramodal, control system -- people have found overlapping networks for covert and overt visual attention, as well as for visual, somatosensory, and auditory attention -- despite the fact that the most influential theoretical model has proposed multiple control systems (Posner's "Attention Networks Model") and despite the fact that clear differences have been found between studies that suggest otherwise. The question whether attentional control is organized by one or more networks is therefore still unresolved, and the dominant view appears oversimplified in this respect.
- In addition, whereas in Posner's model the Posterior Attention System is indicated to be most strongly linked to orienting of attention, other findings and models such as those from Norman and Shallice (1986) and Miller and Cohen (2001), for example, would argue for a much larger influential role of the frontal

cortex. Thus, theoretical models and experimental data are not very tightly linked where it concerns the dominance of frontal or parietal attention control.

- What is also not so tightly linked is evidence gathered with different recording techniques. We have already talked about the mixed findings from brain imaging data. ERP recordings also have been mixed in findings, like finding either primarily posterior activity (EDAN, LDAP) or both frontal and parietal control (ADAN and EDAN and/or LDAP). Furthermore, brain lesion data almost always pointed to the posterior parietal cortex as being crucial for the ability to shift attention in space, with very little evidence pointing to the frontal cortex. On the other hand, neuronal micro-stimulation studies clearly indicated both posterior areas (LIP, PC) and frontal areas (FEF, DLPFC) to be involved in attentional control, as well as subcortical areas (SC). So, evidence gathered from different lines of research does not reveal a clear, unambiguous, picture of top-down attentional control: we are certainly not all on the same page yet.
- With respect to the implicit idea of sequential activation of frontal-parietal and sensory cortices during preparatory delay periods, the few available ERP studies at the onset of this dissertation work that could shed light on the timing of activity in the different brain areas have been very inconsistent in their findings. Some found the EDAN component, indicating posterior onset of attentional orienting, but others lacked an EDAN and found an ADAN component, indicating frontal onset. In addition, the sources of EDAN and ADAN were at the onset of this dissertation work still unknown. The first evidence for the EDAN and LDAP being generated in posterior brain areas (most likely the ventral IPS) and the ADAN originating from frontal brain areas (most likely FEF) came from Van der Lubbe and colleagues (2006). Furthermore, most studies looked at lateralized activity only (attend-left minus attend-right contrast), which ignores the possibility of just as important non-lateralized activity. Thus, at the onset of this work, both the timing of frontal and parietal attentional control activity and the contribution of non-lateralized frontal-parietal control activity was unknown, information that is critical for the understanding of the specific functional role(s) of frontal and parietal brain areas in attentional control.
- With respect to biasing activity, the LDAP, believed to indicate sensory biasing activity, has not always been observed in the earlier ERP studies, surprisingly not even in cases where P1/N1 attention effects were reported for the expected target stimulus (e.g., Nobre et al., 2000). In other words, we don't know yet what the exact relationship is between sensory cortex activity before and after the onset of the task-relevant target stimulus.
- A final puzzle concerns the relationship between the timing of selection (early-versus-late) and the two different neuronal mechanisms hypothesized for biasing-related sensory cortex activity (sensory-gain control mechanism and an increase in baseline firing rates). It appeared that a sensory-gain mechanism would be consistent with early selection and the P1/N1 ERP effects of visual spatial attention. However, how this relates to the mechanism of a tonic, sustained bias in the form of a prestimulus baseline shift is unclear. Also, the

relationship between the two hypothesized biasing-related mechanisms and their possible effects on (the timing of) selective target processing has never been shown. There is not even evidence for two different types of biasing responses in fMRI or ERP data, consistent with these hypotheses. Therefore, how the two hypothesized biasing-related mechanisms of attentional control in sensory cortices are represented in fMRI and/or EEG/ERP data, and how they relate to subsequent timing and form of attentional selection still needs to be elucidated.

1.6 Outline of this thesis

The goal of this dissertation is ***to elucidate the functional significance of preparatory attentional control activity***. In order to find answers to this main question, we will focus on the following aspects of attentional control activity:

1. Is attentional control organized by one particular network or by multiple different networks of brain areas?
2. What is the timing of activity in the frontal and parietal areas within the frontal-parietal attentional control network during attentional orienting and what does it tell us about the function(s) these areas might play in top-down attentional control?
3. Can we find evidence for the existence of two sensory cortex biasing-related mechanisms in EEG data? If yes, how do these two mechanisms then relate to subsequent sensory cortex target processing activity and the timing of selection of task-relevant information?
4. Is attentional control primarily a function of brain areas that can be turned up or down in gain voluntarily, and can we even voluntarily change which areas are recruited? If yes, what implications does such flexible, voluntary, control has on subsequent target processing activity and behavioral performance?

A number of experimental manipulations have been used to guide the study of these aspects of top-down attentional control:

1. **Contrasts**: in the study presented in Chapter 2, the experimental and control conditions were both active (followed by a task on target), and differed only in whether attention needed to be shifted from one to the other target category on a trial-by-trial basis or shifted between blocks of trials. In Chapters 3, 4, and 5, a more passive control-cue condition was included, which was not followed by a discrimination task. Manipulation of contrasts is crucial to test the validity of interpretations of onset of attentional control activity.
2. **Attended feature or modality**: Chapter 2 involved directing attention to a non-spatial visual feature (spatial frequency patterns), whereas in Chapter 3 and 4 attention was directed covertly to a lower right or lower left lower-visual field location (spatial attention). In Chapter 5, attention was directed either to the centrally presented visual or auditory part of a multisensory audio-visual letter

object. These manipulations together test domain generality of attentional control activity.

3. **Recording techniques**: Chapter 3 included a study for which fMRI activity was available, recorded previously and using the exact same paradigm as the presented EEG/ERP study. Together, the combined data sets provided a powerful mix of high spatial and high temporal resolution data. Using the spatial information from the fMRI data in source modeling of the ERP data, we expected to be able to elucidate temporal profiles of frontal-parietal attentional control areas, which could then could provide answers to our questions of their possible separate onsets of control-related activity as well as their functional significance in top-down attention control.
4. **Task/paradigm**: In Chapter 4, three separate visual-spatial attention cueing studies were presented that differed in one key feature from each other in terms of their paradigm; manipulated factors were perceptual task difficulty (easy or hard to detect targets) and motor instructions (when to press a button to indicate having detected a target stimulus). Such a manipulation was expected to reveal knowledge about the functional significance of two EEG derived coexisting markers of visual-spatial biasing-related activity, the "BRN" ERP component and a decrease in power of alpha-band oscillatory activity.
5. **Strategies**: In Chapter 5, participants applied two, pre-experimentally trained, task strategies to deal with the exact same task demands that included cross-modal stimulus and response conflict. Based on findings of possible influence of voluntary strategies on attentional control activity in the other studies presented in this thesis, we expected that purposefully manipulating voluntary strategies would reveal more about the dynamics of attentional control activity. This study thus yielded important information for all our specific research questions.

It is the case that most of the studies presented in this thesis involve visual stimuli. Only one study includes both visual stimuli and auditory stimuli. Such a selective choice in the type of attended stimuli of course by definition limits the generality of the conclusions to other sensory domains, such as taste, touch, or smell. There are, however, enough good reasons to regard this approach nonetheless worthwhile. First of all, we humans are mostly visual beings: Laird (1985), for example, reported that adult humans learn 75% through sight, 13% through hearing, and the remaining 12% through the other senses (smell, touch, and taste). A second reason to study attention mostly in the context of vision and audition is a purely practical one. Most of our knowledge on information processing in the brain is related to the visual system, which happens to have advantages for its study. A clear second modality of high importance to study is audition and auditory attention, and this is therefore included in the cross-modal study of Chapter 5.

Final note for non-expert readers: it is safe to skip reading the detailed studies (Chapters 2-5) and jump immediately to the summary, discussion and conclusions (Chapter 6). Chapter 6 is also available in Dutch as "Samenvatting, discussie en conclusies in het Nederlands".

Chapter 2

Electrocortical correlates of control of selective attention to spatial frequency

Grent-'t-Jong, T., Böcker, K.B.E., & Kenemans, J.L. (2006). Electrocortical correlates of control of selective attention to spatial frequency. *Brain Res., 1105,* 46-60.

ABSTRACT

In the present study, we investigated control of selective attention to spatial frequency patterns, using a cueing paradigm. Subjects either used the instruction embedded in a word cue to prepare for the upcoming test stimulus (transient attention condition) or used the instruction they received before a block of trials (sustained reference condition), under completely similar stimulus conditions. The pattern of differential cue responses between these two conditions, reflecting top–down attentional control processes, was different between two groups of subjects, effectively canceling each other out. Despite comparable behavioral performance on both cues and targets, one group (n = 4) elicited a fronto-central–parietal positivity, starting 500 ms postcue over frontal and prefrontal areas, later including more central and posterior scalp sites, whereas another group (n = 8) started 400 ms postcue over central sites with a negativity, growing in strength over time and stabilizing over fronto-central sites. Only the group of eight subjects showed some evidence of occipital pretarget biasing activity. Independent of group, source modeling of the attentional control activity showed that attentional control was initiated in anterior, not posterior, parts of the brain. Furthermore, different underlying sources were found for both groups, in addition to signs of differential processing of target stimuli. Possible individual differences in attentional control ability and its relation to usage of different brain areas to deal with the task demands are discussed in more detail.

2.1 Introduction

Attention serves to select and guide processing of certain stimuli or responses over others. Setting attention selectively to specific events over others is termed "attentional control". Attentional control can be invoked by changes in task demands or (bottom-up) by salient changes in the environment and also even before the selectively attended events really occur. Top-down control mechanisms of selective attention have been studied now for more than 20 years, initially only with the use of behavioral or event-related potential (ERP) methods, but nowadays, more predominantly by using brain-imaging techniques such as functional magnetic resonance imaging (fMRI). One straightforward paradigm to study these top-down attentional control mechanisms is the so-called cueing paradigm, in which an attention-directing cue is followed by a target stimulus. This paradigm capitalizes on the possibility that attention may be set selectively by the attentional control system before the selectively attended event occurs. The brain responses recorded during the cue-target interval are thought to reflect top-down attentional control activity.

The majority of these attentional control studies have focused on the control of visual spatial attention. The global pattern of results found across brain-imaging (fMRI/PET) studies features three characteristics. First, across most studies, there seems to be a core network of cortical areas implementing attentional control, consisting of parietal areas surrounding the intra-parietal sulcus (sometimes also including more superior parietal areas), and medial-dorsal frontal premotor areas, often including the frontal eye fields (Corbetta and Shulman, 2002; Rosen et al., 1999; Shulman et al., 1999; Vandenberghe et al., 2000; Woldorff et al., 2004). Second, numerous studies also report additional involvement of dorsal and ventral lateral prefrontal areas (Giesbrecht et al., 2003; Hopfinger et al., 2001; MacDonald, III et al., 2000; Weissman et al., 2002; Weissman and Woldorff, 2005). This prefrontal involvement does not seem to depend on whether attention is directed to locations in space or to a non-spatial feature like color. Rather it may relate to demands on working memory (Corbetta et al., 2002) in relation to the anticipated presence of distractors to the target that may even elicit competing response tendencies (Weissman et al., 2002; Yamaguchi et al., 2000). Third, most models on attentional control assume that, in anticipation of the target, a "higher" controlling area "biases" the activity in target-specific areas (e.g., visual cortex), making these areas more selectively sensitive to the cued target features (Desimone, 1998; LaBerge, 2001). Indeed, some fMRI studies have revealed retinotopic overlap between areas activated by instruction cues and those activated by targets (Giesbrecht et al., 2003; Hopfinger et al., 2000). In addition, studies that have used ERPs to study visual spatial attention control mechanisms have confirmed the suggestion of a frontal-parietal network controlling baseline activity in visual cortical areas. More specifically, the better temporal resolution available with this technique revealed that activity over occipital-temporal scalp sites, specific to the location of the expected target stimulus, is initiated later in the cue-target interval than activity over frontal and parietal scalp sites (Harter and Anllo-Vento, 1991; Hopf and Mangun, 2000; Nobre et al., 2000b; Slagter et al., 2005a; Talsma et al., 2005; Yamaguchi et al., 1994b).

Far less effort has been devoted to investigating attentional control (using ERPs) in relation to visual features other than locations in space (Slagter et al., 2005b; Slagter et al., 2005a; Yamaguchi et al., 2000). In the Yamaguchi et al. (2000) study, subjects were cued to local or global features of an hierarchically structured letter. Differential effects of attending to global or local features started as early as 240 ms postcue over right temporal-parietal and left posterior temporal areas. In line with these results, an initial posterior phase of directing attention to the color of an expected target stimulus was reported in two studies by Slagter et al. (2005a,b) (with the onset around 340 ms postcue in one study and around 260 ms postcue in the other study). The pattern of results across these three studies suggests a sequence of first posterior cortical and secondly anterior cortical activity. This pattern may be consistent with the medial-dorsal core network outlined above but with a reverse temporal order of activations as compared to most of the spatial studies discussed above. In addition, it cannot be excluded that the anterior sources are contributed to by lateral, rather than medial prefrontal activation. In one of the two Slagter et al. studies, the posterior-anterior sequence was preceded by an even more posterior (as well as more lateral) activation, which could well originate in the ventral pathway. In addition, the anterior part of the sequence was accompanied by posterior activity suggestive of a biasing effect.

The present study complemented the studies reported by Slagter and colleagues in a number of ways. First, attentional control was investigated in relation to yet another non-spatial visual feature: spatial frequency. Secondly, rigorous measures were taken with respect to the reference condition. Special attempts were made to ensure that it differed from the attentional control condition only in terms of whether the cue could (and should) be used to direct attention selectively. More specifically, cues did not differ in physical aspects between conditions and were very intuitive with respect to the features of the target they were cueing for. This should have ensured quick and easy similar cue discrimination and identification in both conditions, thereby preventing differences in early cue processes that do not reflect top-down attentional control proper. Also, a choice-reaction task with respect to the cue stimuli was added, to ensure that cues would be discriminated equally in attention and reference conditions. Furthermore, test stimuli as well as the task on target test stimuli were similar between the attention and reference condition, preventing differential general strategies in preparation for the anticipated target detection task. The attention and reference condition thus only differed in terms of using the task instruction embedded in the cue on a trial-by-trial basis (leading to transient task preparation) or using a task rule instructed before the onset of a block of trials (leading to sustained task preparation). Using such a tightly controlled design, we expected to find ERP indices of attentional control mechanisms in the context of a non-spatial selective attention task. In particular, we were interested in the temporal sequence of posterior and anterior components of attentional control. Because transient and sustained selective attention have been shown to affect target processing differentially (Eimer, 1997), we also looked at the attentional modulation of the cortical response to the target stimuli, to explore whether these would differ between the two conditions as well.

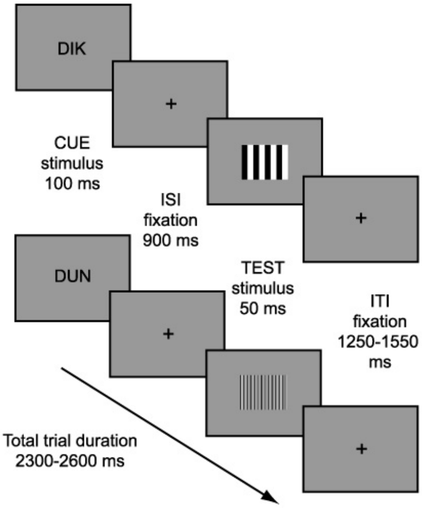


Fig.1 Layout of the trial structure and stimuli as used for both Attention and Reference condition. Word cues ("DIK" and "DUN") were presented for 100 ms and were followed 900 ms later by either a low spatial frequency (0.6 c/d) grating (see upper trial; third panel) or high spatial frequency (4.8 c/d) grating (see lower trial; third panel). Intertrial intervals (ITI) were jittered between 1250 and 1550 ms.

2.2 Methods

2.2.1 Subjects

Twelve healthy volunteers (11 females/1 male, mean age 22.4, range 19-30 years) with normal or corrected-to-normal vision agreed to participate in this study. Two subjects reported a history of concussion of the brain but claimed to be fully recovered. One subject reported epileptical seizures of closely related family members but did not suffer from epileptical seizures herself. No history of psychiatric disease was reported by any of the subjects. All of the subjects reported right-handedness. Subjects were paid € 4.50/h for their participation.

2.2.2 Stimuli and procedure

Subjects were presented with a series of event trials, each beginning with a word cue (S1) at fixation, followed by a test stimulus (S2), also at fixation (non-spatial design; see also overall trial-structure in Fig. 1). Word cues consisted of either the word DIK (Dutch for "thick"; 50% of all cues) or the word DUN (Dutch for "thin"; 50% of all cues), presented with a duration of 100 ms. Both DIK and DUN cues were presented in the letter type Lucida Console (28 pt, bold; width 1.66°, height 0.75°). Test stimuli consisted of square, black-white, square-wave gratings with a vertical orientation, presented with a duration of 50 ms. For each of the cue types, half of the target events consisted of high spatial frequency gratings (HSF; 4.8 c/d, width 6.30°, height 6.64°), and the other half of the target events were of low spatial frequency (LSF; 0.6 c/d, width 6.30°, height 6.64°). Constant Stimulus Onset Asynchronies (SOAs) of 1000 ms were used between S1 and S2 stimuli (cue-target interval). Inter-Trial Intervals (ITIs; S2 next S1) varied randomly between 1250 and 1550 ms.

All stimuli were presented against a grey background in the center of a computer screen, positioned at a distance of 138 cm from the subject's eyes. Series of event trials were presented block-wise in pseudo-random order, meaning that the order of trials within each block was corrected after randomization to ensure a maximum of two equal, subsequently presented S1-S2 pairs of stimuli. The total experiment included 8 blocks (4 Attention and 2 × 2 Reference blocks) of each 240 trials (120 S1-S2 pairs). In all blocks, subjects performed a 2-choice reaction time (RT) task to the S1 cue stimuli (first response, R1) and a Go-Nogo task to the S2 target test stimuli (second response, R2). In the Attention condition, subjects were instructed to press a left button with the left index finger at the presentation of the LSF-cue (DIK) and a right button with the right index finger in case of a HSF-cue (DUN). A subsequent target in this condition was defined as a SF pattern indicated by the cue (DIK-cue meant LSF pattern is target; DUN-cue meant HSF pattern is target). In the case of receiving the cued subsequently presented target pattern, subjects were to press the same button as used for the response to the preceding cue (same response hand for R1 and R2). Subjects were instructed to respond as rapidly and accurately as possible in all cases.

The Reference condition consisted of two separate sub-conditions; a low spatial frequency (Reference Low) and a high spatial frequency control (Reference High) condition (2 blocks each). Cues, as well as subsequently presented gratings, were identical to those used in the Attention condition, but cues were no longer indicative of the target-specific spatial frequency (i.e., non-instructive cues). In the Reference Low condition, the targets were defined (instructed before a block of trials) as the LSF-patterns (thick stripes), irrespective of whether they were preceded by the LSF-cue or the HSF-cue. Similarly, instruction for the Reference High condition defined targets as HSF-patterns (thin stripes), irrespective of which cue was presented before. Response characteristics were the same as in the Attention condition; press left after the LSF-cue and right after the HSF-cue, and use the same response hand for S1 and S2 trials. This setup ensured that, although Reference cues were non-instructive with respect to indicating the task specific spatial frequency for the immediately following test stimulus, Reference cues were still instructive (i.e., controlling) for response hand and response button. Thus, the difference between the Attention and Reference condition(s) should only concern the extraction of target-feature-specific information from the cue, and the use of this information in guiding attentional task preparation for the next test stimulus.

Finally, in all (sub)conditions, subjects received a training block of 96 trials. The order of blocks and conditions was carefully controlled, according to the rule that each block and each (sub)condition should be presented equally on each possible position in the sequence of 11 blocks (including 3 training blocks) over all subjects.

2.2.3 ERP recordings

Electroencephalographic (EEG) data were recorded from 30 tin electrodes (AFz, Fz, F3, F4, F7, F8, FC1, FC2, Cz, C3, C4, CP1, CP2, Pz, P3, P4, P5, P6, PO3, PO4, POz, Oz, O1, O2, O3, O4, T7, T8, P7, and P8, arranged according to the International 10-10 system), mounted in an elastic cap. Horizontal eye movements (HEOG) were monitored by two bipolar tin electrodes placed at the left and right outer canthi of each eye. Vertical eye movements and eye blinks (VEOG) were recorded bipolarly by two tin electrodes, one placed above and the other below the right eye. The forehead was grounded. All scalp electrodes were referred to the right mastoid during recording. Impedances of all electrodes were kept below 5 kΩ. Data acquisition was continuous, with a sampling rate of 200 Hz (each 5 ms), and band pass filtered online between 0.05 and 40 Hz. Recordings took place in an electrically shielded, sound attenuated, dimly lit, experimental chamber.

2.2.4 Behavioral analyses

Performance data were analyzed separately for the 2-choice RT task to the cue stimuli (S1-word cues) and the Go-Nogo task to the test stimuli (S2-spatial frequency target patterns). For both tasks, trials were included in the mean RT only if they were found between 200 and 700 ms poststimulus. Trials that did not match this criterion were excluded, as were error responses (wrong hand-responses to the cues), false alarms (incorrect responses to non-target spatial frequency test stimuli), missed responses, or outlier responses (trials with RTs slower than 700 ms or faster than 200 ms). Repeated measurement ANOVAs with the within-subject factors CONDITION (Attention, Reference), CUETYPE (LSF-cue, HSF-cue), or TARGETTYPE (LSF, HSF), were used to test for significant differences (alpha level 0.05). For the Reference conditions, only trials were included in which the instructed target type was congruent with the cue type.

A second analyses was performed on trials from the Reference condition to address exactly the effect of (in) congruence between instructed target type and cue type. More specifically, the Reference subconditions included both congruent trials, in which the cue type (varying from trial to trial) and the instructed target type matched, as well as incongruent trials in which they did not. These incongruent trials consisted of the HSF-cue from the Reference Low condition followed by an LSF-target and the LSF-cue from the Reference High condition followed by a HSF-target. Such incongruence has several possible undesirable consequences: the cue could induce directing attention to the cued spatial frequency, followed by redirecting to the instructed one; or a right-hand response to an LSF target, because it followed a right-hand response to an HSF cue, involves a switch in stimulus-response mapping, relative to the standard mapping maintained for the cue choice RT throughout all blocks of trials (LSF left, HSF right hand). Especially the former consequence may affect attentional control during the Reference condition, which might be expected to in turn affect the selective processing of S2 targets and non-targets. Repeated measurement ANOVAs were applied to cue and (non-)target stimuli from the Reference conditions separately, using the factors CONGRUENCY (congruent, incongruent) and CUETYPE (LSF cue, HSF cue), or TARGETTYPE (LSF target, HSF target).

2.2.5 ERP analyses

2.2.5.1 Cue-ERPs (S1-trials)

2.2.5.1.1 Trial selection and generation of ERPs

ERPs time-locked to cues (S1 stimuli) were computed separately for LSF cues and HSF cues, and separately for each condition, with an epoch length of 1100 ms, including a prestimulus baseline of 100 ms. Incongruent Reference trials were excluded from the analyses. Only cue trials with correct behavioral responses were included in the averages, and only when the reaction times were between 200 and 700 ms postcue, to ensure that the last 300 ms of the cue-target interval was not contaminated by any late response related activity, but in contrast, only reflected preparatory activity.

Trials contaminated by excessive muscle-related activity, slow drift or amplifier blocking were discarded from the analyses. Artifacts caused by eye movements or eye blinks were corrected before general artifact removal and final averaging, using the regression method developed by Gratton et al. (1983). Furthermore, average ERPs were digitally low-pass filtered with a non-causal, zero-phase shift, running average filter of 9 points, which strongly reduces frequencies at and above 22 Hz at our sampling frequency of 200 Hz. Finally, difference waves were computed between Attention cues (averaged over both cue types) and Reference cues (averaged over both cue types).

2.2.5.1.2 Statistical approach and source localization of significant effects

To detect significant differences between the Attention and Reference condition, an ROI approach was used, including 6 Regions-Of-Interest (ROIs): (1) Prefrontal ROI (F7, AFz, F8), (2) Frontal ROI (F3, Fz, F4), (3) Central ROI (C3, Cz, C4), (4) Parietal ROI (P3, Pz, P4), (5) Parietal–Occipital ROI (PO3, POz, PO4), and (6) Occipital ROI (O1, Oz, O2). For these 6 ROIs, mean ERP amplitudes were computed over 20 data points (100 ms), starting 100 ms postcue and ending at target onset (at 1000 ms postcue). Each of the 100 ms bins and ROIs was then submitted to repeated measurement ANOVAs using the within-subjects factors CONDITION (Attention versus Reference condition), CUETYPE (LSF versus HSF cues), and ELECTRODES (left, midline, right electrode). Significance was assumed for P values < 0.05 (if necessary, Greenhouse-Geisser corrected).

Furthermore, to investigate possible locations of neural generators underlying the significant differences found between the Attention and Reference condition, Grand Average difference waves were submitted to source analyses (using the software package BESA Version 2.2). Dipole fitting included one or two bilateral equivalent current dipoles with symmetrical (mirrored) location and orientation. The default four shell (head, shell, bone, csf) spherical head model was used as well as an energy constraint of 20% (as opposed to 80% for the residual variance; see Berg and Scherg, 1994). Finally, to evaluate onset locations (anterior or posterior) of attentional orienting activity, as well as changes of dipole locations and strength of individual dipoles over time, individual source parameters (dipole location and dipole moments) were estimated and submitted to repeated measurement ANOVA, separately for each contrast of interest.

2.2.5.2 ERPs to test stimuli (S2-trials)

2.2.5.2.1 Trial selection and generation of ERPs

ERPs time-locked to test stimuli (S2 stimuli) were computed, separately per condition and separately for targets and non-targets (collapsed over LSF and HSF), using an epoch length of 700 ms, including a prestimulus window of 100 ms. Trials were included in these ERP averages only if they matched the following inclusion criteria: (1) congruence between instructed target-SF and cue type, (2) preceded by correctly identified cues (correct response hand and RT between 200-700 ms postcue), (3) in the case of a target, correctly identified as such with the proper response hand and within the response window of 200-700 ms poststimulus, and (4) not contaminated by excessive muscle-related activity, slow drift or amplifier blocking. In addition, artifacts caused by eye movements or eye blinks were corrected before averaging, using the regression method developed by Gratton et al. (1983). Furthermore, selection potentials (difference waves between target and non-target ERPs) were computed within each condition separately. Finally, all computed average ERPs were digitally low-pass filtered with a non-causal, zero-phase shift, running average filter of 9 points, which strongly reduces frequencies at and above 22 Hz at our sampling frequency of 200 Hz.

2.2.5.2.2 Statistical analyses of selection potentials

Selective attention to spatial frequency (SF) patterns has been shown (Baas et al., 2002; Kenemans et al., 1993; Kenemans et al., 2002; Martinez et al., 2001a) to involve a sequence of selection potentials (FSP: frontal selection positivity; OSN: occipital selection negativity; fronto-central N2b, and parietal P3b), reflecting selective attention to the task-specific spatial frequency stimuli. In the present study, these selection potentials (reflected in ERP difference waves between targets and non-targets) were investigated both between and within the two main conditions (Attention and Reference condition). Attention effects were identified and tested for significance using windows of averaged data around the peaks of the different attention effects, and a comparable ROI approach as used in the cue-analyses: (1) FSP: frontal [F3, Fz, F4] and prefrontal [F7, AFz, F8] ROIs, (2) OSN; occipital ROI [O3, Oz, O4]; (3) N2b: frontal [F3, Fz, F4] and central [C3, Cz, C4] ROIs, and (4) P3b: parietal [P3, Pz, P4] ROI. The repeated measurement ANOVAs on these ROIs included the within-subject factors CONDITION (Attention, Reference), ATTENTION (targets, non-targets), and ELECTRODES (left, midline, right electrode).

2.3 Results

2.3.1 Behavioral results

2.3.1.1 Responses to cues

Subjects performed a two-choice reaction time task to the cues, indicating the presence of a Low Spatial Frequency (LSF) cue (word "DIK") by pressing a left button with their left index finger, and the presence of a High Spatial Frequency (HSF) cue (word "DUN") by pressing a right button with their right index finger. In addition, they were instructed to press the same button as used for the cue response to indicate that the presented test stimulus matched the cued spatial frequency (in the Attention condition) or the task-rule as instructed before the start of the run (in the Reference condition). Note that this means that during some Reference condition cue-target trials, the spatial frequency mapping was different (incongruent) for cues and targets. These incongruent trials consisted of the HSF-cue from the Reference Low condition (LSF-pattern is always the target) followed by a LSF-target, and a LSF-cue from the Reference High condition (HSF-pattern is always the target followed by a HSF-target). As we discuss in more detail in Experimental procedures, incongruent trials were excluded in the main behavioral analyses (as well as in the ERP analyses), and we included behavioral analyses to test the effect of incongruency on behavior for both cue and target responses of the Reference condition.

Table 1 summarizes all grand-average values (n=12) for mean RTs, percentage of errors or false alarms, percentage of missed trials, and percentage of outliers, separately for the different cue and target conditions. In the main analyses of the 2-choice RT task to cues, concerning the attention and congruent reference conditions, no significant differences between our two conditions were found for mean RTs and percentage of outliers. Subjects responded equally fast in the Attention condition, without differences in percentages of outliers. In contrast, however, significant main effects of CONDITION were found for percentage of errors ($F(1,11)= 6.1$, $p< 0.03$) and missed trials ($F(1,11)= 6.2$, $p< 0.03$). Compared to the Attention condition, subjects made more hand errors in the Reference condition and missed also more cue responses in the Reference condition.

Additional ANOVAs, including both congruent and incongruent cue trials from the two Reference conditions, revealed no effect of CONGRUENCY (neither on mean RTs, nor on any of the accuracy measures).

In sum, cue identification processes were more accurate in the Attention than in the Reference condition but showed no differences in speed of processing. Furthermore, incongruency in the Reference condition did not affect the subjects behavioral performance to the cues.

Table 1. Overview of behavioral performance measurements for 2-choice reaction time (RT) task to cues and Go-NoGo task to test stimuli. LSF and HSF refer to low and high spatial frequency, respectively, and incg and cong to incongruent and congruent mapping. RTs presented in ms.

CUES	Condition	Mean RT	% Outliers	% Missed	% Errors
LSF-cues	Attention	468	3.8	2.2	2.2
HSF-cues	Attention	460	4.2	1.9	2.0
LSF-cues (cong)	Reference Low	482	5.2	3.0	3.5
HSF-cues (incg)	Reference Low	470	5.2	2.4	3.1
LSF-cues (incg)	Reference High	480	5.1	4.8	2.8
HSF-cues (cong)	Reference High	472	5.7	4.2	3.6
TARGETS	**Condition**	**Mean RT**	**% Outliers**	**% Missed**	**% Errors**
LSF-targets	Attention	345	3.0	4.0	0.1
HSF-targets	Attention	355	3.1	3.3	0.2
LSF-targets (cong)	Reference Low	347	1.5	4.3	0.3
HSF-targets (incg)	Reference Low	360	1.9	3.2	0.7
HSF-targets (cong)	Reference High	344	2.3	3.0	0.5
LSF-targets (incg)	Reference High	359	2.9	5.1	1.6

2.3.1.2 Responses to targets

Repeated measurement ANOVAs on congruent LSF and HSF targets from the Attention and congruent Reference conditions did not reveal any significant differences, neither in processing speed (mean RTs), nor in accuracy (percentage of false alarms, missed targets, or outlier responses). The additional repeated measurement ANOVA for all target trials in the Reference conditions (including congruently cued and incongruently cued targets) revealed that subjects responded significantly slower to incongruently cued targets than to congruently cued targets (main effect of CONGRUENCY; F(1,11)= 18.4, p= 0.001).

Because these congruency effects on target responses may actually reflect effects of incongruence on attentional control, they justify the exclusion of incongruent trials from the final ERP analyses (described below).

2.3.2 ERP and source-modeling results

2.3.2.1 ERPs to cues

To detect significant ERP differences between the Attention and Reference condition, a Region of Interest (ROI) approach was used. More specifically, data from 10 time windows (collapsed over 100 ms of data from cue until target onset) and six different ROIs (PreFrontal, Frontal, Central, Parietal, Parietal-Occipital, and Occipital; see Experimental procedures for included electrodes) were submitted to repeated measurement ANOVAs. As can be seen in Figure 2 (upper part; thick solid ERP traces), grand average (n=12) ERP difference wave amplitudes (Attention versus Reference cues, averaged over cue type) were surprisingly small in amplitude or even absent (zero amplitude). This observation was confirmed by the statistical results from the ANOVAs applied on all ROIs and for all 100 ms bins of averaged data within the cue-target interval. No main effects of CONDITION were found in any of the windows and/or ROIs. However, interaction effects between CONDITION and CUETYPE were found between 600 and 700 ms (Prefrontal and Frontal ROIs; $F(1,11)= 8.1$, $p< 0.02$, and $F(1,11)= 8.8$, $p< 0.02$, respectively), and between 900 and 1000 ms (Central, Parietal, and Parietal-Occipital ROIs; $F(1,11)= 7.5$, $p< 0.02$, $F(1,11)= 5.4$, $p< 0.05$, and $F(1,11)= 5.6$, $p< 0.04$, respectively). In addition, CONDITION × CUETYPE × ELECTRODES interaction effects were found between 700-800 ms over Occipital sites ($F(1,11)= 3.5$, $p< 0.05$) and Parietal-Occipital sites ($F(1,11)= 5.2$, $p< 0.02$). Post hoc tests, separately per cue type for all of the CUETYPE interaction effects, however, did not reveal any significant CONDITION effects.

The lack of meaningful significant differences in the cue ERPs between the Attention and Reference condition was surprising and somewhat mysterious at first sight. Should we have included more subjects (i.e., is this due to a lack of power?), or did our Reference condition control too tightly (i.e., was this condition too similar to the Attention condition, leaving no detectable differences)? If either of these two possibilities would have been true, we should have found a too low number of subjects (out of the total group) showing a difference, or a difference between the two conditions for most of the subjects that was too small to become significant, respectively. Neither of these patterns, however, was present in the data. In contrast, careful observation of the individual ERP responses revealed that all individual subjects showed a clear difference between the Attention and Reference condition, especially in the later part of the cue-target interval (starting at approximately 400-500 ms post cue). However, scalp potential distribution patterns of this differential activity differed between two groups of subjects, effectively canceling each other out when averaged together (see both ERP traces and scalp potential distribution maps displayed in Fig. 2).

Visual inspection of the ERP difference waves for individual subjects showed that 4 subjects elicited a pattern of broad fronto-central-parietal positivity in the later part of the cue-target interval (GA4 data in Fig. 2), whereas the remaining 8 subjects elicited a pattern of broad negativity mainly over fronto-central scalp sites in the same latency windows (GA8 data in Fig. 2). This classification of the subjects into two different groups of respectively 4 and 8 subjects (based on their individual ERP profiles) was confirmed by a K-means cluster analyses (2 clusters) on individual ERP difference wave amplitude values over time (using five consecutive 100 ms bins of averaged data between 500-1000 ms postcue from four frontal ERP channels; Fz, Cz, F3, and F4). Specifically, based on the amplitude values of the five windows, all 8 GA8 subjects were categorized in one cluster for each of the 4 electrodes; and all 4 GA4 subjects were categorized in a second cluster for each of the 4 electrodes, except for two electrodes for one subject. Thus, based on the observation and classification of two different groups showing clear differences between the two conditions -- indicative of attentional control activity -- in the absence of an overall difference, we decided to investigate attentional control activity per group separately. For reasons of clarity, a direct comparison between the groups is postponed until subparagraph 2.3.2.4.

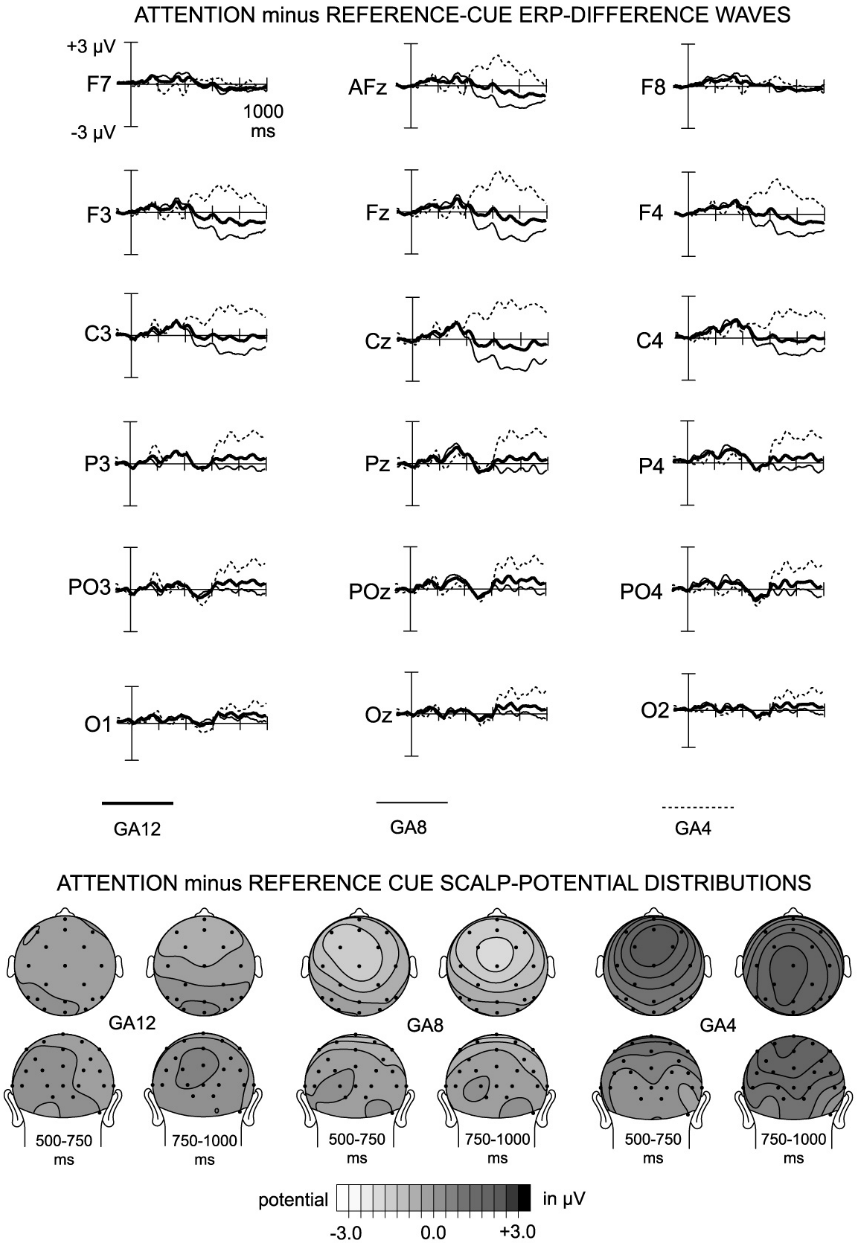


Fig. 2 Upper panel with ERP traces shows overlays of cue-ERP difference waves between Attention cues and Reference cues for all subjects (GA12: n=12), and two subgroups of subjects (GA8: n=8 and GA4: n=4), separately, on 18 channels covering almost the whole scalp. Positive polarity is plotted upwards and ERP-traces lasted until target onset. The lower panel displays scalp potential distribution maps (top-view and back-view) for two windows of averaged data (500-750 ms and 750-1000 ms postcue), for all three groups, separately as described above for the ERPs.

2.3.2.2 ERPs to cues: analyses, separately per group

As could be expected on the basis of the opposite ERP patterns, statistical analysis of both these groups of subjects (GA8 and GA4) separately revealed many significant differences between the two main conditions, in contrast to the lack of any significant effect when all subjects were taken into account (GA12). To start with the group of eight subjects (GA8), an early CONDITION × ELECTRODES interaction effect was present over central scalp sites (central ROI: C3, Cz, C4) between 100 and 200 ms ($F(1,7)= 5.8$, $p< 0.05$). Attention cues evoked a greater central positivity (maximum amplitude at Cz) in this time window than Reference cues did. Thereafter, a negative difference between the two conditions started to emerge at 400-500 ms over central sites, lasting until target onset, in the meantime spreading over frontal (700-1000 ms), prefrontal (600-1000 ms), parietal (600-700 ms), and occipital sites (900-1000 ms). At central sites, CONDITION × ELECTRODE interaction effects were found between 400-900 ms (smallest $F(1,7)= 5.2$, $p< 0.03$), as well as a main effect of CONDITION between 900 and 1000 ms ($F(1,7)= 7.7$, $p< 0.03$). Prefrontal sites started to become significant between 600 and 700 ms ($F(1,7)= 6.0$, $p< 0.02$) and stayed significant throughout the rest of the cue-target interval (smallest $F(1,7)= 6.8$, $p< 0.03$). Frontal sites started later than the prefrontal sites (700-800 ms; $F(1,7)= 8.3$, $p< 0.03$), but also remained significant until target onset (smallest $F(1,7)= 8.5$, $p< 0.03$). Furthermore, parietal sites showed significant differences between conditions (main effect of CONDITION) between 600 and 700 ms only ($F(1,7)= 5.9$, $p< 0.05$). Finally, in the last window before target onset (900-1000 ms), a CONDITION × ELECTRODE interaction effect was present over occipital sites ($F(1,7)= 5.5$, $p< 0.03$). This reflects the very small negativity visible in the GA8 difference wave (Fig. 2) at Oz and O2 at the uttermost end of the cue-locked epochs. No interaction effects including the factor CUETYPE were found in any of the windows, suggesting that attentional control processes did not differ depending on the spatial frequency (and respond hand) information embedded in the cue.

The group of four subjects (GA4) showed a different pattern, although most of the effects were again found over anterior parts of the scalp. The earliest effect for this group was found over prefrontal, frontal, and central sites between 500 and 600 ms. Prefrontal sites showed a CONDITION × CUETYPE interaction effect ($F(1,3)= 10.8$, $p< 0.05$), resulting from a larger amplitude difference between the two conditions for the HSF-cue (mean amplitude 1.0 μV) than the LSF-cue (mean amplitude 0.2 μV), and revealed a CONDITION × ELECTRODE interaction effect ($F(1,3)= 33.9$, $p< 0.02$). In the same window, the frontal sites showed a CONDITION effect ($F(1,3)= 28.2$, $p< 0.02$) and the central sites a CONDITION × ELECTRODE interaction effect ($F(1,3)= 11.5$, $p< 0.03$). The same three ROIs also revealed CONDITION × ELECTRODE interaction effects in the next window between 600 and 700 ms postcue (prefrontal ROI: $F(1,3)= 35.3$, $p< 0.001$; frontal ROI: $F(1,3)= 34.9$, $p< 0.001$; central ROI: ($F(1,3)= 10.1$, $p< 0.03$). Thereafter, only the prefrontal ROI showed significant CONDITION × ELECTRODE interaction effects (700-800: $F(1,3)= 21.8$, $p< 0.02$; 800-900 ms: $F(1,3)= 11.5$, $p< 0.05$). All

CONDITION × ELECTRODE interaction effects resulted from higher amplitude differences at the medial electrodes, compared to the lateral electrodes.

In sum, the two groups were comparable in that they had most of their effects over medial anterior scalp sites. The groups differed, however, in the polarity of the attention effects (GA8 negative, GA4 positive), in onset latency (GA8 earlier than GA4), location of onset (GA8 over central sites, GA4 most prominent over frontal and prefrontal sites, less prominent over central sites), and extent of their activity (GA8 including also some posterior channels (parietal and occipital) in some latency windows).

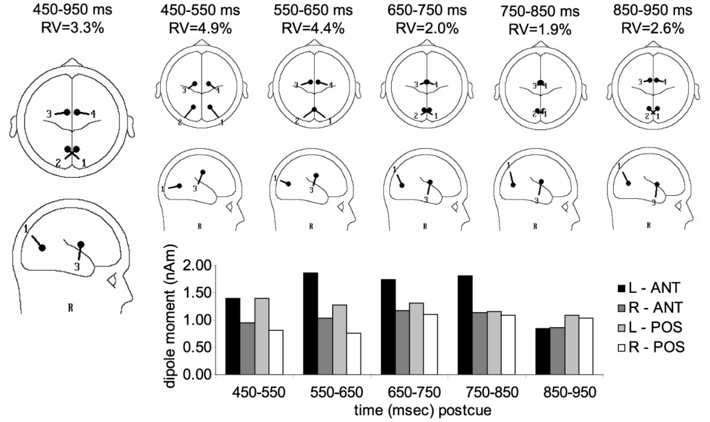
2.3.2.3 Source modeling of cue-induced attentional control activity

Assuming a frontal-parietal network of brain areas as the most likely generators, to model the grand average difference topographies for the two groups, we started with two equivalent current dipole pairs with symmetrical orientation and location. The default four shell (head, shell, bone, csf) spherical head model was used, as well as an Energy Criterion of 20% (Berg and Scherg, 1994). Figure 3 (left enlarged figures) displays the results of the best fits for the total window between 450 and 950 ms postcue (a window best overlapping with the effects for both groups), as well as for 5 subwindows of 100 ms within this window, for both groups separately. These grand-average solutions found for both datasets turned out to be very good, with all of the fits resulting in less than 5% Residual Variance (RV) in any of the windows.

As in Kenemans et al. (2002), models for the individual-subject difference topographies were also estimated. The mean RV and standard error (stderr) across individuals for the 450- to 950-ms window amounted to 9.0% and 1.4% for GA4, and 15.1% and 3.6% for GA8), respectively. Individual location coordinates were expressed as positions in a normalized head with a radius of 1. Across individuals, the mean locations of the anterior sources seemed to be more lateral and anterior for the GA4 group (X location (medial to lateral) = ±0.345, stderr 0.131; Y location (posterior to anterior) = 0.439, stderr 0.161; Z location (inferior to superior) = 0.261, stderr 0.082), than the sources found for the GA8 group (mean X = ±0.216, stderr 0.071; mean Y = 0.172, stderr 0.046 mm; mean Z = 0.239, stderr 0.070). The location of the posterior sources showed the same trend to being more lateral for the GA4 group (mean X = ±0.086, stderr 0.171; mean Y = -0.390, stderr 0.015 mm; mean Z = 0.167, stderr 0.050) than for the GA8 group (mean X = ±0.003, stderr 0.144; mean Y = -0.342, stderr 0.057; mean Z = 0.145, stderr 0.041), but this effect was less consistent throughout time (they moved to more medial and frontal locations over time).

This pattern is consistent with the grand-average results depicted in Figure 3 but was not confirmed by an ANOVA for the group effect on the individual x-locations of the anterior and posterior sources. Only an expected main effect of location in the y-direction (anterior-posterior axes) became significant, independent of group (F(1,10)= 138.3, p= 0.000); mean y-location (averaged over all 12 subjects) was 0.306, and -0.366 for anterior and posterior sources respectively).

This effect simply reflects the fact that the two dipole pairs were located in different parts of the brain, one pair located significantly more anterior than the other. The more interesting group effects were restricted to a trend for a TIME × GROUP interaction effect for y-location (p= 0.060), consistent with the observed movement of the posterior sources over time for the GA4 group.


GRAND-AVERAGE (n=8): cue-difference waves negative potentials

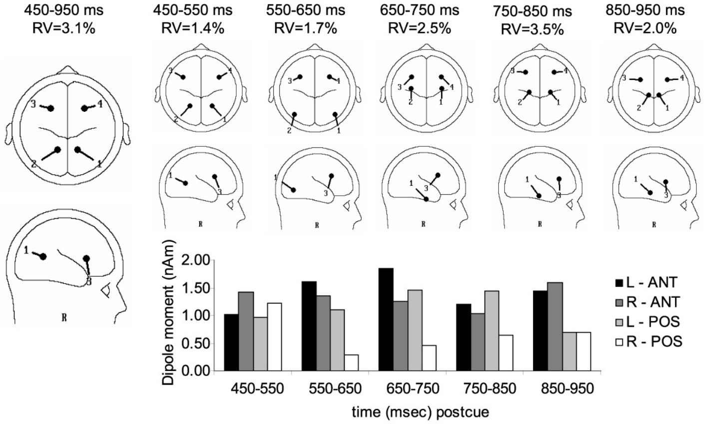

GRAND-AVERAGE (n=4): cue-difference waves positive potentials

Fig. 3 Both upper and lower panel display grand average source solutions for late cue-induced attentional control activity, separately for both subgroups of subjects (upper panel displays solutions for group of 8 subjects; lower panel for group of 4 subjects). Larger heads on the left show the solutions found for the total window of interest between 450 and 950 ms postcue, using a 2 × 2 symmetrical dipole-pair fitting procedure. The upper two rows on the right site display the solutions in 5 different time windows within the larger window displayed on the left, again for a 2 × 2 dipole-pair procedure. Bar diagrams show dipole moments for anterior and posterior dipoles as a function of time.

The relative timing of activations of anterior versus posterior sources is shown in the bar diagrams in Figure 3. Apparent differences were tested using the dipole moments for the 4-source solutions in each window (subsequent windows of 100 ms between 450 and 950 ms postcue) in a repeated measurement design including the within subject factors ANTPOS (Anterior, Posterior) and HEMISPHERE (Left, Right) and a between GROUP factor (GA8, GA4). This analysis revealed a main effect of ANTPOS between 550 and 650 ms (F(1,10)= 10.0, p= 0.010) and a main effect of HEMISPHERE (F(1,10)= 4.0, p= 0.028) in the same window, with mean dipole-moments pointing to stronger anterior activity (1.5 nAm and 0.9 nAm for anterior and posterior sources respectively, averaged over hemisphere) and stronger left hemispheric activity (1.5 nAm and 0.8 nAm for left and right hemisphere sources respectively, averaged over antpos). In addition, in the last window between 850 and 950 ms postcue, an ANTPOS × GROUP interaction effect was found (F(1,10)= 5.0, p= 0.050), with mean dipole moments showing a cross-over effect on the ANTPOS factor (0.9 nAm and 1.1 nAm for anterior and posterior sources for the GA8 group, and 1.5 nAm and 0.7 nAm for anterior and posterior sources for the GA4 group respectively, averaged over hemisphere). In conclusion, anterior activations preceded posterior ones in time for both groups. For the GA4 group, the anterior activation was relatively more persistent in the late time segment, and the posterior sources gradually shifted to anterior locations across time since the cue.

2.3.2.4 Direct comparisons between groups

Clearly different patterns were observed between groups in terms of differential ERPs as presumably related to attentional control. This prompts two question. First, were there any behavioral differences between groups suggestive of differences in the efficacy of attentional control, or in strategy? Second, did the difference between groups for the (Attention minus Reference) contrast reflect differences between groups for the Attention or for the Reference condition?

As to the first question, post hoc analyses including the factors CONDITION, CUETYPE (or TARGETTYPE), and GROUP did not reveal any significant (interactions with) GROUP effects on any of the behavioral parameters assessed in the initial analyses (as described in Section 2.2.1). As to the second question, Figure 4 shows ERPs to Attention and Reference cues separately, with GA8 and GA4 waveforms superimposed. Significant GROUP × CONDITION effects were observed from 500 to 1000 ms latency (Central and Frontal ROIs, 5.1 < F(1,10) < 25.5), from 600 to 1000 ms latency (Parietal, 5.7 < F(1,10) < 13.7), from 700 to 1000 ms latency (Parietal-Occipital, 6.6 < F(1,10) < 9.6), and from 900 to 1000 ms latency (Occipital, F(1,10)= 8.7). To meet possible concerns about Type I errors in relation to unequal sample sizes (8 versus 4), the GA8 group was split into 4 subjects with the largest late (Attention minus Reference) difference wave and 4 with the smallest one. Both subgroups were tested against the GA4 group separately, and for both the pattern outlined above was replicated, except for three individual time windows, each in a specific ROI.

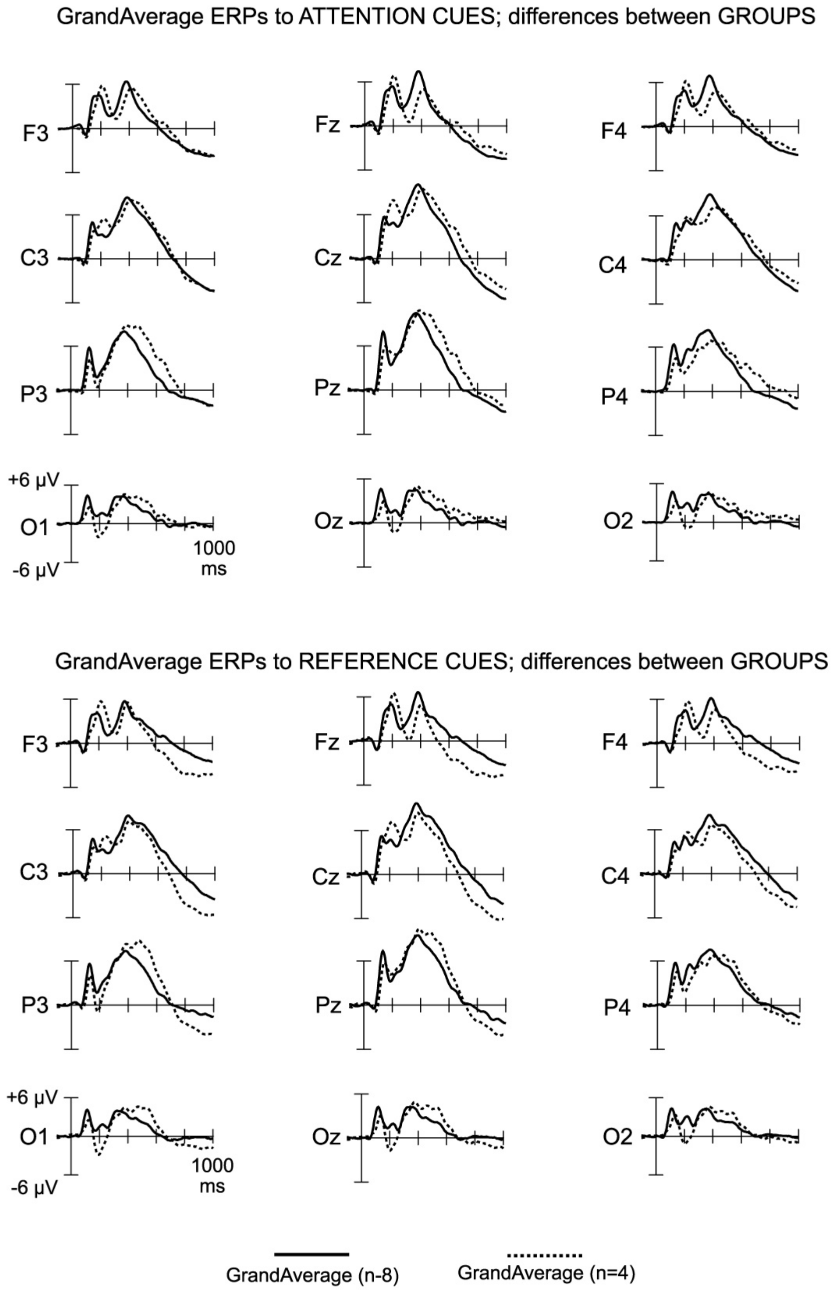


Fig. 4 Overview of group effects per condition. Upper panel: Cue-locked ERP overlays for the two groups (GA4 and GA8) for the Attention condition. Lower panel: Same for Reference condition. Positivity plotted upwards. Epochs last until S2 onset.

As can be seen in Figure 4, some differences between groups are present both for the attention and the reference condition and therefore do not contribute to the group difference in difference waves (Attention minus Reference). Other differences have different polarities across conditions, e.g., more late anterior negativity for the GA8 group in the Attention condition, but for the GA4 group in the Reference condition. This might be taken to suggest that the negative difference wave for GA8 versus the positive one for GA4 reflect differences in attentional control processes in both the Attention and the Reference condition. However, it is equally possible that the differences between groups in the two conditions reflect to a substantial extent simple main effects of GROUP. For example, suppose that the "true" attentional control values are 0 in the Reference condition for both groups, and in the Attention condition −2 and 2 for GA8 and GA4, respectively. Then an additional simple main effect of Group (e.g., 2 for GA8 versus 0 for GA4, in both conditions) would result in observed values of 0 (GA8) and 2 (GA4) in the Attention condition and of 2 (GA8) and 0 (GA4) in the Reference condition, very much like the pattern of late anterior differences depicted in Fig. 4.

In sum, we conclude that that there were clear interactions between the groups factor and CONDITION, which may reflect genuine differences in attentional control mechanisms, which were however not paralleled by differences in performance.

2.3.2.5 ERPs to test stimuli

Figure 5 shows an overview of ERP difference waves (target minus non-target selection-potentials, averaged over spatial frequency) on channels best representing the four attention effects of interest (FSP, OSN, N2b, and P3b). Selection potentials are shown separately per condition (Attention and Reference Condition), as well as for the same three Grand Averages (n= 2, n=8, and n=4) as used for the analyses of the cue ERPs. As can be seen in the figure (middle and most right ERPs), the two groups did not only show different patterns in their cue-responses, but also in their responses to test stimuli. As stated, behaviorally the two groups could not be distinguished from each other, despite these different patterns of selection potentials.

In the ERP analyses, the FSP was tested statistically on both the prefrontal ROI [F7, AFz, F8] and the frontal ROI [F3, Fz, F4] with repeated measurement ANOVAs in a factorial design (factors ATTENTION (target, non-target), CONDITION (attention, reference) and ELECTRODES), using time windows of 20 ms of averaged data between 140 and 260 ms latency. For the GA8 group, an ATTENTION × CONDITION × ELECTRODE interaction effect was found between 180-220 ms for the prefrontal ROI ($F(1,7)= 6.4$, $p< 0.04$) and frontal ROI ($F(1,7)= 7.2$, $p< 0.01$). Post hoc tests separately per condition revealed that the FSP reached significance only in the Attention condition (ATTENTION × ELECTRODE effect for prefrontal ROI, $F(1,7)= 22.9$, $p< 0.01$; ATTENTION effect for frontal ROI, $F(1,7)= 31.0$, $p< 0.01$). No significant FSP was elicited in this group for the Reference condition. Mean FSP amplitudes for this group at the prefrontal and frontal ROIs were 0.88 and 1.66 µV for the Attention condition, and 0.72 and 0.67

µV for the Reference condition. The FSP for the GA4 group was much larger in amplitude (mean amplitudes at the prefrontal and frontal ROIs 2.03 and 2.70 µV for the Attention condition and 1.18 and 1.59 µV for the Reference condition) but had also an earlier onset and a longer duration (ATTENTION × ELECTRODE interaction effect between 160-260 ms for prefrontal ROI, F(1,3)= 13.4, p< 0.04; main effect of ATTENTION between 160 and 240 ms for frontal ROI, F(1,3)= 12.3, p< 0.04). Although no interaction was found between ATTENTION and CONDITION effects for this group, ATTENTION effects were still tested separately per condition, to allow comparison with the pattern found for the GA8 group. These tests revealed that no significant FSP was elicited in the Reference condition, as was found for the GA8 group, but a significant FSP was present in the Attention condition on both prefrontal and frontal ROIs (ATTENTION × ELECTRODE effect for prefrontal ROI, F(1,3)= 10.2, p< 0.05; ATTENTION effect for frontal ROI, F(1,3)= 19.3, p< 0.03). Thus, in both conditions, an FSP was only found in the Attention condition and was significantly earlier and longer lasting for the GA4 group than the GA8 group.

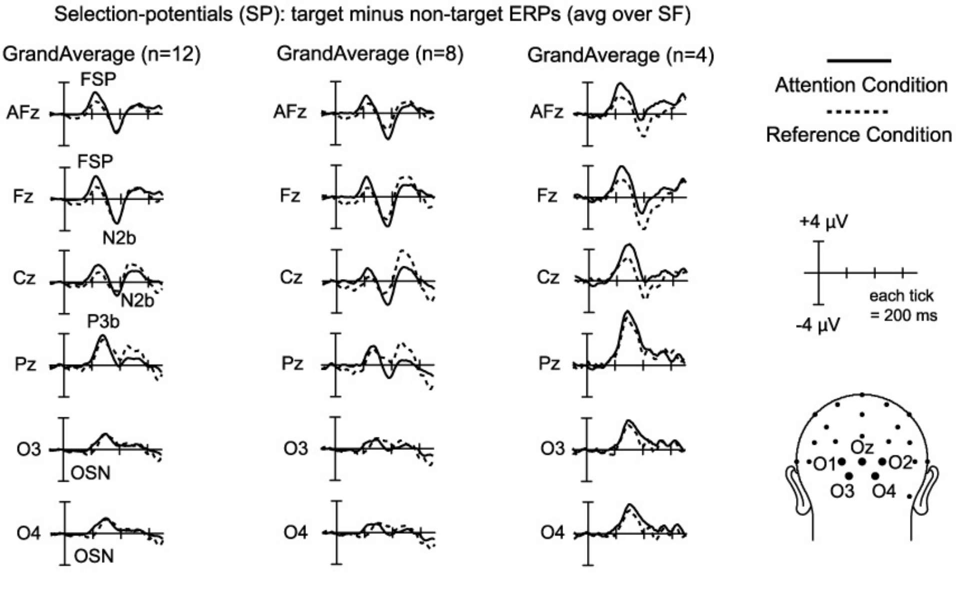


Fig. 5 Selection potentials (SPs) to test stimuli (target minus non-target ERPs; averaged over spatial frequency), displayed for all subjects (left: n=12 traces), a subgroup of eight subjects (middle: n=8 traces), and the remaining four subjects (right: n=4 traces). SPs are shown on those channels best representing the SPs of interest (FSP, OSN, N2b, and P3b).

Both groups showed little to no evidence of an OSN over occipital scalp sites. Only the GA8 group analyses exhibited a significant ATTENTION × ELECTRODE interaction effect between 180 and 220 ms (Occipital ROI; F(1,7)= 7.4, p< 0.03), but this certainly did not reflect a robust selection negativity across these electrode sites. The N2b was not significant for the GA4 group, not even in the Reference condition. The GA8 group, in contrast, exhibited an N2b in both conditions, becoming significant between 360 and 400 ms posttarget over both frontal ROI (ATTENTION effect; $F(1,7)= 5.6$, $p< 0.05$) and central ROIs (CONDITION × ATTENTION effect; $F(1,7)= 14.9$, $p< 0.01$). The P3b was clearly significant for both the GA8 and the GA4 groups but, as with the FSP difference, differed in duration and amplitude between the groups. For the GA8 group, the P3b was significant from about 200-500 ms, with an ATTENTION effect (averaged over conditions) between 200 and 300 ms ($F(1,7)= 11.0$, $p< 0.02$) and a CONDITION × ATTENTION interaction effect between 300 and 500 ms ($F(1,7)= 15.0$, $p< 0.01$). The later interaction effect was caused by a prolonged P3b for the Reference condition, compared to the Attention condition (see Fig. 5, middle panel, P3 and P4 ERPs). The GA4 group showed highly significant P3bs between 200-600 ms over parietal cortex ($F(1,3)= 312.1$, $p< 0.001$), irrespective of condition.

2.4 Discussion

In the present study, directing attention selectively on a trial-by-trial basis to one of two grating patterns (low or high spatial frequency), was compared to using selective attention in a sustained way throughout a block of trials. We expected to find the same pattern of effects as found in two earlier ERP studies (Slagter et al., 2005b; Slagter et al., 2005a) on attentional control to color (i.e., earliest effects over posterior scalp sites, followed somewhat later in time by a more anterior effect). The results from the present study, however, were not consistent with these earlier findings. Specifically, in relatively early phases of the cue-target interval, activation was significantly greater for the anterior, relative to the posterior sources.

This anterior precedence was present in two groups of subjects that were distinguished based on waveforms and scalp topographies. Both groups showed a pattern of initially mainly anterior activity, but with opposite polarity (thus canceling each other out). More specifically, the activity for the largest group of 8 subjects started as a negative difference over central sites between 400 and 500 ms, growing in strength over time, thereby stabilizing over a broader fronto-central region. In addition, this group emitted a small occipital negativity in the last 100 ms before target onset, independent of cue type. The pattern found for the remaining 4 subjects consisted of a positive difference, starting between 500 and 600 ms over frontal and prefrontal sites, growing rapidly in strength over time, thereby expanding to a broad frontocentral-parietal positivity until target onset. In contrast to the other group, this group did not show significant late posterior occipital activity.

These results are unexpected and surprising in a number of ways. First of all, comparing ERP responses to the cues in the Attention and Reference condition over all subjects surprisingly yielded no meaningful significant differences between these conditions during the entire cue-target interval. Careful inspection of the differences between conditions on the level of individual subjects, including cluster analysis, revealed that the lack of overall results was caused by opposite patterns of differential activity generated by two distinctive groups of subjects, effectively canceling each other out when taken together. Such differential effects across subsets of subjects have not been reported before for top-down control of attention. However, a growing number of studies, focusing on relations between working-memory capacity and attentional control, have described patterns of individual differences suggestive of brain networks involved in those processes (Gevins and Smith, 2000; Kane et al., 2001; Osaka et al., 2003). Both the groups of Gevins and Smith and Kane and colleagues, for example, have suggested that high-span working memory capacity subjects are better able to focus and sustain attention to task performance, than subjects with low working memory capacity. In addition, Osaka et al. (2003) showed that this better attentional control ability in high-span subjects is supported strongly by the medial frontal areas, as part of the attentional control network. Although we do not have any evidence that the present two groups of subjects can be dissociated on the basis of their working memory capacity profiles, the suggestion of better use of attentional control as based on medial frontal areas in high-span subjects, pointed out by Osaka et al., fits the strong medial frontal sustained negativity during attentional orienting as revealed in the GA8 group.

Secondly, despite their clearly different ERP-profiles on both cues and targets, the two groups could not be distinguished on the basis of their behavioral performance. This can be explained as resulting from a floor effect because obviously the task on both cues and targets was not difficult, leaving simply not enough room for improvement. On the other hand, despite the fact that no differences between the two groups were obtained for task performance on the targets, the groups did show differential selection potential profiles. The GA4 group exhibited earlier and greater FSP and P3 components under these similar performance levels. A comparable pattern was described recently by Roche et al. (2005) as exhibited by more absent-minded subjects. The authors suggested that the greater activity arises from neural substrates of response inhibition in order to accomplish the same task performance as less absent-minded participants. Thus, in other words, more absent-minded subjects have to compensate more during processing of task-relevant stimuli. In the present study, this could explain the profile found for the GA4 group target ERPs because this group did not emitted an N2b, a component known to be linked to attentional orienting (Lange et al., 1998; Wijers et al., 1989a), whereas the GA8 group showed clear N2b components. Taking into account the clear medial frontal location of the N2b component, this suggests that the GA8 group used a more efficient variant of attentional control, while the GA4 group had to rely on other, compensatory, strategies to achieve the same performance level.

Thirdly, the present results do not support an early posterior start of attentional control activity, as was reported before. In contrast, source-modeling results clearly favored an anterior start over a posterior one, and this was true for all subjects, despite all the other differences elicited by the two subgroups. Slagter et al. (2005b) suggested that the early posterior cue activity most likely reflects generic processes involved in generating the attentional set, because the observed differences in early posterior activity could be explained in terms of differences across tasks in demands placed on processes involved in updating of the attentional set. Note that this reasoning is in fact not contradicted by the present results because in the present study demands did NOT differ between conditions, as reflected in similar behavior to the cues, and posterior activity preceding anterior activity was NOT found. Thus, the present study underscores the idea of early posterior activity as resulting from differential cue translation processes.

A fourth unexpected finding is the lack of clear biasing activity in the present study. Does this mean that we cannot prepare for spatial frequency? Some evidence of at least occipital activity that could represent biasing activity was found in the last 100 ms before target onset in the GA8 group, although this was not target feature specific. If our suggestion is correct that this group exhibited better attentional control ability, then biasing obviously has to be initiated by frontal brain areas, an idea suggested before by a number of authors (LaBerge, 2002; Miller and Cohen, 2001). The fact that we did not find evidence for target-feature dependent biasing effects might simply be a result of the design features; that is, it is very likely that there was not enough time for proper biasing activity to become full blown. As was proposed by LaBerge (2001), posterior preparatory activity needs time to build up, at least a second, and in the present study the cue-target interval was exactly 1 s, and subjects also had to perform an additional choice RT task during that second. Alternatively, the task on target was too simple to require strong prebiasing occipital activity to facilitate target-selective processes later on.

Finally, behavioral results collected for both the cue discrimination task as well as for the detection task on targets, revealed no significant differences in speed of responding between conditions. The only difference that was found concerned accuracy of the cue responses and consisted of better task performance (less errors and omissions) to the cues in the transient Attention condition than in the more sustained attention Reference condition. This pattern of result cannot easily be explained by a speed-accuracy trade-off on the basis of subjects strategy differences between the transient and sustained condition. That is, if subject would have chosen a more liberal strategy in one of the two conditions, they would have responded both faster and less accurate, with the opposite pattern if their strategy would have been more conservative (Strayer and Kramer, 1994). This was clearly not the case. We suggest that a possible alternative explanation for the present findings could be that subjects allocated more attentional resources in the transient Attention condition because of the second task embedded in the Attention cues (translation in terms of target spatial frequency) that was absent in the Reference condition, as has been described for dual-task performance on integral objects before (Kramer et al., 1985).

A last point to consider concerns the contribution of motor preparation. The right hemisphere may be more specialized for low-SF processing and the left hemisphere more for high-SF processing (e.g., Yamaguchi et al., 2000). Directing attention to low versus high SFs then could involve differential processing in the right and left hemisphere, respectively. In the present study, behavioral responses to low-SF cues were always left-sided (right-hemisphere controlled) and those to high-SF cues always right-sided. This could have interacted with attentional control so as to produce right-hemisphere dominance for low-SF cues, and left-hemisphere dominance for high-SF cues, and perhaps stronger so for the Attention than for the congruent Reference condition, in which the motor requirements were identical but attention presumably did not have to be directed that much. However, the only sign of lateralized attentional control was not specific for low-versus high-SF cues but concerned stronger left-hemisphere involvement for both.

2.5 Conclusion

The present results indicate that top-down control visual attention to features other than location originates in anterior cortical areas. This anterior activity may guide more posterior areas to prepare for the upcoming stimulus event. These attentional control mechanisms, however, are not used by all subjects in the same way. The present findings suggest individual differences that not only affect the way subjects deal with the task demands, but probably also which brain areas they use for task preparation. The interaction between individual differences and attentional control abilities clearly needs further investigation.

Furthermore, the present results again bring to the fore the problem of a valid operationalization of attentional control. The fact that the earliest effects of directing of attention in both visual spatial and visual non-spatial cueing paradigms have been found in posterior areas in some studies and in anterior areas in other studies might be due to the differences in the exact processing components (and their on- and offset timing) isolated by the contrast between experimental conditions that was intended to reveal just "attentional control". For example, relatively non-specific differences in task demands between the attentional control and the reference condition may result in relatively rapid differences in posterior cortical areas. That is, differences between conditions in the amount of time needed to identify the cue and translate its meaning into an attentional set (processing steps that all seem to be more likely to activate posterior than anterior areas) could lead to earliest effects over posterior brain areas. One way to estimate and eliminate this interpretation problem is to include a behavioral discrimination tasks on the cues, as shown in the present study. Any posterior difference between the attentional control and the reference condition that remains without behavioral evidence for speed and/or accuracy differences between conditions can be considered pure attentional control activity. Anything else should perhaps be viewed more as attentional modulation due to differences in general task demands of extracting the target-specific task-relevant information from the cues, rather than as correlates of subsequently initiated top-down attentional control processes (see also van Velzen and Eimer, 2003).

Chapter 3

Timing and sequence of brain activity in top-down control of visual-spatial attention

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ABSTRACT

Recent brain imaging studies using functional magnetic resonance imaging (fMRI) have implicated a fronto-parietal network in the top-down control of attention. However, little is known about the timing and sequence of activations within this network. To investigate these timing questions, we used event-related electrical brain potentials (ERPs) and a specially designed visuo-spatial attentional cueing paradigm, applied as part of a multi-methodological approach that included a closely corresponding event-related fMRI study using an identical paradigm.

In the first 400 ms post cue, attention-directing and control cues elicited similar general cue-processing activity, corresponding to the more lateral subregions of the fronto-parietal network identified with the fMRI. Following this, the attention-directing cues elicited a sustained negative-polarity brain wave that was absent for control cues. This activity could be linked to the more medial frontal-parietal subregions similarly identified in the fMRI as specifically involved in attentional orienting. Critically, both the scalp ERPs and the fMRI-seeded source modelling for this orienting-related activity indicated an earlier onset of frontal versus parietal contribution (~400 versus ~700 ms). This was then followed (~800-900 ms) by pretarget biasing activity in region-specific visuo-sensory occipital cortex.

These results indicate an activation sequence of key components of the attentional control brain network, providing insight into their functional roles. More specifically, these results suggest that voluntary attentional orienting is initiated by medial portions of frontal cortex, which then recruit medial parietal areas. Together, these areas then implement biasing of region-specific visuo-sensory cortex to facilitate the processing of upcoming visual stimuli.

3.1 Introduction

At each and every moment of our lives we are deluged with sensory stimuli coming at us from multiple directions and through our various sensory modalities -- much more than we can fully process. The critical function of attention allows us at each moment to continuously select and extract the most important information from this flood of sensory inputs in order to provide those stimuli with fuller processing.

In the visual modality, if one covertly directs attention (i.e., without moving the eyes) to a location in the visual field, stimuli that occur in that location are discriminated or detected faster and/or better than at other locations in the visual field (Downing, 1988; Posner et al., 1980). Previous brain-imaging and electrophysiological studies (Handy et al., 2001; Heinze et al., 1994; Hopfinger et al., 2000; Mangun et al., 1998; Mangun and Hillyard, 1991; Woldorff et al., 1997) have shown that this behavioral improvement is associated with increased evoked brain-activity responses in early visual sensory areas for stimuli that occur at the attended location. In addition, the directing of visual spatial attention is associated with increased activity in a network of mainly dorsal frontal and parietal cortical brain areas (Corbetta et al., 1993; Corbetta, 1998; Corbetta and Shulman, 2002; Giesbrecht et al., 2003; Gitelman et al., 1999; Handy et al., 2001; Kastner et al., 1998a; Nobre et al., 1997; Vandenberghe et al., 2001). It is thought that this frontal-parietal network may facilitate a biasing of the system in advance towards task-relevant information by enhancing baseline activity in feature-specific visual areas that will be processing the visual stimuli (Chelazzi et al., 1993; Fu et al., 2001; Hopfinger et al., 2000; Kastner et al., 1999; Luck et al., 1997; Reynolds et al., 1999; Woldorff et al., 2004).

While previous brain imaging studies of the top-down control of visuo-spatial attention have helped delineate which brain areas exert control over stimulus processing, the various mechanisms by which this is implemented are still unclear. Apart from the finding of pre-target baseline shifts in visual areas that may facilitate upcoming target processing and that may be induced by top-down signals from the frontal-parietal control network, little is known about the timing and sequence of activations within this fronto-parietal network and their temporal relationship to such biasing. To date, no studies have addressed questions as to whether these areas act together in temporal concert, or whether there is some specific temporal sequence of the different components. Knowledge of the timing and sequence of activation within this network is important, because it could provide us with more specific information on functional specificity of these regions for attentional orienting, including which parts initiate and/or sustain the directed attention.

This incomplete understanding is partly due to the difficulty of comparing the various studies on top-down attentional control, due in part to their different methodologies and different design structures. Various event-related potential (ERP) studies, for example, have looked at top-down control of attention (Harter and Anllo-Vento, 1991; Hopf and Mangun, 2000; Nobre et al., 2000b; Slagter et al., 2005a; Yamaguchi et al., 1994b). These have typically used the event-related capabilities inherent in ERPs, applied to the cueing paradigm developed in behavioral studies in which an instructional attention-directing cue is followed by a target stimulus (Posner et al., 1980; Talsma et al., 2005). By time-locked averaging of the responses separately to the cues and to the targets, these studies have extracted the brain-wave activity triggered by each of them. However, none of these studies have reported the underlying neural sources of the cue-related ERP activity associated with attentional control, making their observations difficult to compare with hemodynamically based (i.e., blood-flow-based) functional imaging studies (e.g., those using positron emission tomography [PET] and fMRI).

On the other hand, PET and fMRI studies of attentional control have generally been structured rather differently from the ERP studies, and they have also had their limitations. First, and most critically, hemodynamically based fMRI signals are too sluggish to be able to reveal temporal aspects of the activations within the control network (e.g., timing differences between the frontal and parietal activations). Secondly, although ERP studies have generally used the relatively short cue-target intervals used in behavioral studies (~1 sec), event-related fMRI cueing studies have typically used much longer intervals (e.g., 4-10 sec or so), mainly to be able to deal with the severe overlap of the hemodynamic response signals to the cues and the targets. Using such longer cue-target intervals, however, is likely to invoke different cognitive processes or subject strategies, adding to the difficulty of comparing to the electrophysiological data. Third, the responses extracted to the attention-directing cues have often included general processing of the cue (e.g., interpreting its meaning), and thus have not exclusively reflected attentional orienting. Alternatively, the analyses have employed a contrast between directing attention toward one stimulus aspect versus toward another stimulus aspect, thereby subtracting out the overall orienting activity.

Considering the limitations from earlier fMRI studies, we previously designed a fast-rate event-related cueing fMRI study (Woldorff et al., 2004), with shorter cue-target intervals that are much more comparable to those used in ERP and behavioral studies, and with control-cue trials that controlled for general cue processing. In that study, participants received instructional cues telling them either to attend (Attend cues) covertly to a location in the lower left or lower right visual field to detect a faint grey dot that might (or might not) be presented there, or cues telling them to not orient their attention (Interpret cue) on that trial (see schematic trial structure in Fig. 1). When the target did occur on the active-attend trials (Attend-cue-plus-target trials), it could come at either 900 ms (early) or 1900 ms (late) randomly, but on some trials targets would not occur at all (Attend-cue-only trials). Participants were also instructed to delay their response to any detected target until the onset of a "report" signal toward the end of the trial, thereby helping to minimize motor-preparation activity during the cue-target interval. This hierarchical design, with Attend-cue-plus-target trials, Attend-cue-only trials, and Interpret-cue trials, allowed us to separate not only cue-related from target-related activity, but also cue-induced attentional orienting activity from more general cue-processing related activity. Results from this fMRI study showed a clear dissociation between the more lateral subregions of the fronto-parietal network, which were activated similarly by both Attend-cue and Interpret-cue trials, and the more medial frontal and parietal subregions, which were much more strongly activated by the Attend cues. This pattern of results indicated that the lateral parts of the fronto-parietal network were involved in more general aspects of cue processing, such as cue-symbol interpretation and decisional processes based on that interpretation (i.e., whether to orient), whereas the more medial fronto-parietal network activity was more specifically related to the process of orienting of visual spatial attention.

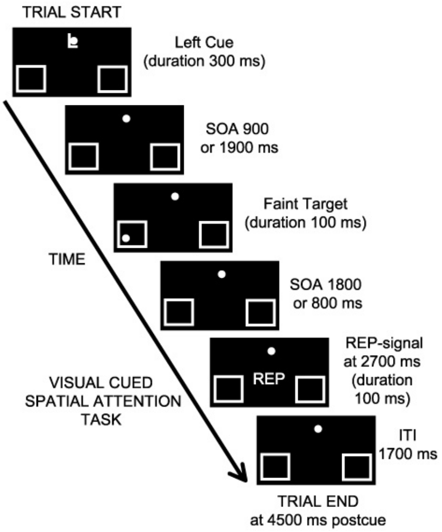

Fig. 1. Example of an attend-left-cue-plus target trial.

A centrally presented left cue (letter L) instructed the participant to covertly attend to the lower left visual field box to detect an upcoming faint dot target that might be presented there. A target could appear either early or late (50% probability) following the cue, and at the valid location only. An end-of-trial (REP-signal) presented at 2700 ms post-cue signalled the participant to press a button to report if they had seen a target. Other trial types included attend-right-cue-plus-target, attend-left-cue-only (no target), attend-right-cue-only (no target), interpret-cue (also no target) and nostim trials (no cue nor target).

As noted above, the fMRI results alone cannot delineate the temporal characteristics of these activations. In the present study, we therefore recorded EEG and event-related potentials (ERPs) using the exact same paradigm. Although fMRI and EEG recording techniques measure different aspects of brain activity -- and thus can not be expected to have a perfect one-to-one relationship -- various studies have shown close correlation between intracranially recorded local field potentials, including event-related time-extended local field potentials, and the event-related BOLD response used in fMRI (e.g., Logothetis et al., 2001). Moreover, numerous studies have also shown considerable correlation between scalp-recorded ERP components and fMRI BOLD responses, supporting the usefulness of comparing and combining the results gathered with the two methods. For example, successful attempts to combine ERP data with results from a comparable fMRI dataset have been described for early sensory ERP components, such as the visual P1 and N1 components (Di Russo et al., 2003; Mangun et al., 1998; Martinez et al., 2001b; Noesselt et al., 2002), the face-specific N170 wave (Henson et al., 2003; Horovitz et al., 2004), the frontal target-detection-related N2 (Iidaka et al., 2006; Swainson et al., 2003), the error-related negativity associated with incorrect target-detection responses (Mathalon et al., 2003; Ullsperger and von Cramon, 2001), the auditory sensory N1 component, and the mismatch negativity (MMN) elicited by auditory deviants in a a stream of repeated stimuli (Doeller et al., 2003; Liebenthal et al., 2003; Mulert et al., 2005; Opitz et al., 1999; Opitz et al., 2002), as well as for later ERP components, such as the target-detection-related P3b (Bledowski et al., 2004a; Bledowski et al., 2004b; Ford et al., 2004; Menon et al., 1997; Rowan et al., 2004), the language-related N400 component (Matsumoto et al., 2005; Rossell et al., 2003), and slow anticipation-related potentials, such as the CNV (Hinterberger et al., 2003; Nagai et al., 2004). Accordingly, we hypothesized that the present combined ERP-fMRI source modelling approach would help elucidate the timing and sequence of activations within the fronto-parietal network, knowledge that would be useful in understanding the roles of these areas in attention control.

3.2 Methods

3.2.1 Participants

Sixteen healthy participants with normal or corrected-to-normal vision gave written informed consent, approved by the Duke University Institutional Review Board, and participated in this experiment. Thirteen participants (4 females / 9 males, mean age 22, range 18-41, all right handed) were included in the final analyses. Data from the other three participants were excluded from the analysis, for a number of reasons: either because more than 30% of their trials were contaminated with eye blinks, eye movements, muscle activity, or excessive drift of scalp potentials. Participants were either paid $10/hour or received university class credits for their participation.

3.2.2 Stimuli and procedure

As in our corresponding previous fMRI study (Woldorff et al., 2004), subjects were presented with a series of event trials, each beginning with an instructional letter cue at fixation (center of the screen), which was sometimes followed by a target. These instructional cues were either the letter L, R, or P, which instructed the subject either to covertly attend to a boxed location in the lower left ("L") or lower right ("R") visual field (3 deg lateral and 3 deg below horizontal meridian), or to not orient attention away from fixation ("P"). Targets consisted of a small faint grey dot presented on a black background in the lower visual field box on the cued side, which could occur in one or the other of two possible corners (closest or farthest away from fixation). The dots differed in level of greyness ranging from 10 to 19% grey (0% being equal to the completely black background), thus ranging in difficulty from trial to trial. For each target-containing trial, the target was chosen randomly from across this range to ensure that the subjects could not predict the difficulty level and therefore needed to prepare maximally on each trial. Subjects received at least two practice runs of 64 trials each (total run time of 4 min 48 sec per run) to familiarize themselves with the task, followed by 12-14 runs (also 64 trials each) during which EEGs were recorded.

The trial structure used in this ERP study was identical to the one used in the earlier analogous fMRI study (Woldorff et al., 2004). In Attend trials ("L" or "R" cues), subjects were instructed to determine whether a faint visual target (dot) occurred at the cued location. In Attend-cue-plus-target trials (25% of all trials), a target would occur either early (50% probability) at 900 ms, or late (50% probability) at 1900 ms after cue onset. In Attend-cue-only trials (25% of all trials), no target was presented. On Interpret-cue trials ("P" cues; 25% of all trials) it was also the case that no faint dot target would occur. In addition, as in the fMRI study, 25% so-called "NoStim" trials (periods of fixation only) were included, randomized with the other trials types, to facilitate the removal of response overlap from previous trials (Buckner, 1998; Burock et al., 1998; Busse and Woldorff, 2003).

In all trial types (other than NoStims), an End-Of-Trial (EOT) stimulus (the letters REP) was presented below fixation and midway between the upper part of the outlined target-boxes, 2700 ms after trial onset (see Fig. 1). For Attend-cue trials ("L" and "R" cues), participants were instructed to press a button with their right index finger if they had observed a target in that trial. In order to minimize motor preparation within the cue-target interval on these trials, participants were explicitly instructed not to prepare for any response during the cue-target interval and to wait until the onset of the REP/EOT signal to respond. The EOT stimulus was, however, presented in all cue-only and cue-plus-target trials (including interpret-trials) in order to equate sensory processing demands across conditions. Finally, trial onset-to-onset intervals were 4500 ms for all possible trial types, including NoStims.

3.2.3 ERP recordings

The EEG was recorded from 64 electrodes mounted in a custom-designed electrocap (Electro-Cap International, Inc.) and referenced to the right mastoid during recording. The 64 channels of these caps were equally spaced across the cap and covered the whole head from above the eyebrows to lower aspects of the occipital lobule (slightly past the inion). In previous work (Woldorff et al., 1997; Woldorff et al., 2002), further refined and confirmed here, the average electrode positions of this cap were determined in Talairach space, facilitating source modelling using and/or comparing with the activations from the fMRI study.

Eye blinks and eye movements were monitored by horizontal and vertical EOG electrodes for later rejection of trials with such artifacts. Vertical eye movements and eye blinks were detected by two electrodes placed below the orbital ridge of each eye, each referenced to the electrodes above the eye. In addition, subjects were encouraged to delay their blinks to the window following the report signal (2700 ms after the cue). Horizontal eye movements were monitored by two electrodes placed at the outer canthi of the eyes. Subjects were trained before starting the experiment on being able to covertly move their attention without moving their eyes. In addition, during recordings of their EEG data, eye movements were monitored by using a video zoom lens camera. Analyses of the horizontal EOG data indicated that the number of rejected trials due to eye movements was very low in all conditions (~3%), and did not significantly differ between the different conditions. Electrode impedances were maintained below 2 kΩ for the mastoids, below 10 kΩ for the facial electrodes, and below 5 kΩ for all remaining electrodes. All 64 EEG channels were continuously recorded with a band pass filter of 0.01 to 100 Hz and a gain of 1000 (SynAmps amplifiers from Neuroscan, Inc.) and digitized with a sampling rate of 500 Hz. Recordings took place in an electrically shielded, sound attenuated, dimly lit experimental chamber.

3.2.4 Behavioral recordings and analyses

Behavioral data of each participant was monitored and analyzed online using a custom in-house behavioral monitoring and analysis system. The output of these analyses was used during the experiment to continuously titrate task-difficulty (by adjusting perceptual contrast of the targets) to keep the participant's behavior at the same level (~80% hit rate) as in our earlier corresponding fMRI study. Target reaction times were also monitored online, although due to the delayed response, such reaction time information mainly just indicated that the participant was reasonably engaged in the task.

3.2.5 ERP analyses

3.2.5.1 Cue-ERPs (S1-trials)

ERPs time-locked to the cues were averaged separately for Interpret-cue and Attend-cue trials with an epoch-length of 3200 ms (including 400 ms pre-stimulus baseline). To increase signal-to-noise ratios for the cue response, Cue-only trials were averaged together with Cue-followed-by-late-target trials, separately for Right and Left cues as well as collapsed over both Right and Left cues. Trials in which targets followed cue presentation early (i.e, at 900 ms) were not included in these response averages, so that the whole 1900 ms cue-target interval could be analyzed for cue-triggered activity. It should be noted, however, that the possibility of having a target occur at both early and late time periods ensured that participants needed to process the cue and orient their attention as soon as possible and to maintain that attention throughout the interval. Artifact rejection was performed off-line before averaging by discarding epochs of the EEG that were contaminated by eye movements, eye blinks, excessive muscle-related potentials, drifts or amplifier blocking when these artifacts were detected in the window of interest (-200 until 1900 ms post-cue). Furthermore, the averages were digitally low-pass filtered with a non-causal, zero-phase running average filter of 9 points, which strongly reduces frequencies at and above 56 Hz at our sampling frequency of 500 Hz. Additional processing of the data included re-referencing of all channels to the algebraic mean of the two mastoid electrodes. To assess orienting-specific activity, difference-waves were computed for "Attend-minus-Interpret-cues" (Attend-cue-only trials plus Attend-Cue-followed-by-late-target trials minus Interpret-cue trials). Finally, spherical-spline-interpolated topographic voltage maps

(Perrin et al., 1989) of grand-averaged ERP-traces were derived for a series of consecutive time windows to visualize scalp distribution changes over time.

3.2.5.2 ERPs to target stimuli (S2-trials)

ERP averages time-locked to Early and Late targets were calculated, separately for the Right and Left target conditions, along with analogous averages for Early and Late "No-Target" trials (analogous points in time on cue-only trails where a target could be expected but did not appear). These "No-Target" trials were subsequently subtracted from the corresponding Target trials in order to correct for overlap of cue-induced attentional-orienting activity (Woldorff, 1993), which was expected to differ for Left and Right cues. If not corrected for, the differential overlap for left and right cues would have confounded the target-induced ERP responses. In order to increase signal-to-noise ratios, following the correction for possible overlap, Early- and Late-target ERPs were averaged together, separately for Right and Left-targets. Finally, these overlap-corrected Right(Early+Late)-target-evoked ERPs were subtracted from overlap-corrected Left(Early+Late)-target-evoked ERPs to extract target-induced contralaterality of response to assess any cue-induced pre-target priming or biasing.

3.2.5.3 Statistical analyses

Statistical analysis for the cue-induced attentional-orienting effects (frontal-parietal network activity) included within-subject repeated-measures analyses of variance (ANOVAs) of the ERP amplitudes using the factor ATTENTION (with Attend-Right and Attend-Left cue-only and cue-followed-by-late-target trials collapsed together versus Interpret-cue trials). Separate ANOVAs were computed for data averaged over all sample points within sequential windows of 100 ms postcue and separately for each electrode site. To correct for multiple comparisons, the significance-level threshold (p-value) was lowered to 0.01 (corresponding F(1,12)= 9.30).

Biasing activity over occipital cortex that was evoked by the cues (i.e., the late cue-induced biasing related negativity or BRN - see Results) was tested with repeated-measures ANOVAs on mean ERP amplitudes in 200 ms windows between 500-1900 ms postcue, using the factors CUETYPE (Left cues versus Right cues) and HEMI (Left versus Right hemisphere). Electrodes included in these ANOVAs were restricted to 4 left parietal-occipital sites (O1, O3, TO1, and P3) and 4 right parietal-occipital sites (O2, O4, TO2, and P4). Because of the very specific planned comparisons used in this analysis, significance was assumed for F(1,12) values larger than 4.7, corresponding to a p-value of 0.05. The same electrode sites were used in repeated measures ANOVAs of the ERP amplitudes of the Right and Left-target trials (collapsed across Early and Late), to test contralaterality of the N1-component between 175-225 ms post targets (factors included TARGETTYPE [Right versus Left targets] and HEMI [Left versus Right hemisphere].

3.2.5.4 ERP source analysis

Finally, ERP source analysis -- using the BESA software (Brain Electrical Source Analysis, Version 2.2M) -- was performed on the Attend-minus-Interpret cue Grand-Average (n=13) difference waves, which predominantly reflects attentional-orienting processes. In this study, we were able to constrain the number and possible source locations by using activated loci found within the identical contrast in our previous corresponding fMRI study. The fMRI locations were seeded (fed) into BESA, using their Talairach locations and the Talairach-to-Spherical transformation parameters from our cap electrodes. The default four-shell, spherical, head model was used in modelling of those sources. Allowing orientation to vary, the seeded sources were fit in the latency window of statistically significant attentional-orienting activity, keeping their locations constrained to the fMRI-locations. An Energy-Criterion of 50% was used, which helps minimize interactions during the iterative modelling procedure between sources that are relatively close to one another. The source analyses were applied to both the grand-average and the single-subject attentional orienting difference wave activity. The single-subject analyses were accompanied by statistical analyses of the dipole strengths over time (averaged over 100 ms of data and over hemisphere) of the estimated source activity.

Lastly, early cue-induced attentional orienting activity (500-600 ms) was modelled in a second "free-source-modelling" approach, using a single symmetrical dipole-pair, optimizing both location and orientation. Final solutions of this analysis were transformed back into Talairach space and compared to the fMRI-seeded sources.

3.3 Results

3.3.1 Frontal-Parietal Attentional Control Network Activity

Cue-triggered ERP waveforms time-locked separately to the Attend-cues (collapsed across Attend Left and Attend Right) and to the Interpret Cues are shown in Fig. 2a. For approximately the first 400 ms, traces for the Attention-directing cues and Interpret cues closely overlapped everywhere across the scalp, beginning to differentiate only after that time. By 600 ms, activation for Interpret cues had essentially returned to baseline, whereas that evoked by Attend cues during the rest of the cue-target interval took the form of a sustained, mostly bilateral negativity over frontal, central, and parietal scalp sites. In the difference waves, computed for the contrast between those Attend and Interpret cues (Fig. 2b), the early evoked responses to both cue types (until 400 ms) thus essentially subtracted out, leaving the strong fronto-central-parietal negativity in the rest of the cue-target interval. Because these attentional-orienting activations over frontal, central, and parietal sites did not show any consistent contralaterality relative to the direction of attention, these data were collapsed across this dimension, and we have focused on the attend cue versus the interpret cue trials over these sites.

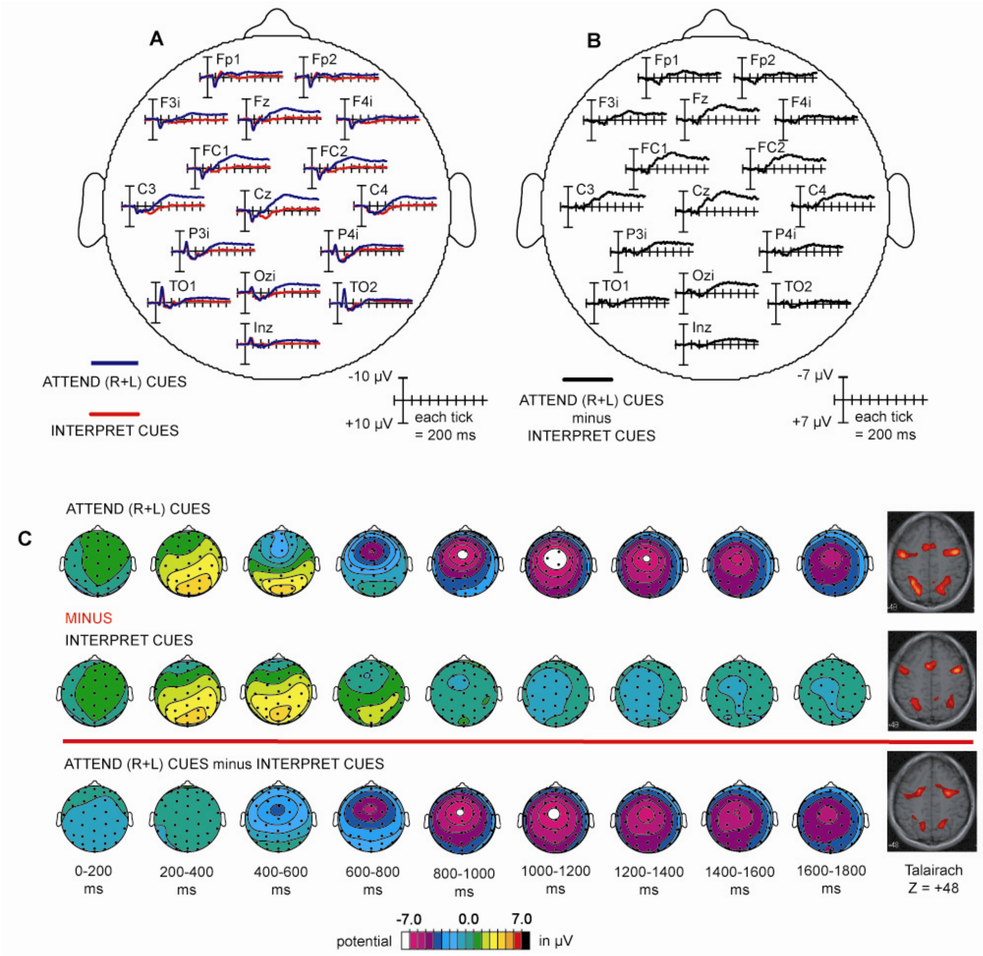

Fig. 2 Cue-related ERP and fMRI responses.
(A) Grand-average (n=13) ERP traces from 16 channels across the scalp of the cue-triggered responses to Attend-cue trials (collapsed over Right and Left, and also across cue-only and cue-plus-late-target trials), overlaid on the cue responses for Interpret-cue trials, starting 200 ms before cue-onset until 1900 ms (which was the onset of a target on trials with a late target). (B) Grand-Average (n=13) ERP difference-waves of the Attend-cue responses minus Interpret-cue responses from 2a. (C) ERP topographic maps of these scalp-potential distributions, averaged over 200 ms windows, for Attend Cues, Interpret Cues, and their difference waves, starting at the onset of the cues and ending 100 ms before the time of a possible late target presentation. On the right are shown the corresponding fMRI activations (at Talairach height of z=+48) for the Attend-cue-only and Interpret-cue responses (corrected for overlap), and for the Attend-cue-vs-Interpret-cue contrasts observed in the identical conditions in the corresponding Woldorff et al. (2004) fMRI study.

The scalp potential topographic distribution maps across time for Attend cues, Interpret cues, and their difference waves are shown in Figure 2c. These maps, like the traces in Figure 2a and 2b, show clearly that the early ERP activity triggered by

Attend cues and Interpret cues was very similar out to 400 ms postcue. Thus, in the subtraction of these responses (bottom row, Fig. 2c), this early activity subtracts away, leaving the sustained negativity beginning at around 400 ms and lasting throughout the entire cue-target interval. These maps also show that the early part of the attentional-orienting negativity (from around 400 to 800 ms postcue) had a clear frontal distribution, whereas over the next few hundred milliseconds the activity progressively spread posteriorly over the scalp to include central and parietal sites.

Repeated measurement ANOVAs, applied to the ERP response amplitudes and computed for consecutive windows of 100 ms across the cue-target interval, confirmed the presence of a fronto-central-parietal sustained negativity by showing highly significant main effects of ATTENTION (Attend versus Interpret cues) between 400-1900 ms postcue on all electrodes covering medial frontal, central, and parietal scalp sites (F(1,12) values between 9.3-78.1, all p's < 0.01). However, the point in time after 400 ms in which this differential activity became significant varied systematically between frontal, central, and parietal scalp locations. More specifically, these attentional-orienting effects were significant over frontal sites beginning in the 400-500 ms window postcue (F(1,12) values between 9.4-22.4, all p's < 0.01), over central sites beginning at 500-600 ms postcue (F(1,12) values between 9.3-36.0, all p's < 0.01), and over parietal sites beginning at 700-800 ms postcue (F(1,12) values between 9.9-27.1, all p's < 0.01). At around 1000-1200 ms, the scalp distribution of the attentional-orienting difference wave activity stabilized, with no apparent further change in distribution across the rest of the cue-target interval out to 1900 ms. This result suggests that the sustained activity for the rest of the cue-target interval stayed relatively constant in source configuration.

Due to the identical trial structures and contrasts between the ERP and fMRI studies, these ERP results could be mapped to the activations seen in the corresponding conditions in the fMRI study (see right panels in Fig. 2c). Therefore, the early ERP activity (prior to 400 ms) that was similarly triggered by both the Interpret cues and Attend cues presumably corresponds to the general cue-processing related activity in such areas as visual sensory cortex and the lateral fronto-parietal network that were similarly activated for the Interpret and Attend cues in the fMRI (Fig. 2c; upper two rows). Similarly, the later sustained negativity remaining after the subtraction (Fig. 2c; lowest row) that continued only for the Attend cues would be expected to reflect the orienting-specific activation and to correspond to the more medial fronto-parietal areas activated mainly by the Attend cues in the fMRI data (Fig. 2c; bottom row, right).

With respect to the timing of activation within the different components of the orienting-specific activity in the medial fronto-parietal network, a number of observations pointed to an onset delay in the parietal areas compared to the frontal areas. First, as noted above, the attentional-orienting negativity, seen in the ERPs and the topographic plots, began with a more frontal distribution and started to become significant a couple of hundred milliseconds earlier over frontal scalp sites than over parietal ones. The earlier onset over frontal sites relative to more posterior locations can be seen particularly clearly in overlays of the ERP traces from the frontal and parietal scalp sites directly above the medial fronto-parietal network areas identified in the fMRI using the identical contrast, with onsets at about 400 and 650 ms, respectively (see Fig. 3a, top, left and right hemisphere scalp ERPs).

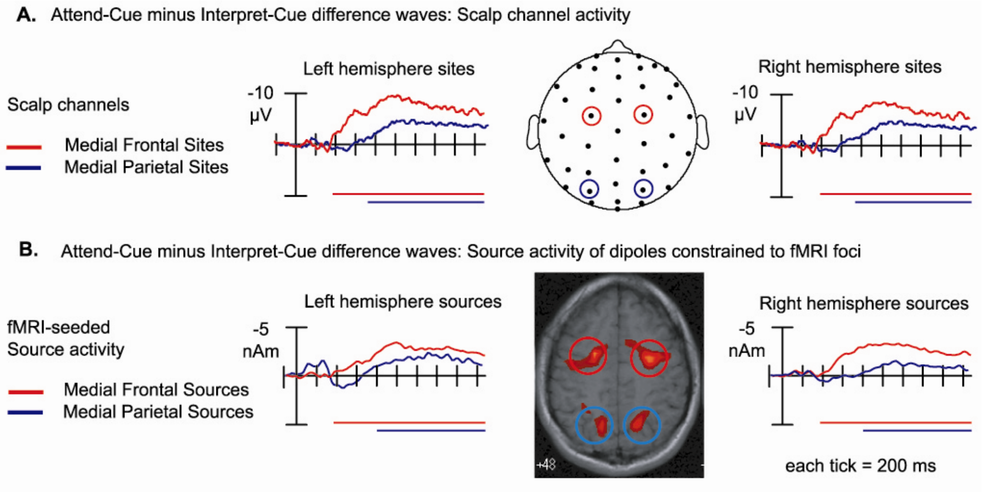

Fig. 3 Timing of activity in the medial frontal-parietal attentional orienting network.
(A) Grand-Average (n=13) ERP traces selected from channels located at scalp sites above the medial frontal and medial parietal fMRI loci for the difference waves derived from the contrast of Attend-cues versus Interpret-cues. The traces for the frontal and parietal scalp are overlaid, showing the temporal delay for the parietal relative to the frontal scalp sites. Below the ERP traces, the horizontal colored bars indicate the windows in which the attentional orienting activity across participants was significant at the frontal channels (red) and at the parietal channels (blue). (B) Overlay of the estimated source activity waveforms for the medial frontal and medial parietal sources, separately for each hemisphere, also showing the relative delay for the parietal relative to the frontal sources. These source activity waveforms resulted from source modelling of the Grand-Average (n=13) ERP-difference-wave for Attend cues versus Interpret cues, using dipoles constrained to fMRI centroids of activity (obtained from Woldorff et. al 2004). Below the source activity waveforms, the horizontal colored bars represent the windows in which the attentional orienting activity across participants was significant for the estimated frontal source (red) and parietal source (blue) activity waveforms.

Secondly, as another way to approach relative timing issues, as well as to additionally relate these ERP activations to neuroanatomical brain regions, ERP source analysis was applied to the attentional-orienting difference wave activity using information from the analogous fMRI contrast. More specifically, two pairs of dipoles were placed at the centroids of the medial frontal and medial parietal fMRI activations, and iterative best fit modelling of their orientation was applied to the ERP distributions (fMRI centroid locations are circled in Fig. 3b, middle panel, fMRI overlays; fMRI activation coordinates in Talairach space (Talairach and Tournoux, 1988) were x=-23, y=-4, z=46 [left middle frontal cortex, BA6], x=27, y=1, z=46 [right middle frontal cortex, BA6], x=-18, y=-58, z=48 [left parietal (precuneus), BA7], and x=20, y=-57, z=50 [right parietal (precuneus), BA7]). Using such an fMRI-seeded source modelling approach with location-constrained dipole sources, 95% of the variance for the observed ERP distribution was explained (Residual Variance [RV] = 5%) across the entire time period of the attentional orienting effects (400-1900 ms postcue). Moreover, as was the case with the overlays of the frontal versus parietal scalp ERP traces, overlays of the analogous estimated source activity waveforms from these medial frontal and parietal sources (Fig. 3b; left and right hemisphere source waveforms) also argue that the onset of the sustained frontal activity leads that of the sustained parietal activity by several hundred milliseconds, with onsets at around 400 ms and 700 ms, respectively. Note that there also appeared to be small earlier negative and positive blips in the left parietal source waveforms, present even before 400 ms. Several considerations suggest that these are likely to be artifactual, however. First, these small blips possibly derive from the fact that, although the model dipole parameters were optimized for the window in which there was significant attentional orienting activity on the scalp (400-1900 ms), the source-modelling program automatically returns an estimate of source activity amplitude for all sources and for all time points. Thus, the estimates of source amplitude activity at the other time points outside the window (e.g., before 400 msec) are likely not very accurate. Second, there were no significant differences between Attend cues and Interpret cues (attentional orienting activity represented by the difference-wave activity) over parietal scalp sites before 700 ms. And finally, in the statistical analysis of the source waveforms estimated for the individual subjects (see below), the parietal sources were not significantly active before 800 ms. Thus, these small early blips in the left parietal source waveforms are unlikely to reflect reliable activity effects.

Thirdly, source analyses were performed on the orienting-related difference wave activity of individual subjects, and the resultant estimated dipole strengths statistically analyzed across subjects. Residual variance found for the individual-subject dipole solutions, using fMRI-seeded sources with optimized best-fitting orientations, ranged from 3.8% to 20.3%, calculated across the entire window of 400-1900 ms. Consistent with the observed onset timing differences seen in the grand averages, the statistical analyses of the estimated dipole strengths revealed significant activity in the two medial frontal sources starting at 400 ms (400-1900 ms: t-values between -3.2 and -7.1, all p's < 0.01), whereas the later-onsetting sustained medial parietal sources started to become significantly activated several hundred milliseconds later (800-1900 ms, t-values between -2.7 and -3.9, all p's < 0.03). Again, note that these results argue against a possible early parietal onset, even though the estimated grand-average left parietal source waveform might suggest a small amount of earlier transient parietal activity (Schicke et al., 2006).

Fourth, if our conclusion of an earlier onset for frontal versus parietal activation is correct, then the frontal sources alone should provide a fairly good fit in a time window in which the frontal sources are active but the parietal ones are not yet active. Thus, to test this prediction, source analyses were applied to the window of 500-600 ms using just the two medial frontal sources alone, and, indeed, these explained 96% of the distribution (RV=4%). In contrast, the two parietal sources alone had a considerably worse fit (RV=13%) in this time period, leading to fits with orientations pointing very anteriorly.

Fifth, to provide additional converging evidence, we performed a "free fit" (i.e., both locations and orientations allowed to vary, not imposing any locational constraints from the fMRI results) of a bilaterally symmetric dipole pair during the 500-600 ms latency range. Again, consistent with our hypothesis that the frontal sources initiated the attentional orienting during this latency range, this free fit resulted in source locations in medial frontal cortex (RV=4.4%), with Talairach coordinates fairly close to the medial frontal fMRI-derived sources (within 1 cm in all dimensions; left frontal [x=-18, y=-8, z=45] and right frontal cortex [x=18, y=-8, z=45]).

Sixth, additional analyses were performed to assess the relative contribution of the frontal and parietal sources over the entire time period of significant sustained activity. More specifically, the explained variance was computed in successive 200-ms windows between 500-1900 ms using the frontal sources alone, the parietal sources alone, and the frontal and parietal sources combined (Fig. 4a). In the early windows, the figure reaffirms what was noted above, namely that in the early windows, the two medial frontal sources alone provided a particularly good fit by themselves, and considerably better than the parietal locations alone. Thereafter, the frontal sources by themselves still explained most of the variance in the data, but substantially less well. This could be taken as further evidence that additional sources had become active in the later part of the window. Indeed, as shown in Figure 4a, adding the two parietal sources in the later part of the time window substantially improved the fit, whereas they added little in the earlier time range.

And lastly, we performed an additional analysis of the attentional orienting activity to provide further evidence for the addition of two parietal sources that onset later, in contrast to a model in which the two frontal sources alone are possibly just growing in strength over time. In this analysis, shown in Figure 4b, the ERP distribution in the 500-600 ms range, a period in which only the frontal sources are presumably active, was subtracted from a later distribution between 1100-1200 ms, by which time our model suggests that the parietal sources have become substantially activated. If only a single frontal dipole pair were being activated in both time windows, differing solely in strength of activation between these two windows, this subtraction should reveal differential activity that also had a clearly frontal distribution, similar to that in the 500-600 ms window. If, however, the later window includes substantial activity that is generated by additional, more posterior areas, then this subtraction should yield a residual activation with a more posterior distribution on the scalp. This latter possibility is exactly the pattern that is shown in Figure 4b, in which this subtraction leaves a distribution with a posterior parietal maximum. In addition, we note that scaling of the early frontal-only activity (i.e. the distribution at 500-600 ms) up to the level of the later frontal-level amplitude (by multiplying all potentials across the scalp with the factor representing the ratio between the maximum amplitude in the two windows) before performing the subtraction from the later window revealed a very similar pattern, still leaving a clearly posterior residual distribution (see Fig. 4c). This analysis thus provides additional evidence of the existence of posterior sources that onset later in time, and which would thus be well-explained as deriving from the parietal activations seen in the fMRI in the identical contrast.

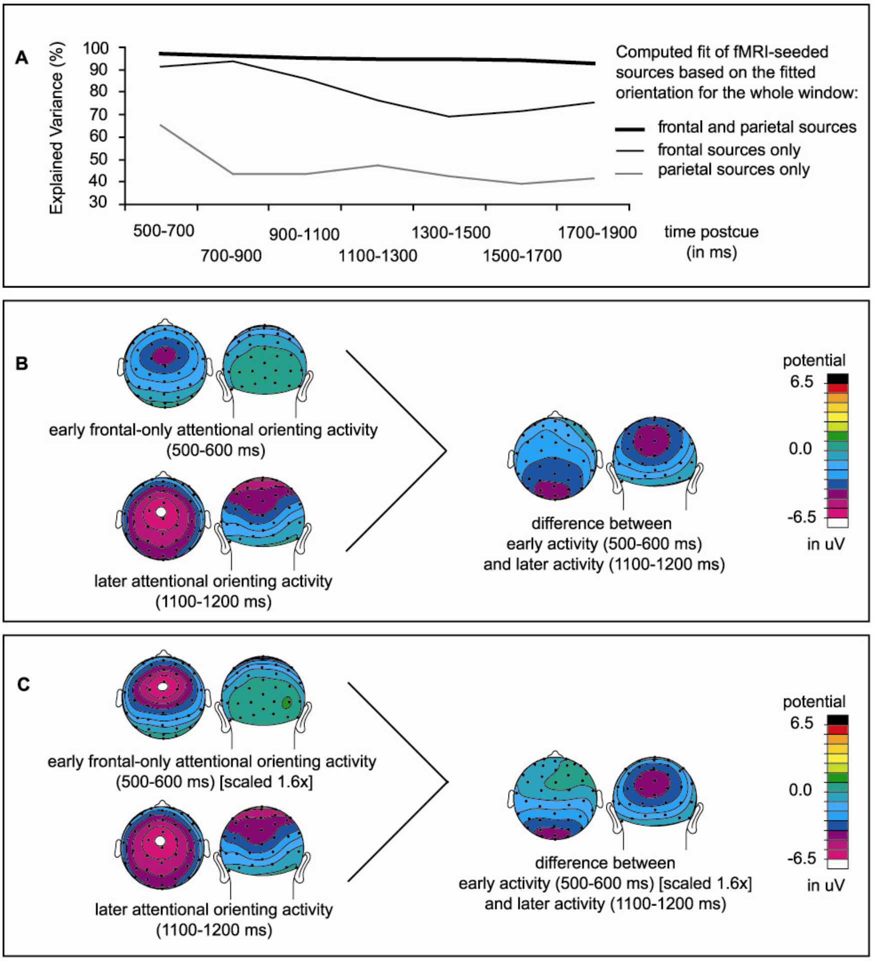

Fig. 4 Evidence for robustness of the 4-source fronto-parietal model of the attentional orienting activity. (A) Explained variance of three different source configurations (frontal only, parietal only, and both frontal and parietal) for the Grand-Average difference wave activity between Attend and Interpret cue responses. These were computed across time (500-1900 ms) in windows of 200 ms, using the locations and orientations of the sources from the initial fMRI-seeded solution. (B) Topographic distributions of the Grand-Average attentional orienting activity at 500-600 ms (upper left map), at 1100-1200 ms (lower left map), and the calculated difference between these. (C) same as (B) but with the attentional orienting activity between 500-600 ms being scaled in amplitude first, before the subtraction from the activity during the distribution at later window (i.e., amplitudes at all channels from the early activity were first multiplied by a factor 1.6 to approximately match the amplitude of the midfrontal activity in the later window between 1100-1200 ms).

3.3.2 Pre-Target Biasing Activity in Occipital Cortex

Figure 5 shows back-view topographic plots of the activity triggered by the attention-directing cues in 200 ms bins between 500-1900 ms postcue, separately for Attend-Left and Attend-Right cues (two top rows). These figures suggest a relative enhancement of negative-wave activity over posterior scalp sites contralateral to the direction of attention, in addition to the large, superior, bilateral negativity reaching back to parietal sites that was discussed above. The contralaterality of this effect (relative to the direction of attention) over occipital sites can be seen more clearly in the difference waves computed from ERP responses to the "*Attend-Left minus Attend-Right cues*" (bottom row), with this subtraction resulting in a relative negativity over right occipital cortex and a corresponding relative positivity over left occipital cortex. This Attend-Left-minus-Attend-Right cue-related difference activity of contralateral negativity and ipsilateral positivity with respect to the direction of attention can be seen to begin at around 700 ms postcue and to build up in strength over time until the onset time of the possible late target presentation. At the right side of the figure (far right column), topographic plots of a corresponding subtraction of the responses to "*Left and Right targets*" are displayed for the N1-latency window (corrected for overlap from preceding cue-related activity - see Methods). Comparing, it can be seen that the pattern of differential hemispheric activity elicited by the cues prior to target occurrence

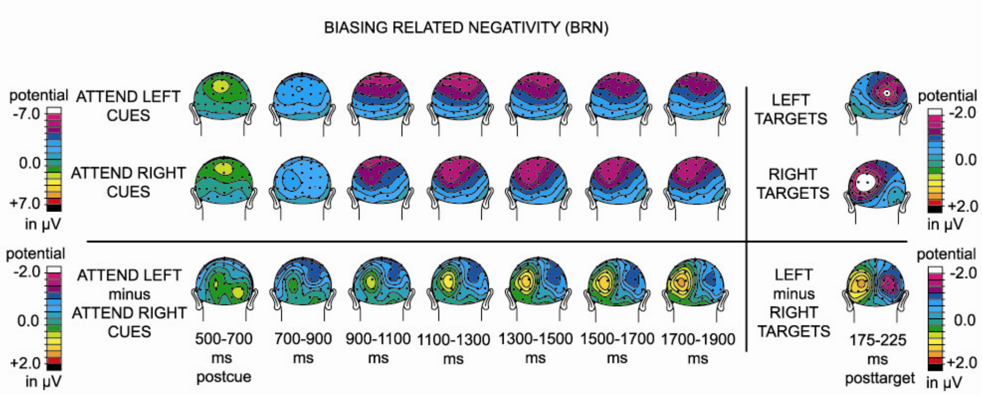

Fig. 5 Pretarget visual cortex biasing.
Grand-Average (n=13) ERP topographic plots (back view) time-locked to Attend-Left cues (upper left row), Attend-Right cues (middle left row), and the difference between Attend-Left and Attend-Right cues (lower left row), averaged over 200 ms bins, starting 500 ms post-cue until the onset of late targets at 1900 ms. Far right column shows N1-latency back-view topographic plots for Left-Targets (upper right), Right-Targets (middle right), and the Left-minus-Right Target difference-wave (lower right). All Target-related activity is corrected for overlap from previous cue activity. Note the build up and then maintenance of the biasing-related negativity (BRN) over occipital cortex contralateral to the direction of attention, and the similarity of the scalp-potential distributions of this biasing-related activity to the N1 differences between Left and Right targets.

showed a strikingly similar scalp-potential distribution to the post-target N1 difference-wave activity. In that this activity matches the idea of preparatory activity building up over time in areas later recruited for target processing, we have termed this activity a Biasing-Related-Negativity (BRN).

The contralaterality of the BRN with respect to the cued site was confirmed by significant interactions between CUETYPE (Attend-Left vs. Attend-Right cues) x HEMI (left vs. right hemisphere) beginning at 900 ms postcue and increasing across the rest of the cue-orienting period (tested in 200 ms bins of averaged data: F(1,12) values between 8.2-16.2, p's between 0.015-0.000) over left and right parietal-occipital scalp-sites (left: O1,O3,TO1,P3; right: O2,O4,TO2,P4). Between 700-900 ms, the effect was only tending toward significance (F(1,12)= 3.8, p= 0.07). Finally, the same parietal-occipital scalp sites predictably revealed highly significant contralateral N1 components to the unilateral targets (TARGETTYPE x HEMI effect between 175-225 ms; F(1,12)= 37.58, p= 0.001).

3.4 Discussion

The present study combines high-density ERP recordings with fast-rate event-related fMRI data from an identical visual attentional cueing paradigm to investigate the executive control of visual spatial attention. Previous neuroimaging studies and neuropsychological lesion data had implicated a fronto-parietal network in attentional control. In addition, in our own recent fMRI attentional cueing study (Woldorff et al., 2004), we had used both attention-directing cues and "cue-interpretation" control trials, revealing a functional distinction between the lateral parts of this network as being more involved in general cue processing (such as cue interpretation) and the more medial parts as being more specific for the orienting of visual spatial attention. In addition, the fMRI data included a reflection of pre-target biasing of the specific visual cortical areas that would be processing the upcoming target. The temporal characteristics of the activations of the various parts of this system, however, had not previously been established.

Here we report results from the ERP study, using an identical cueing paradigm as in the fMRI experiment, to help delineate the timing and sequence of the various parts of this network. To begin with, the temporal resolution of the ERPs, in conjunction with the paradigm structure, provided a clear temporal separation between general cue processing activity, manifested as similar ERP activity until 400 ms postcue for the attention-directing cues and interpret cues, and subsequent activity that was more specific for attentional orienting, identified as a sustained broad negativity elicited by only the attention-directing cues and lasting throughout the cue-target interval. In addition, due to the identical nature of the contrasts to those in the fMRI, the early general cue-processing ERP activity was associable with the more lateral subregions of the fronto-parietal network as delineated by the fMRI, whereas the later sustained negative wave activity for the attention-directing cues could be linked to the more medial regions of this network.

Moreover, this combined data set allowed further parcellation of the sustained negative-wave brain activity that was specific for the attention-directing cues. In particular, both ERP traces at the scalp and multiple fMRI-constrained source modelling analysis of the ERP data indicated that the initial part of this sustained orienting-specific activity beginning at 400 ms postcue derived primarily from the frontal cortical regions, with the parietal contribution not beginning till after 700 ms. Additional analyses further indicated that this was then followed (beginning ~800-900 ms postcue) by pre-target biasing activity of specific visual cortical areas contralateral to the direction of attention in preparation for the to-be-detected visual target stimulus.

3.4.1 Combining fMRI and ERP results

The above model assumes that there are electrophysiological correlates of both the frontal and the parietal areas activated in the fMRI. This assumption, however, has some associated caveats. Not only do these two methods measure different aspects of brain activity (electrical field potentials during neuronal activity versus metabolic demands resulting from that neuronal activity), it is also the case that some fMRI sources might not be seen in the ERPs (e.g., activity in deep brain structures) and, conversely, there can be circumstances in which there may not be any fMRI correlate(s) for certain ERP components of interest (e.g., very transient effects). In the current study, however, we believe that we have been able to create enough likely overlap between the possible results from the two studies to justify a direct comparison with fMRI-seeded source-modelling. First, we have minimized many of the possible sources of differences between the two data sets by using exactly the same event-related paradigm and the same timing parameters in the two studies, and then mapping the activations derived from identical contrasts in the two studies. Secondly, the focus of this fMRI-ERP mapping is on the sustained attention-related preparatory activity. The electrical correlates of this activity are both quite large in amplitude (~7 µV) and sustained for many hundreds of milliseconds, making it that much more likely to correlate well with increased metabolic demands (and thus fMRI BOLD activity) in the areas of the brain involved in these processes (as compared with electrical activations of a much smaller amplitude or transient nature). It would actually be very surprising if these very large and very sustained electrical activations on the scalp did not result in an increase in metabolic and thus fMRI activity somewhere in the brain. Moreover, since there was such a robust set of fMRI activations (i.e., the frontal and parietal activations) isolated during the identical paradigm using an identical contrast, these fMRI activations seem likely to be the generating sources. Lastly, a recent study has reported that such tonic, sustained activity reflected by slow cortical potentials recorded at the scalp do seem to correlate well with an increase in metabolic demands reflected by fMRI BOLD responses (Schicke et al., 2006). Thus, although there are not always one-to-one relationships between ERP and fMRI activity, in certain circumstances (such as the current one), relating the two data sets together seems quite reasonable.

Nonetheless, despite the likely correspondence between the two activation data sets, we have tested this assumption in several other ways, including an additional one not described in the Results section. In particular, another possible source-configuration model to consider for the attentional orienting activity is that, despite there being both a frontal and a parietal pair of potential sources implicated by the identical contrast in the fMRI, perhaps there is only contribution from one frontal source-pair that shifts its orientation posteriorly across time, with no contribution from the parietal pair. This, however, does not seem to be very likely. To begin with, although the frontal pair alone explains the early activity extremely well (RV < 4%), an analysis in the later windows of a model using the frontal sources alone (even allowed to optimally shift in orientation) yielded a fit of the data that was considerably worse than the frontal-parietal model described above (e.g,, from 1100-1300 ms the RV was ~12% versus 4%, particularly fitting poorly toward the back of the head). Even more importantly, a frontal dipole source pair that has shifted its orientation posteriorly would be expected to give rise to the spatial peak on the scalp being shifted posteriorly (indeed, our additional modelling simulations confirm this would be the case). In contrast, as can be seen in Figure 2c, this is not the observed pattern in the data; rather, the spatial peak is quite stationary during the entire interval. In actuality, the changes in the distribution of the attentional activity over time appears much more like one in which the frontal negativity expanded over time to cover the more posterior areas, while still maintaining similar, or even greater, activation over frontal areas, rather than the shifting of one activation pattern backward. This is, as we’ve noted, very well-fit by the two-pair (frontal and parietal) model, with the parietal pair coming on line later than the frontal. Moreover, the shifting backward of the orientations of ERP sources, in and of itself, does not seem very physiologically plausible, unless, possibly, if it were due to the coming on line later of differential portions within the frontal sources that happened to point backward. However, considering the clear and robust posterior (i.e., parietal activations) seen in the fMRI in an identical contrast, this shifting hypothesis, besides not fitting the distributions nearly as well, seems considerably less plausible than our model in which the source of this increased posterior distribution at longer latencies is actually due to the later onsetting of contribution from these parietal sources.

In addition, various consideration and analyses of the ERP data alone, without explicitly incorporating the fMRI, also implicate a match to the frontal and parietal fMRI activations and indicate the onset of frontal activity prior to a parietal source. For example, Figure 2C shows a clear distribution spread over time, including first only frontal cortical areas, and then later over central and then parietal areas. In addition, the ERP-overlays of frontal and parietal recording sites (see Fig. 3a) also clearly points to parietal activity starting later than frontal activity. And last but not least, Figure 4b and 4c show that when the early activity (either unscaled or scaled) is subtracted from the later activity on the scalp, it leaves a clearly posterior distribution of activity over parietal scalp. All these aspects of the ERP data alone are very suggestive of an onset at 400 ms of orienting-related activity in frontal cortex, followed a couple hundred milliseconds later by the addition of parietal cortex activity, thus convergent with the ERP source analyses seeded by the corresponding fMRI activity foci.

Thus, these data suggest the following sequence of functional activity in response to an attention-directing instructional cue. In the first 400 ms or so, there is general cue processing, including cue sensory processing (in visual cortex) and cue-symbol interpretation (largely in lateral regions of the frontal-parietal network). Following this, the more medial portions of the frontal cortex initiate activity that is more specific for the orienting of attention, followed a couple hundred milliseconds later by medial parietal activity. This relative latency delay for the medial parietal onset suggests that the initial medial frontal activity for attentional-orienting may signal the parietal regions to activate, which may in turn help facilitate the specific biasing activity in visual cortex shortly later. Lastly, our data also suggest that, after activation initiation, both the frontal and parietal regions appear to maintain sustained levels of activity throughout the cue-target interval. This suggests that, although there is different onset timing of their sustained activations, they presumably continue to work together in maintaining the appropriate attentional state and resulting target-location specific preparation of relevant sensory areas.

3.4.2 Functional Interpretation of the Results

The critical role of the frontal cortex in the activation pattern in the present study fits well with some current theories concerning its central role in executive and attentional control. In particular, frontal regions have been described as being involved in keeping track of task goals and actively maintaining a representation of stimulus-response associations (Miller and Cohen, 2001), as controlling temporal aspects of the task such as linking past sensory memory traces to future (motor) goals (Fuster, 2001), as expressing preparation based on hypotheses about most likely identity and task-relevancy of the upcoming stimulus (Ivry and Knight, 2002), as regulating selection of task relevant stimuli and responses in an attentional set (Corbetta and Shulman, 2002), or as controlling sustained attentional activity in posterior areas that express attentional preparation (LaBerge, 2002). In the context of these theoretical notions, the present study suggests that the more lateral frontal regions, along with the lateral parietal ones, play a role in more general executive processes. In the present study, these more general executive processes would appear to include activity in the first 400 ms following a symbolic instructional cue that involve interpreting the meaning of that cue and making a decision as to what to do based on that interpretation, processes that needed to be performed for both the Attend cues and the Interpret cues. Moreover, the present results suggest that, following these initial more general executive processes, the medial frontal regions then specifically perform regulatory control over the initiation and maintenance of the orienting of visual spatial attention. The temporal characteristics of the activations suggest that this attentional control may involve these medial frontal regions signalling or triggering the parietal regions to activate and facilitate the biasing of visual areas to enhance the processing of expected goal-relevant stimuli. Thus, this activation pattern for the medial frontal regions supports its role in keeping track of task goals and in controlling and coordinating other regions to help accomplish those goals (Miller and Cohen, 2001) .

Functional interpretation of parietal contribution to attentional control has been described as generating spatial stimulus-response mapping patterns of activity (Colby and Goldberg, 1999), as establishing or switching of task-sets or spatial stimulus-response associations (Corbetta and Shulman, 2002; Yantis et al., 2002), as rehearsal of to-be-memorized locations in spatial working memory (Postle et al., 2004), and as modulating neuronal activity in visual cortex (Han et al., 2004). As noted above, the present results suggest that the more lateral parietal subregions, together with the lateral frontal subregions, are involved in the initial cue-symbol interpretation and decisional processes based on that interpretation. Following these processes, and then following activation of the medial frontal regions that appear to initiate the specific orienting of attention toward the task-relevant stimuli / location, the medial parietal regions would appear to activate and stay active throughout the cue-target period, presumably participating in the triggering of the biasing seen shortly after in visual sensory cortex.

With respect to the baseline shift in target-location specific visual areas, this mechanism of attentional control over expected upcoming processing of task-relevant stimuli has been linked in previous ERP studies to a component termed a "Late-Directing-Attention-Positivity (LDAP)" (Harter and Anllo-Vento, 1991; Hopf and Mangun, 2000; Yamaguchi et al., 1994a). Our observed biasing related activity over occipital-parietal cortex (what we are terming biasing-related negativity, or BRN), however, differs from these previous findings in a number of ways. First, the present BRN consists of a pattern of increased negativity over occipital areas contralateral to the direction of attention, whereas the LDAP shows the opposite pattern (contralateral positivity). Secondly, the BRN steadily increased in strength across the cue-target interval and continued its highest level of activity until target onset, and even beyond, when no target is presented (i.e., in cue-only trials). The LDAP, in contrast, has been described by some researchers to be more transient in nature and to disappear shortly before target onset (Hopf and Mangun, 2000). Thirdly, an LDAP-like component has been found to be elicited not only during visual-spatial orienting, but also when attention is directed towards expected locations of auditory or tactile events (Eimer et al., 2002), suggesting that such a component may reflect a more general aspect of target preparation than just the modulation of baseline activity in target-location specific visual-sensory areas. Finally, the onset latencies of the BRN observed here and previously reported LDAP responses differ in that the BRN appears to need more time to build-up than the LDAP. Even though the target could appear moderately early (900 ms), the BRN did not begin till around 800-900 ms post-cue, whereas the LDAP has mostly been observed in an earlier window between approximately 500-700 ms postcue.

The discrepancies between our BRN and the LDAP component might be related to different design parameters used in the present study compared to some previous ERP studies, such as somewhat longer delays between cues and targets, the use of only validly cued target locations, and the use of delayed rather than speeded responses to targets. Alternatively, these two components might reflect different underlying mechanisms of target-specific biasing activity. For example, the LDAP or earlier-latency lateralized activity could reflect processing related to the establishment of stimulus-response mapping representations (Eimer et al., 2002; Praamstra et al., 2005), whereas the BRN might reflect the specific sustained baseline shift that biases target-specific brain areas to enhance perceptual sensitivity and that is maintained across the attentional-orienting time period. Lastly, the relatively late start of the biasing in the present study could be related to the specific manipulation of probability and timing of target occurrence in the present study (moderately early or late, sometimes not presented), as suggested recently by Correa and colleagues (Correa et al., 2006). More specifically, for example, had we included trials in which the target could have come earlier (e.g., by 400-800 ms postcue), both the attentional orienting control activity and the biasing activity may well have begun earlier.

3.5 Conclusions

In conclusion, our results provide evidence for different functional roles of the various brain areas involved in visual spatial attentional orienting by revealing differential temporal characteristics during the cue-target interval. First, the combined pattern of ERP and fMRI data suggest that the initial processing of the cue in the first 350-400 ms involves the analysis of its sensory content and the decoding of its instructional meaning. These processes are presumably performed in visual cortex and then in lateral frontal and parietal areas, respectively, and are carried out even when the cue instructs to not orient attention (e.g., the interpret-cue control trials in this study). Secondly, after this initial general cue processing, the more medial frontal areas initiate attentional orienting, including triggering the onset and maintenance of medial parietal cortex activation. These areas in turn have a role in rendering a biasing of activity in those specific sensory areas that will later receive incoming signals from target stimuli. Together they prepare the system to successfully identify hard-to-detect targets. Future research should assess whether this model of visual-spatial attentional control can be generalized to other attentional-control processes and/or to more complex task situations.

Chapter 4

Differential functional roles of slow-wave and oscillatory-alpha activity in visual sensory cortex during anticipatory visual-spatial attention

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ABSTRACT

Markers of preparatory visual-spatial attention in sensory cortex have been described both as lateralized, slow-wave, event-related-potential (ERP) components and as lateralized changes in oscillatory-EEG alpha power, but the roles of these markers and their functional relationship are still unclear. Here, three versions of a visual-spatial cueing paradigm, differing in perceptual task difficulty and/or response instructions, were used to investigate the functional relationships between posterior, oscillatory-alpha changes and our previously reported posterior, slow-wave, Biasing-Related-Negativity (swBRN) ERP activity. The results indicate that the swBRN reflects spatially specific, pretarget, preparatory activity sensitive to the expected perceptual difficulty of the target-detection task, correlating in both location and strength with the early sensory-processing N1 ERP to the target, consistent with reflecting a preparatory baseline-shift mechanism. In contrast, contralateral event-related decreases in alpha-band power were relatively insensitive to perceptual difficulty and differed topographically from both the swBRN and target-N1. Moreover, when response instructions emphasized making immediate responses to targets, compared to prescribing delayed responses, contralateral alpha-ERD activity was particularly strong and correlated with the longer-latency target-P3b activity. Thus, in contrast to the apparent perceptual-biasing role of swBRN activity, contralateral posterior alpha activity may represent an attentionally maintained task set linking stimulus-specific information and task-specific response requirements.

4.1 Introduction

Covertly shifting attention to a location different from where the eyes are directed increases the likelihood of being able to rapidly and accurately process stimuli presented at that location (Posner et al., 1980). The prevailing view is that these behavioral improvements are brought about by preparatory activity induced by a frontal-parietal attentional-control network (reviewed in Corbetta and Shulman, 2002), which in turn is thought to initiate and maintain a state of goal-directed, stimulus-specific readiness for expected target stimuli. This stimulus-selective perceptual-processing readiness is often referred to as sensory biasing (e.g., Foxe et al., 2005; Grent-'t-Jong and Woldorff, 2007; Hopfinger et al., 2000; Kastner and Ungerleider, 2001), and it is thought to be accomplished by a prestimulus baseline shift of activity in stimulus-selective sensory areas, which in turn is believed to lead to the increase in perceptual sensitivity (Desimone and Duncan, 1995; Kastner et al., 1999; Luck et al., 1997).

Although there is substantial consensus on this general model of anticipatory, visual-spatial, attentional control, certain aspects of this model are still unclear. One aspect that is still not very clear, for example, is the precise nature of the target-location-specific biasing activity in sensory cortex that appears to be contingent upon frontal-parietal attentional control, activity that would be expected to be particularly clearly manifested during the later part of the cue-target delay interval in cueing paradigms. Electroencephalographic (EEG) recordings from human participants in such paradigms have revealed both oscillatory changes (particularly in the alpha frequency range) as well as a number of slower event-related potential (ERP) changes. In regards to ERP markers, sensory-cortex pretarget ERP activity was initially reported as a contralateral positive-polarity wave, termed the Late-Directing-Attention-Positivity (LDAP, e.g., Eimer et al., 2002; Green et al., 2005; Harter et al., 1989; Hopf and Mangun, 2000; Jongen et al., 2006; van der Lubbe et al., 2006). More recently, however, contralateral negative-polarity preparatory ERP activity have been reported (Dale et al., 2008; Grent-'t-Jong and Woldorff, 2007; Van der Stigchel et al., 2006), which have been referred to as the Late-Directing-Attention-Negativity (LDAN) in one of these studies (Van der Stigchel et al., 2006), and as the Biasing-Related-Negativity (BRN) in another (Grent-'t-Jong and Woldorff, 2007).

The functional interpretations of these markers have varied greatly between studies. For example, the positive-polarity LDAP was initially postulated as reflecting an increase in the excitability of visual occipital cortical neurons enhancing the response to the target stimulus (Harter et al., 1989), and later as reflecting the buildup and maintenance in occipital-temporal areas of an attentional trace of the expected visual target (Hopf and Mangun, 2000). Subsequently, this positive-polarity posterior wave was interpreted as reflecting parietal cortex activity related to the deployment and maintenance of spatially specific attention at the cued location (Eimer et al., 2002; Eimer et al., 2003), as encoding of the to-be-ignored location (rather than the to-be-attended) location (McDonald and Green, 2008), or as a marker of covert manual response preparation (Gherri et al., 2009;

Praamstra et al., 2005), with the last of these deviating substantially from a location-specific "perceptual" biasing interpretation. The posterior negative waves contralateral to the direction of attention (BRN/LDAN), on the other hand, have been interpreted by our group as reflecting baseline shift activity that biases target-specific brain areas to enhance perceptual sensitivity, following the instantiation of attentional control activity in the fronto-parietal network (BRN: Grent-'t-Jong and Woldorff, 2007), and by others as reflecting a combination of "pre-target oculomotor programming" and "attentional orienting" (LDAN: Van der Stigchel et al., 2006).

In addition to ERP markers of preparatory activity, ample evidence exists for the involvement of induced preparatory *oscillatory* signals, especially in the form of late, sustained, spatially selective, occipital-parietal cortex modulations of ongoing activity in the alpha band (8-14 Hz). As with the ERP components, some variability has been reported in the directionality (polarity) of these spatial-location-specific alpha frequency modulations. For example, some studies have reported observing predominantly sustained pre-target *decreases* (desynchronization) in oscillatory alpha power over occipital or parietal scalp sites *contralateral* to the direction of attention (Kelly et al., 2009; Sauseng et al., 2005; Thut et al., 2006; Trenner et al., 2008; Yamagishi et al., 2005), whereas others have reported observing predominantly sustained pre-target *increases* (synchronization) in alpha power over *ipsilateral* sites (Kelly et al., 2006; Rihs et al., 2007; Worden et al., 2000). In general, decreases in visual-cortex alpha power have been interpreted as reflecting cortical activation or enhanced cortical excitability, whereas increases in alpha power have been linked to cortical deactivation (Pfurtscheller, 2001) and/or to active decoupling of cortical processing or disengagement of visual attention (Fu et al., 2001; Vanni et al., 1997). More recently, the ipsilateral alpha power increases seen in visual-spatial cueing studies have also been interpreted as an active inhibition mechanism (Kelly et al., 2006; Rihs et al., 2007) for the purpose of suppressing task-irrelevant or distracting visual input, an interpretation along the lines of the inhibition-timing hypothesis put forward by Klimesch and colleagues (Klimesch et al., 2007).

These observations of different EEG/ERP markers of preparatory visual-cortex activity, along with their widely varying functional interpretations, lead to two important questions that comprise the focus of the current study. First, what is the relationship between our previously reported slow-wave Biasing-Related-Negativity ERP marker and previously reported oscillatory alpha-band markers of pretarget sensory-cortex activity, and second, what are the functional roles of the neural activations these markers reflect?[1] Answering these questions is of considerable interest for at least two reasons. First, it is still unclear whether ERP and oscillatory markers reflect different aspects of a related underlying mechanism (see also

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[1] Because the basic paradigm of the present studies, which manipulates attention within the lower visual field, has previously been shown to trigger a negative-polarity contralateral BRN component over posterior scalp in the absence of any positive-polarity contralateral LDAP wave, the contralateral posterior ERP effect that we will be focusing on here will be the negative-polarity BRN.

studies by: Green and McDonald, 2010; Kelly et al., 2009). And secondly, the fact that so many different functional roles have been presented for the different visual-spatial attentional control markers that have been observed in the literature (LDAP/BRN ERP effects, alpha power changes) points to the possibility that there might actually be more than one process or mechanism reflected by these visual-field-specific preparatory activations in visual cortex. Thus, gathering better understanding of the functional roles reflected by these markers has the potential to improve and/or extend our current understanding of the mechanisms of top-down attentional control.

In order to investigate these questions, the current study used a multi-experiment approach that entailed analyses of three variants of a visual-spatial attentional control ERP paradigm, one variant of which we have reported on previously (Grent-'t-Jong and Woldorff, 2007). The basic paradigm in all three experiments consisted of a foveally presented instructional cue (attend right, attend left, or control cue) that could be followed shortly later by a faint target dot in a lower left or right visual-field location, with the target needing to be detected and reported by a button press when it occurred. The main variations of this general paradigm in the three experiments reported on here included a manipulation of perceptual task difficulty (harder or easier detection) and a manipulation of behavioral-response instructions (responding immediately following the target or being delayed until after the onset of a visual report signal). Manipulating perceptual task difficulty was used to study sensitivity of the preparatory BRN and alpha-band marker activity to perceptual degradation, as such sensitivity would favor the interpretation of a baseline-shift mechanism for enhancing the sensory processing of the expected target. Response instructions were manipulated in order to investigate the possible involvement of sensorimotor linkage activity during the delay period, which would favor an interpretation related to engendering the task-set or stimulus-response mapping. Such an interpretation would fit well with data from single-cell and multi-unit studies in non-human primates suggesting that parietal regions not only code for the spatial position of an expected target stimulus or saccade location, but also for its current task-set, including behavioral relevance or valence (see review Bisley and Goldberg, 2010).

4.2 Methods

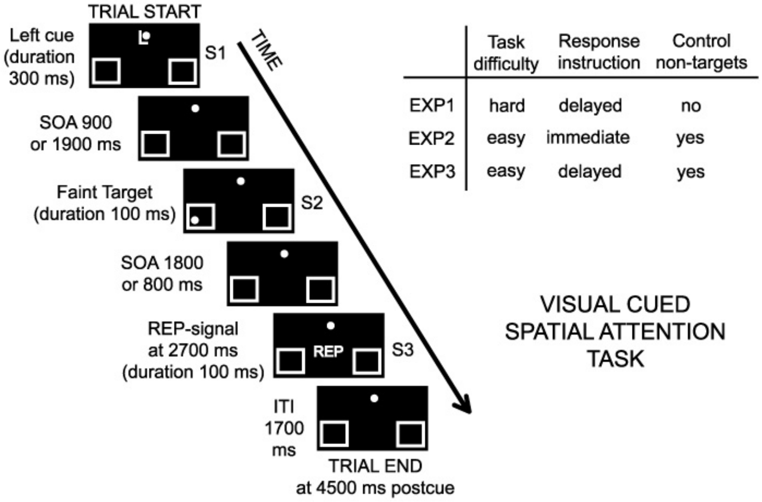
4.2.1 Participants

A grand total of 59 healthy (primarily University student) participants with normal or corrected-to-normal vision gave written informed consent to participate in this study as approved by the Duke University Institutional Review Board. The participants were divided across three independently-run experiments (abbreviated in the remainder of the article as exp1, exp2, and exp3). Included in the final analysis were 16 participants for exp1 (6 females, mean age 21 yrs, stdev 5.8 yrs, 2 left handed), 16 participants for exp2 (10 females, mean age 24 yrs, stdev 8.0 yrs, 5 left handed), and 16 participants for exp3 (10 females, mean age 24 yrs, stdev 5.5

yrs, all right handed). Data from the remaining 11 participants were excluded from the analyses because of excessive eye blinks, eye movements, muscle activity, or skin-potential drift. Participants were either paid $10 per hour or received university class credits for their participation.

4.2.2 General paradigm

Participants were presented with a series of visually presented compound-event trials. Each of these lasted 4500 ms and began with an instructional upper case letter cue ("L", "R", or "P") at fixation, which was sometimes followed by a target stimulus, but which always ended with an End-of-Trial or report signal (see Figure 1 for an example trial). The cues instructed the participants to *covertly shift attention* for that trial to a boxed location in the lower left ("L") or lower right ("R") visual field (3 deg lateral and 3 deg below the horizontal meridian) while maintaining central fixation (attention-directing cues), or *to not shift attention* on that trial and just continue to maintain central fixation ("P", control or "interpret" cues).



	Task difficulty	Response instruction	Control non-targets
EXP1	hard	delayed	no
EXP2	easy	immediate	yes
EXP3	easy	delayed	yes

Fig. 1 Task paradigm. Left panel shows an example of an attend-left-cue-plus-target-trial. The box on the right contains information on different task/paradigm manipulations used in the three experiments in this study. In all experiments, a centrally presented cue (here, the letter "L") instructed the participant to covertly attend to the lower left visual-field box to detect whether a faint-dot target stimulus was presented there in the period shortly following. On trials with a target, it could appear either early or late (50% probability) following the cue, at the cued location only. An end-of-trial signal (the letters REP) presented at 2700 ms post-cue signalled the participant in exp1 and exp3 to press a button to report if they had seen a target, and signalled the end of the response window in exp2. Other trials included attend-right-cue-plus-target, attend-left-cue-only (no target), attend-right-cue-only (no target), control-cue-only (no target), control-cue-plus-non-target (only in exp2 and exp3), and no-stim trials (no cue, no target).

Targets consisted of a small, faint, unilateral, grey dot presented on a black background in the box on the cued side (100% validity). In exp1 (some of the data from which were included in our earlier published study, Grent-'t-Jong and Woldorff, 2007) these faint grey dots occurred only after attend cues and were titrated for perceptual difficulty by changing the contrast level so that the detection rate averaged around 80%. In exp2 and exp3, all target dots had the same level of contrast that was clearly above threshold level, making the detection substantially easier. In addition, the faint dots could also be presented after the control cues in these two experiments, in which case they were task irrelevant and thus to be ignored.

For all trial types (other than "nostims", see below), an End-Of-Trial or report signal (the letters REP, for "report") was presented directly below fixation (see Figure 1) 2700 ms after cue onset. Participants in exp1 and exp3 were instructed to press a response button with their right index finger *after* this REP signal, whereas participants in exp2 were told to respond immediately following the detection of a target dot, *before* the REP signal. In sum, the three experiments were identical in most aspects, but differed in either perceptual task-difficulty and/or response instruction, as well as on the inclusion of task-irrelevant dots following control cues (For a quick overview of the key differences between the experiments, see the Table in the upper right corner of Fig. 1). Task-irrelevant dots were included in two out of the three experiments to provide a baseline for extracting expected attention effects (attended dots versus control dots) on target occipital P1/N1 and/or parietal P3b component activity.

With respect to trial types, 25% of all trials were "attend-cue-plus-target" trials in which a target occurred either early (900 ms) or late (1900 ms) after cue onset (50% probability). A similar number of the trials (25%) were "attend-cue-only" trials in which only cues were presented, still requiring a covert shift of attention but no target was presented. Another 25% of trials consisted of "control-cues" instructing to not shift attention. On these control trials in exp1, no faint target dot would occur (i.e., 25% "control-cue-only" trials). In exp2 and exp3, however, half of the control-cue trials were followed by faint dots (which were task irrelevant and to be ignored), randomly presented in the left or right lower-visual-field boxes, either early or late (50% probability), whereas the other half were "control-cue-only" trials. The remaining 25% of the trials consisted of "nostim" trials (periods of fixation only), which were randomized with the other trial types in order to provide a jittering of the inter-trial intervals that would be necessary for effective fMRI versions of these experiments (e.g., Woldorff et al., 2004). In all experiments, participants received at least two practice runs of 64 trials each, followed by 12-14 experimental runs, each consisting of 64 trials and a run-time of 4.8 minutes, during which EEG was recorded.

4.2.3 Recordings

The EEG was recorded from 64 electrodes mounted in a custom-designed, extended-coverage electrocap (Duke64-cap layout, made by Electro-Cap

International Inc, Eaton, Ohio) and referenced to the right mastoid during recording. The 64 channels were equally spaced across the cap and covered the head from above the eyebrows to the lower occiput (slightly below the inion).

Vertical eye movements and eye blinks (VEOG) were recorded from two electrodes placed below each eye, referenced to the scalp electrodes above the eye. Horizontal eye movements (HEOG) were recorded from two electrodes placed on the outer canthi of the eyes, referenced to each other. Eye movements were also monitored on-line with a video zoom-lens camera. Participants were trained before starting the experiment on covertly orienting their attention without moving their eyes. Analyses of the horizontal EOG data indicated that the number of rejected trials due to eye movements was indeed very low in all conditions in all experiments (3-7%) and did not significantly differ between the different conditions or experiments.

Electrode impedances were maintained below 2 kΩ for the mastoids, below 10 kΩ for the EOG electrodes, and below 5 kΩ for all remaining electrodes. All EEG and EOG channels were continuously recorded with an online band-pass filter of 0.01 to 100 Hz (SynAmps amplifiers from Compumedics Neuroscan Inc, Charlotte, NC) and digitized with a 500-Hz sampling rate. Recordings took place in an electrically shielded, sound attenuated, dimly lit, experimental chamber. Stimuli were presented using the Presentation software package (Neurobehavioral Systems Inc, Albany, CA).

4.2.4 Behavioral data analyses

Behavioral performance estimates were extracted from the analyses of hit rates and false-alarm rates. Because the focus of this study was on the long-lasting preparatory activity induced by the cues, hit rates were determined based on the trials in which the targets occurred late in the cue-target interval, whereas false alarm rates were estimated from cue-only trials. Reaction-time data were not analyzed, because the delayed responses used in two of the three experiments rendered comparisons of those measures not meaningful. For comparisons between the experiments, the statistical analyses of hit rates included mixed-design repeated-measures ANOVAs (rANOVAs), including the between-subject factor EXPERIMENT (exp1, exp2, exp3) and the within-subject factor LOCATION (right, left). Mixed-design rANOVAs for false-alarm rates included the between-subject factor EXPERIMENT (exp1, exp2, exp3) and the within-subject factor CONDITION (attend-left/right collapsed, control-cue). Significance in all statistical tests was inferred for p-values lower than 0.05.

4.2.5 EEG data analyses

EEG analyses were performed using EEGLAB 7.1.3.14b (Delorme and Makeig, 2004), after downsampling of the data to 250 Hz. Cue-only and cue-plus-late-target trials were extracted from both the attend-cue and control-cue conditions (i.e., cue-plus-early-target trials were excluded from all analyses, although the inclusion of these trials in the paradigm engendered more rapid attentional shifting across all the trials). The epochs analyzed for cue-related activity included data between 400 ms precue and 1900 ms postcue onset, whereas epochs for target-related activity included data between 200 ms pretarget and 800 ms posttarget onset. Cue and target ERPs were extracted from the same set of preprocessed trials.

Preprocessing started with the removal of trials that contained high-amplitude muscle artifacts or were clearly contaminated by eye blinks or eye movements. Trials with eye blinks were only rejected if the blink occurred around stimulus presentation times (-200 to +300 ms around cue and target onsets). Residual blink contamination was subsequently removed using independent components analysis (ICA) in the EEGLAB Matlab Toolbox[2]. After these preprocessing steps, the data were divided into three separate analysis pipelines, one for the cue ERPs, one for target-related ERP activity, and one for the cue-induced changes in alpha-band (8-12 Hz) power.

To extract the cue-induced, slow-wave, ERP activity, the data from the cue-only and cue-plus-late-target trials were collapsed together. Target ERPs were extracted only from the cue-plus-late-target trials. Both cue and target ERP averages were imported into ERPSS (ERP analysis software package; UCSD, San Diego, CA) for further analyses. These analyses included re-referencing of the data for all channels to the algebraic mean of the two mastoid electrodes, and the generation of contra-minus-ipsilateral activity (averaged across attend-right-cue and attend-left-cue trials to improve signal-to-noise ratio). In addition, to minimize overlap with cue-induced alpha-band activity, slow-wave cue-locked ERPs were computed by applying a low-pass filter to the data. This low-pass filter consisted of a 41-data-point running-average filter, which at our converted sampling rate of 250 Hz comprised a 164-ms boxcar filter kernel that strongly attenuates signal contributions from frequencies above 6 Hz. For target-locked ERPs the data were filtered with a 7-data-point (28-ms) running-average low-pass filter that attenuates activity above 35 Hz.

For extracting the induced alpha-band responses, the analysis pipeline started with the computation of averaged Event-Related Spectral Perturbations (ERSPs) with the EEGLAB toolbox, separately for each condition and for each channel, using Fast Fourier Transforms (FFTs) of single trials with a frequency resolution of 1.95 Hz. Subsequently, averaged event-related induced alpha-band (8-12 Hz) responses were extracted for all channels from these data. These data were then further analyzed and plotted in ERPSS similar to the cue ERPs (i.e., re-referenced to averaged mastoids and converted into contra-minus-ipsilateral data).

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[2] This approach differs from the one taken in the earlier published study containing data from exp1 participants (Grent-'t-Jong & Woldorff, PLoS Biology, 2007) in that in the earlier study all trials with eyeblinks in the time windows of interest were excluded from the analyses, whereas in the present study ICA detection and removal was used. As a consequence, the datasets from more of the participants (16 versus 13 before), as well as more trials from the individual participants, could be included, thereby increasing overall power.

4.2.6 Statistical analyses of EEG data

Lateralized attend-cue-induced changes (contra-minus-ipsilateral activity) in slow-wave ERP and alpha-band activity were estimated across the cue-target interval in consecutive windows of 250 ms of averaged data from 400-1900 ms postcue onset, relative to a precue baseline window of 400 ms. Statistical tests included data from two occipital-parietal regions of interest (ROIs), consisting of sites approximately equivalent to O1, PO3, PO7, and PPO5 on the left (in the 10-5 system: Oostenveld and Praamstra, 2001) and O2, PO4, PO8, and PPO6 on the right. Significant contralaterality of the slow-wave ERP and alpha-band changes were tested within these ROIs using rANOVAs.

For target-related activity, the amplitudes of the sensory ERP components P1 (90-110 ms) and N1 (exp1: 175-225 ms; exp2 and exp3: 150-200 ms) over the occipital-parietal ROI were tested for significant contralaterality with rANOVAs, using a 200-ms pretarget baseline. In addition, possible early attention effects (attended targets versus nontargets) on these sensory P1/N1 components were tested for significance in exp2 and exp3 only, as exp1 lacked irrelevant non-targets as a baseline condition. In addition, longer-latency target attention effects in exp2 and exp3 were tested on the mean amplitude (350-500 ms) of the parietal P3b component, a component believed to represent stimulus-evaluation and decision-making processes (see e.g. review by Kok, 2001). Statistical tests for early (P1/N1) attention effects on the targets included rANOVAs with the within-subjects factor ATTENTION (attended targets, ignored non-targets). Repeated-measures ANOVAs for the later latency parietal P3b component included an additional factor of ROI (left parietal ROI: channels [PPO5, PO3, PPO3h]; midline parietal ROI: channels [CPz, Pz, POz]; and right parietal ROI: channels [PPO6, PO4, PPO4h]).

4.3 Results

4.3.1 Behavioral performance

Analyses of behavioral performance focused primarily on the accuracy measures of hit rates and false-alarm rates. Hit rates were at their expected level of accuracy, matching the titration goal of approximately 80% for the hard detection task in exp1 (75.9%, stderr 2.1%) and the goal of substantially easier detection tasks in exp2 and exp3 (exp2: 98.9%, stderr 0.4%; exp3: 94.8%, stderr 1.2%; see also Table1). Post-hoc specific pairwise mixed-design rANOVAs indicated a significantly lower overall hit rate in exp1 compared to both exp2 (main effect of EXPERIMENT, $F(1,15)= 119.2$, $p< 0.001$) and exp3 (main effect of EXPERIMENT, $F(1,15)= 68.8$, $p< 0.001$). Hit rates were higher in exp2 relative to the delayed-response conditions of exp3 (main effect of EXPERIMENT, $F(1,15)= 9.4$, $p< 0.01$). Finally, false-alarm rates were generally low (on average across all experiments between 0.1-2.0%; more details in Table 1), and were found to not differ significantly between experiments.

Table 1. Overview of grand-average (n=16 in each experiment) parameters of behavioral performance, separately for the three included experiments.

				% hits		% false alarms		mean RTs	
	Task difficulty	**Response instruction**	**Task-irrelev. targets**	**Right targets**	**Left targets**	**Attend trials**	**Control trials**	**Right targets**	**Left targets**
EXP1	hard	delayed	no	79.4 (1.9)	72.4 (2.5)	2.0 (0.4)	0.2 (0.1)	n.a.	n.a.
EXP2	easy	immediate	yes	99.1 (0.1)	98.6 (0.1)	0.1 (0.1)	1.6 (0.4)	408 (14.8)	421 (15.9)
EXP3	easy	delayed	yes	94.4 (1.4)	95.3 (1.2)	0.6 (0.2)	0.9 (0.4)	n.a.	n.a.

In sum, the analyses of behavioral performance indicated proper overall attention and task compliance in all three experiments, while also showing the intended manipulation of perceptual task difficulty.

4.3.2 Target ERPs

The analyses of the target ERPs focused on early sensory components (P1/N1) at the selected occipital-parietal scalp ROIs and on the longer-latency parietal P3b component in the left, middle, and right parietal ROIs. In all three experiments, the occipital P1 amplitude to the faint target dots peaked between 90-110 ms. P1 amplitudes were generally very small, presumably because of the target being small and relatively faint, and were not significantly different in amplitude over the left and right ROIs as a function of target location. Attention effects on the P1 (i.e., larger for attended target dots vs. task-irrelevant nontarget dots) could be assessed only for exp2 and exp3 in that exp1 had no nontarget-dot condition. These tests showed significant ATTENTION effects on the P1 amplitude in exp3 ($F(1,15)= 6.1$, $p< 0.03$), but not in exp2 ($p> 0.38$).

The first target ERP component that was significantly larger contralateral versus ipsilateral to the location of the target as well as to the direction of attention was the occipital-parietal N1 component (see Fig. 2), peaking between 175-225 ms in exp1 and between 150-200 ms post-target onset in exp2 and exp3. The latency difference of the target N1s between experiments is presumably a result of the manipulation of perceptual contrast (being fainter in exp1 compared to exp2 and exp3), as perceptually degrading a stimulus is known to diminish the amplitude and to delay the peak activity of early sensory components (Johannes et al., 1995). Contralaterality of the N1 component was confirmed by a main effect of TARGET LOCATION in all three experiments (exp1: $F(1,15)= 52.6$, $p< 0.001$; exp2: $F(1,15)= 46.6$, $p< 0.001$; exp3: $F(1,15)= 52.8$, $p< 0.001$). ATTENTION effects on these contralateral N1 components, again assessable only for exp2 and exp3, were again found for exp3 ($F(1,15)= 17.9$, $p< 0.001$) only. In exp2, the overall ATTENTION effect for the N1 across all occipital ROI channels did not quite reach significance ($p= 0.06$), but there was a significant ATTENTION x ELECTRODE interaction effect ($F(1,15)= 3.9$, $p< 0.03$). Post-hoc tests revealed that only the more superior channels of the ROI (PO3/PO4 & PPO5/PPO6) showed a significant N1 amplitude enhancement ($F(1,15)= 5.4$, $p< 0.03$).

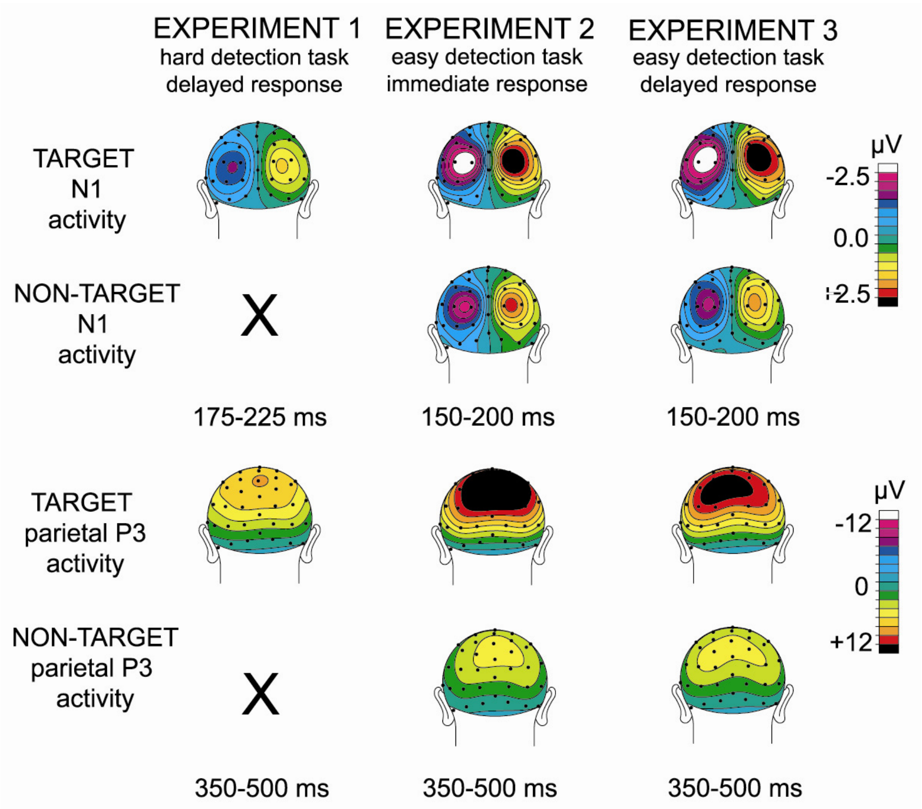


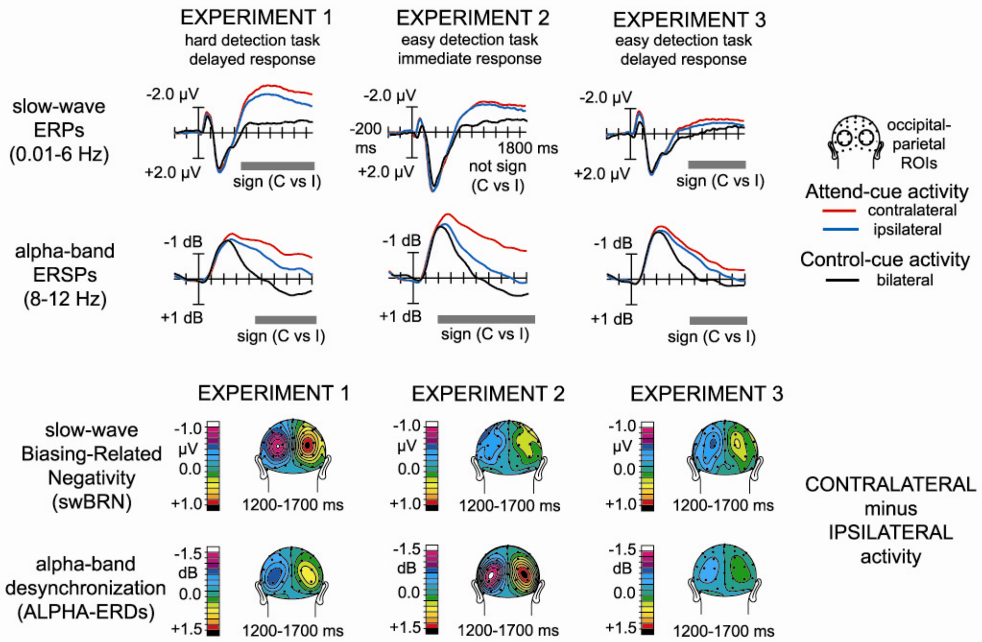
Fig. 2 Distributions and attention effects of target N1 and P3b ERP components. *Top two rows:* Grand-average (n=16) distributions of early N1 activity (contralateral-minus-ipsilateral activity on the left; right side is opposite subtraction and thus contains redundant information) elicited by target (following attend cues) and non-target faint dots (following control cues; only in exp2 and exp3). *Bottom two rows:* Grand-average (n=16) distributions of P3b activity (non-lateralized), again separately for targets and non-targets. Columns separate the results from the three different experiments.

Finally, clear ATTENTION effects were found on the parietal P3b component (see Fig. 2: peaking between 350-500 ms post-target onset) in both exp2 ($F(1,15)= 71.7$, $p< 0.001$) and exp3 ($F(1,15)= 20.5$ $p= 0.004$). In addition, in exp2 only, an ATTENTION x ROI interaction effect was found ($F(2,30)= 17.6$, $p< 0.0001$) that resulted from attention effects being larger over the left parietal than over the middle and right parietal ROIs (attention effects were on average 9.63 μV, 7.38 μV, and 7.50 μV over left, middle and right parietal ROIs respectively).

In sum, the presence of clear early and late attention effects on the target ERPs in exp2 and exp3 indicates that subjects were attending as instructed even when target detection was relatively easy.

4.3.3 Cue-induced preparatory occipital slow-wave BRN and alpha band activity

Sensory cortex preparatory activity was studied by investigating target-location-specific changes in cue-induced slow-wave ERP activity (0.01-6 Hz) and oscillatory event-related alpha-band (8-12 Hz) activity (see Fig. 3).



<u>Fig. 3 Cue-locked pretarget preparatory activity in visual cortex.</u> *Top panel:* Grand-average (n=16) traces, shown separately for the three experiments, of cue-locked slow-wave (0.01-6 Hz) ERPs and alpha-band (8-12 Hz) event-related desynchronization (ERD) activity. These are shown over contralateral (red traces) and ipsilateral (blue traces) occipital ROIs for the attend condition, collapsed across attend-right and attend-left cues, and for the control condition (black traces), collapsed across right and left ROI channels, from 200 ms before to 1900 ms after cue onset, for cue-only and cue-plus-early-target trials only. Grey bars underneath the traces indicate significant differences between contralateral and ipsilateral responses to attend cues, revealing significant slow-wave BRN (swBRN) or alpha-ERD (event-related desynchronization) preparatory activity. *Bottom panel:* Corresponding topographical distributions of the contralaterality of the swBRN and alpha-ERDs difference-wave activity between 1200-1700 ms following cue onset. Contralaterality of distribution is calculated as contralateral-minus-ipsilateral activity relative to the left hemisphere, so the activity over the right hemisphere reflects the inverse of the subtraction (i.e., ipsilateral-minus-contralateral).

4.3.3.1 Slow-wave ERP activity

All cue types (attend right, attend left, control cues) triggered a late-onsetting, sustained negative-polarity ERP wave over occipital-parietal scalp sites that was smallest and mostly bilateral for control-cue trials, somewhat larger for attend-cue between contralateral and ipsilateral activity reflects the ERP biasing marker previously termed the Biasing-Related-Negativity (Grent-'t-Jong and Woldorff, 2007), which we will refer to here as the "swBRN" because of the explicit 6 Hz low-pass filtering we applied to the ERP data in the current study. Exp1 triggered clear swBRN activity, whereas exp3, and particularly exp2, yielded much weaker versions of these responses. The rANOVAs revealed that the contralateral swBRN was significant between 650-1900 ms in exp1 (p-values all < 0.01), and between 900-1900 ms in exp3 (p-values all < 0.01), but did not reach significance (p-values all > 0.1) in any test window in exp2 (see Table 2 for more details). Additional rANOVAs, testing for differential late swBRN activity across experiments (1200-1700 ms data only), revealed a main effect of EXPERIMENT (F(2,30)= 27.4, p< 0.0001). Post-hoc specific pairwise comparisons showed that the late swBRN activity differed significantly between exp1 and exp2 (F(1,15)= 50.5, p< 0.0001) and between exp1 and exp3 (F(1,15)= 25.0, p< 0.0001), but not between exp2 and exp3 (p= 0.21), which both included easy-to-detect targets.

Table 2. Overview of the results of repeated-measures ANOVAs on contra-minus-ipsilateral occipita-parietal ROI data, separately for swBRN and alpha-ERD activity, and separately for each experiment. Results include all F(1,15) tests across 6 sequential windows of 250 ms between 400 and 1900 ms postcue (n.s. means "not significant": p-values higher than 0.05).

Contra-versus-Ipsilateral slow-wave BRN activity over occipital-parietal ROI						
	experiment 1		**experiment 2**		**experiment 3**	
BRN activity	**F(1,12)**	**p-value**	**F(1,12)**	**p-value**	**F(1,12)**	**p-value**
400-650 ms	n.s.		n.s.		n.s.	
650-900ms	9.5	0.0076	n.s.		n.s.	
900-1150 ms	21.7	0.0003	n.s.		12.5	0.0030
1150-1400 ms	18.0	0.0007	n.s.		23.1	0.0002
1400-1650 ms	17.6	0.0008	n.s.		9.6	0.0073
1650-1900 ms	23.6	0.0002	n.s.		10.0	0.0064
Contra-versus-Ipsilateral ALPHA ERD activity over occipital-parietal ROI						
	experiment 1		**experiment 2**		**experiment 3**	
ALPHA ERDs	**F(1,12)**	**p-value**	**F(1,12)**	**p-value**	**F(1,12)**	**p-value**
400-650 ms	n.s.	[0.0580]	11.9	0.0036	n.s.	[0.0709]
650-900ms	n.s.	[0.0522]	25.3	0.0002	n.s.	[0.0546]
900-1150 ms	8.7	0.0098	27.5	0.0001	5.7	0.0300
1150-1400 ms	6.5	0.0220	30.1	0.0001	17.2	0.0009
1400-1650 ms	7.3	0.0164	27.8	0.0001	9.6	0.0074
1650-1900 ms	9.6	0.0073	31.3	0.0001	14.2	0.0019

4.3.3.2 Alpha-band (8-12 Hz) fluctuations

In contrast to the swBRN activity, alpha-band responses showed a fairly consistent pattern across the three experiments. All cue-types triggered an initial strong decrease in alpha-band power (compared to precue baseline power) until about 400-500 ms postcue onset. Following this initial alpha-band event-related desynchronization (ERD) elicited by all cue-types, alpha-band power in control-cue trials moved quickly back to baseline level and even somewhat beyond (giving rise to a small degree of alpha event-related synchronization [ERS]). Alpha power in attend-cue trials, on the other hand, moved more slowly back to baseline level, particularly over scalp sites contralateral to the direction of attention. In contrast to the pattern for the swBRN, this ERD effect was particularly strong in exp2 relative to exp1 and exp3. Repeated-measures ANOVAs revealed that the alpha-ERDs were significantly lateralized (larger contralateral versus ipsilateral to attention) between 900-1900 ms in exp1 (all p-values < 0.03), between 400-1900 ms in exp2 (all p-values < 0.01) and between 900-1900 ms in exp3 (all p-values < 0.03). Additional rANOVAs, testing for differential late alpha-band power changes across experiments (1200-1700 ms data only), revealed a main effect of EXPERIMENT (F(2,30)= 16.1, p< 0.0001). Follow-up post-hoc pairwise comparisons indicated that the late alpha-ERDs differed significantly between exp1 and exp2 (F(1,15)= 20.2, p< 0.0001) and between exp2 and exp3 (F(1,15)= 25.8, p< 0.0001), but not between the two studies with delayed responses, exp1 and exp3 (p= 0.1).

In summary, very different patterns were found for the two markers of pretarget preparatory activity in visual cortex. The swBRN activity was strongest and earliest when the target stimulus was expected to be perceptually difficult to detect (exp1). Surprisingly, no significant swBRN was found in exp2, whereas a small but significant one was found in exp3, despite differing only in response instructions (immediate in exp2, delayed in exp3). In contrast, alpha-ERD responses were much more consistent across studies, thus showing much less sensitivity to perceptual task difficulty. The alpha-ERD marker appeared more sensitive to response instructions, however, starting earlier and becoming stronger when immediate response were required (exp2) compared to when they were delayed (exp1 and exp3).

4.3.4 Direct analyses of differences between marker responses across experiments

The different response patterns of the two markers, summarized in Figure 4, were investigated further by direct analyses across the three experiments, using a mixed-design rANOVA that included the within-subject factor MARKER (magnitude of change in swBRN or alpha-ERD activity) and the between-subject factor EXPERIMENT (exp1, exp2, or exp3). Both a significant main effect of MARKER (F(1,2)= 13.6, p< 0.001) and a significant MARKER x EXPERIMENT interaction effect (F(2,45)= 23.3, p< 0.0001) were found. In addition, pairwise post-hoc comparisons revealed that the pattern of change in magnitude of the swBRN and alpha-ERD activity was significantly different between exp2 and exp1 (main effect of MARKER: F(1,1)= 15.6, p< 0.001 and a MARKER x EXPERIMENT interaction effect: (F(1,30)= 29.8, p< 0.001), and between exp2 and exp3 (main effect of MARKER: F(1,1)= 29.2, p< 0.001, and a MARKER x EXPERIMENT interaction effect: (F(1,30)= 30.1, p< 0.001), whereas no such differences were found between exp1 and exp3 (no MARKER effect: p= 0.29, and no MARKER x EXPERIMENT effect: p= 0.33).

In conclusion, these results suggest that the marker responses in the immediate-response conditions of exp2, lacking a clear swBRN but showing the strongest alpha-ERD responses of all three experiments, were qualitatively different from those recorded in the delayed-response conditions of exp1 and exp3,

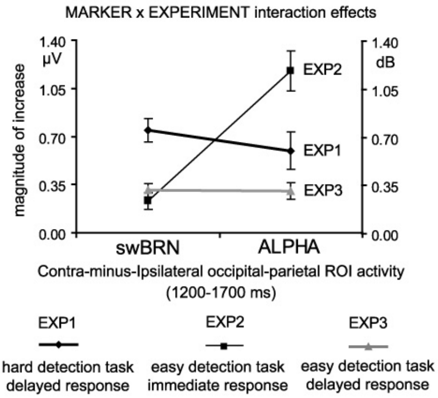


Fig. 4. swBRN and alpha-ERD marker activity across experiments

These show a qualitatively different pattern of preparatory activity for exp2, compared to exp1 and exp3, indicating an especially strong effect of the manipulation of response instructions on the alpha-ERDs.

which induced both swBRN and alpha-ERD activity, mainly differing in strength (i.e., quantitatively) between the two experiments.

4.3.5 Topographical distributions

Another clear difference between the two preparatory-activity markers was the scalp potential distributions (TOPOs) (see TOPOs in Fig. 3 and scalp-current density [SCD] maps in Fig. 5). The distribution of the swBRN appeared to be more superior and medial, whereas the alpha-ERDs seemed to extend further inferiorly and laterally over occipital-parietal scalp sites. We explicitly tested for the presence of statistical distributional differences between the two markers using scalp-current-density transformed data (in order to focus on local distributions) extracted between 1200-1700 ms postcue onset from exp1, an experiment that induced clear activity for both markers. In addition, we compared the marker distributions from exp1 with the target-N1 distribution from that experiment. We reasoned that if one, or both, of these markers reflects a baseline-shift biasing mechanism to improve perceptual sensitivity for processing the targets, one would expect this baseline-shift activity to occur over scalp sites closely corresponding to those where the contralateral target-N1 sensory component peaked.

Figure 5 provides an overview of the results of this analysis. Repeated-measures ANOVAs were performed on the contra-minus-ipsilateral topographic distributions, using the factors of MARKER (swBRN versus alpha-ERD, swBRN versus target-N1, alpha-ERD versus target-N1, in pairwise comparisons) and ELECTRODES (four occipital-parietal ROI channels), revealed significant MARKER x ELECTRODE interaction effects for the swBRN versus alpha-ERD distributions ($F(2.2, 32.4)= 4.8$, $p< 0.02$, Greenhouse-Geisser (GG) corrected) as well as for the contrast of the alpha-ERDs and target-N1 distributions ($F(2.5, 37.9)= 9.2$, $p< 0.0001$, GG corrected), whereas no significant differences were found between the swBRN and the target-N1 distributions ($p= 0.96$). Inspection of the distributions indicated that the swBRN and the target-N1 distributions had the same focal peak distribution within the ROIs, whereas the alpha-ERDs had a broader and more diagonal swath of peak activity that reached from medial parietal scalp locations to more infero-lateral ones (Fig. 2). Thus, it appears that the alpha-ERD power changes were *hemifield* specific but not so target-location specific, differing in distribution from the target N1, whereas the swBRN was both *hemifield* specific *and target-location* specific. As a result, the swBRN would seem to be more likely than alpha-ERDs to reflect a baseline-shift mechanism.

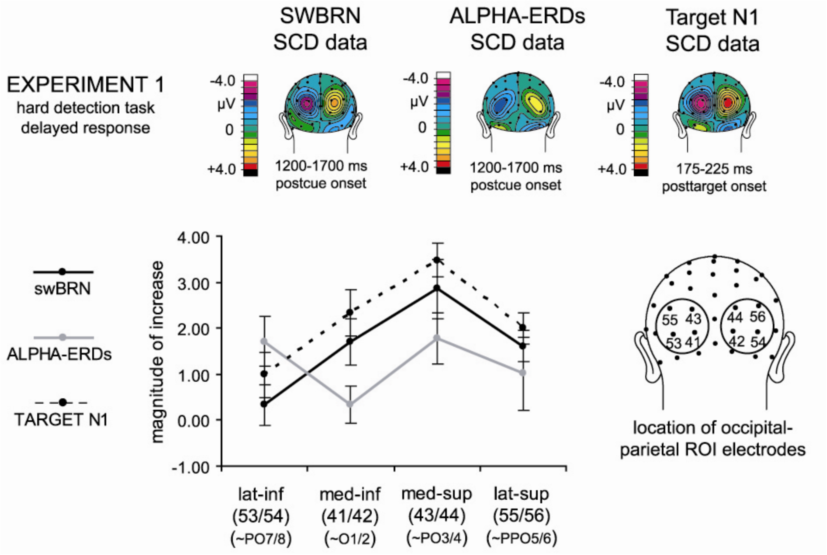


Fig. 5. Comparison between swBRN, alpha-ERD and target-N1 distributions. Top panel shows grand-average (n=16) scalp current density distribution data from exp1, separately for swBRN, alpha-ERDs, and target-N1 activity, plotted over posterior scalp sites (left hemisphere displays contra-minus-ipsi activity, right hemisphere ipsi-minus-contra activity). Bottom panel shows the mean activity and standard error of the mean for all three components, separately for each of the 4 channels included in the occipital-parietal ROI (see for exact locations the lower right cartoon head). Note the pattern of activity across sites differed for the alpha-ERD relative to the swBRN and target-N1.

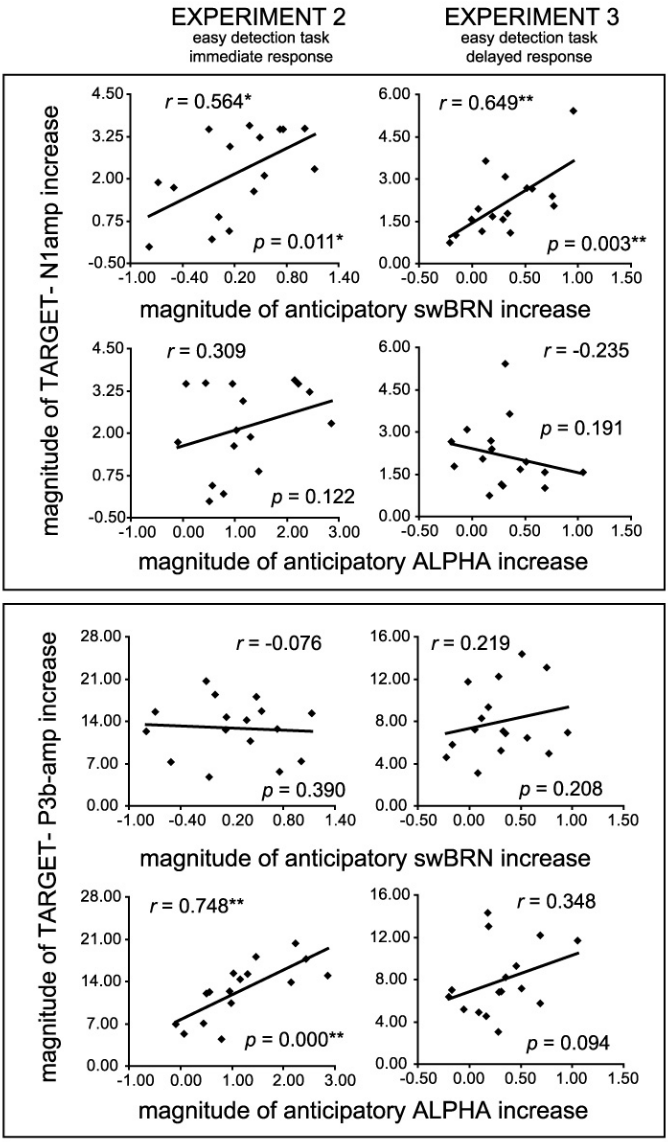
4.3.6 Correlations between preparatory biasing markers and target ERP activity

The functional roles of the swBRN and alpha-ERD were further investigated by correlating the preparatory activity of each of these with the subsequent brain responses to the targets (Fig. 6). In particular, using Pearson's *r* correlation statistics, activity levels of the cue-triggered contra-minus-ipsilateral swBRN and alpha-ERD activity between 1200-1700 ms were tested for their possible correlation across subjects with the amplitudes of the contra-minus-ipsilateral sensory target-N1 (150-200 ms) over the lateralized occipital-parietal ROIs and with the longer-latency parietal target-P3b (350-500 ms) over the left, middle, and right parietal ROIs (i.e., where these ERP components were shown to be affected by attention). These pretarget swBRN and alpha-ERP activity marker were also assessed for their possible correlations with the mean target-detection reaction times (exp2 only) and hit rates (both exp2 and exp3). Data from exp1 were excluded from these analyses, because the online titration of perceptual task-difficulty level in that experiment would likely have confounded the correlations of interest. We predicted that if the swBRN indeed reflects a baseline-shift mechanism, as our main analyses seemed to suggest, then a correlation between the swBRN and target N1 amplitude should be observed, whereas such an effect would likely be absent for the alpha-ERDs, because its topographic distribution did not match the N1 distribution well. Supporting this notion, target N1 amplitudes were found to correlate positively with the preceding cue-triggered swBRN activity (see Fig. 6; upper box, first row, right and left column) in both experiments (exp2: r = 0.564, p= 0.011; exp3: r = 0.649, p= 0.003), but not with the preceding alpha-ERDs (see Fig. 6; upper box, second row, right and left column). Thus, increased target N1 amplitudes were preceded by stronger swBRN preparatory activity, thereby further linking the swBRN marker to a functional role of increasing baseline activity for enhancing sensory and perceptual processing.

Table 3. Complete overview of results of Pearson's r correlational analyses between preparatory swBRN and alpha-ERD activity and magnitude of increase in target P3b amplitude, as recorded over left, middle and right parietal ROIs.

		Experiment 2 easy detection task immediate response	**Experiment 3 easy detection task delayed response**
swBRN activity vs target P3b amplitude	Left parietal ROI	r = -0.076 / p = 0.390	r = 0.219 / p = 0.208
	Mid parietal ROI	r = -0.169 / p = 0.265	r = 0.226 / p = 0.200
	Right parietal ROI	r = -0.221 / p = 0.206	r = 0.327 / p = 0.108
ALPHA-ERD activity vs target P3b amplitude	Left parietal ROI	r = 0.748 / p = 0.000**	r = 0.348 / p = 0.094
	Mid parietal ROI	r = 0.652 / p = 0.003**	r = 0.324 / p = 0.110
	Right parietal ROI	r = 0.662 / p = 0.003**	r = 0.260 / p = 0.166

The pattern of correlations between the swBRN and alpha-ERDs and the later parietal P3b in exp2 and exp3 were less straightforward, but in part showed the converse pattern. A complete overview of all the parietal ROI correlations is presented in Table 3. More specifically, preparatory swBRN activity did not correlate with the P3b amplitude in either of the two experiments in any of the parietal P3b ROIs, or collapsed across all of them (see Fig. 6, left parietal ROI correlations in lower target P3b box, first row, right and left column). In contrast, alpha-ERD activity correlated significantly with P3b amplitude in exp2 (Fig. 6; lower box, second row, right column; r = 0.748, p< 0.001), although not in exp3 (Fig. 6; lower box, second row, left column; r = 0.348, p= 0.094). In addition, in exp2, the alpha-ERDs correlated more strongly with the P3b over the left parietal ROI (r = 0.748, p< 0.001) than over the middle (r = 0.652, p= 0.003) and right (r = 0.662, p= 0.003) parietal ROIs, mirroring the stronger left parietal effects found for attention effects on the target P3b amplitudes in that experiment. Thus, a stronger decrease in alpha-band power (larger alpha-ERDs) resulted in a subsequently higher target P3b amplitude (especially over left parietal sites), but only when response instructions favored immediate-response decisions and executions, and not when responses were delayed.



<u>Fig. 6. Anticipatory swBRN and alpha-ERD activity and their correlations across subjects with subsequent target N1 and P3 activity.</u> Scatterplots showing the correlations (Pearsons r-coefficients and corresponding, one-tailed, p-values) between the contra-minus-ipsilateral magnitude of increase of swBRN and alpha-ERD activity between 1200-1700 ms postcue and subsequently elicited magnitude of increase of the contra-minus-ipsilateral N1 amplitudes (upper panels) and the longer-latency P3b (lower panels) to the targets, separately for exp2 (left column) and exp3 (right column). N1 activity is averaged over the four channels of the occipital-parietal ROI, and the P3b activity is from the left-parietal ROI where maximum correlations were found in exp2. All activity is collapsed across attend-right and attend-left conditions.

Finally, correlational analyses between preparatory swBRN and/or alpha-ERD activity and subsequent behavioral performance (hit rates and mean reaction times) were performed for the two studies that could be tested (exp2 and exp3), but no significant correlations were found. Although all these correlational relationships were in the direction of a positive relationship with task performance, the p-values were all larger than 0.3, except for the correlation between swBRN activity and hit rates in exp3 (easy detection/delayed response), which was 0.08 (r = -0.37). In other words, in exp3, participants with stronger preparatory swBRN activity (greater contralateral amplitude decrease) tended to show better target-detection performance (higher hit rates). Considering the rather small number of target trials in these experiment, however, we hypothesize that we may not have had sufficient power for these correlational analyses with behaviour to reach significance.

4.3.7 Within-subject marker correlations

Finally, although clearly significant differences were found between the swBRN and alpha-ERDs markers of visual-spatial biasing activity, these significant differences could in theory be heavily driven by individual differences, as all tests used between-subject variance. Thus, as a final test, we also explored the relationship between swBRN and alpha-ERD activity at a within-subject level by selecting data from exp1 (which included both markers), looking for different swBRN activity in a subject-based median-split of the single-trial amplitudes of the occipital-parietal alpha activity between 1200-1700 ms.

For this final test (results summarized in Fig. 7), trials were sorted by the induced alpha-power desynchronization, separately for attend-right and attend-left cue trials on the channel of strongest swBRN activity found in the grandaverage (that is, channel 43 [~PO3] for attend-left cues and channel 44 [~PO4] for attend-right cues) between 1200 and 1700 ms post-cue onset. After sorting, the data was split for each subject individually into two datasets of high and low alpha ERSPs (median split). Subsequently, averaged alpha-ERSP and slow-wave ERP data was extracted for further analyses, comparable to the original analyses on the whole dataset. Finally, the data from 6 windows of 250 ms of averaged data between 400 and 1900 ms was submitted to rANOVAs, separately for both markers, including the factor CONTRAvsIPSI (contralateral, ipsilateral), and MSDATA (median-split: data1, data2). As would be expected, due to the sorting, these data showed large differences in the alpha ERSPs, which was also reflected in the rANOVAs showing significant CONTRAvsIPSI x MSDATA interaction effects for the alpha-ERSPs (upper traces in Fig. 7) between 1150-1400 ms ($F(1,15)= 12.2$, $p< 0.01$) and between 1400-1650 ms ($F(1,15)= 16.6$, $p= 0.001$). In contrast, for the same trials, there was no evidence of any such interaction effects in any of the tested windows for the swBRN (lower traces in Fig. 7).

In conclusion, in the current multi-experiment study, changes in the magnitude of alpha-ERD activity did not appear to correlate with changes in the magnitude of swBRN activity in the same trials, supporting the view that these two markers indeed reflect different processes.

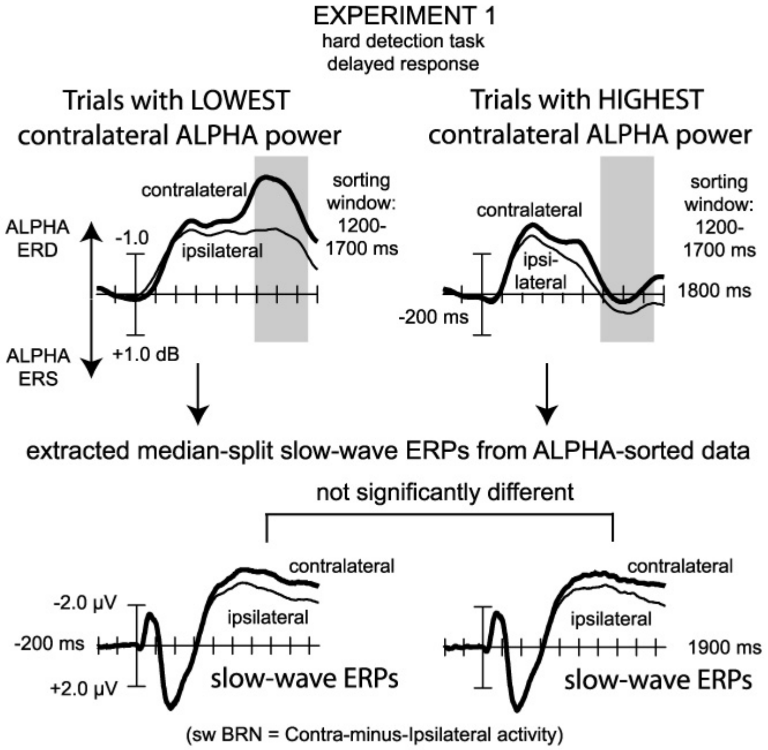


Fig. 7. Within-subject marker correlations across trials in exp1. Top panel shows grand-average (n=16) median-split alpha-ERSP activity, separately for the contralateral and ipsilateral occipital-parietal ROIs. These activitation traces were extracted from alpha-power-sorted data at the contralateral scalp sites that showed maximum overlapping lateralized alpha and swBRN responses (PO3/PO4) between 1200-1700 ms post cue onset. Bottom panel shows the corresponding swBRN ERP responses extracted from these alpha-sorted median-split datasets. Note that, despite the very large, contralateral, alpha-power differences resulting from the median-split separation imposed, the swBRN responses (contralateral minus ipsilateral ERPs) did not show any difference in magnitude between these two sets of trials.

4.4 Discussion

In the current study, we used different variants of a cued visual-attention paradigm in three separate experiments to investigate the functional roles of two markers of pretarget preparatory neural activity in visual cortex, namely the slow-wave Biasing-Related-Negativity (swBRN) ERP component and the simultaneously induced alpha-ERD activity. The results provide strong support for the view that these markers do not reflect the same underlying mechanism of preparatory sensory cortex activity. First, the swBRN was very sensitive to the manipulation of perceptual task difficulty, and not to the manipulation of response instructions, whereas the alpha-ERDs showed the opposite pattern. Second, the activity of these two markers did not correlate in either their strength or timing of onset. Third, their location over occipital-parietal scalp sites also differed, showing a broader swath of hemifield-specific responses with a more inferior maximum for alpha-ERDs, and a more superior, hemifield- and target-location-specific response for the swBRN activity, with the latter corresponding more closely to the N1 sensory-ERP distributions of the targets that would follow. Fourth, a further dissociation was found between the across-subject correlation of the amplitudes of both markers with the activity elicited by the targets that followed. More specifically, the swBRN correlated strongly with early sensory-evoked target-N1 amplitude, but not with that of the later parietal P3b activity, whereas alpha-ERDs did not correlate with the early N1, but correlated with the later P3b activity. Finally, the strengths of the swBRN and alpha-ERD activity also did not correlate across trials within subjects.

4.4.1 Functional significance of the Biasing-Related-Negativity

The sensitivity of the swBRN component to the perceptual difficulty level of the expected target stimulus and its correlation with subsequent early sensory N1 activity over identical brain areas is in line with the predictions from our previously proposed model (Grent-'t-Jong and Woldorff, 2007). This model, based on the combination of ERP recordings with fMRI measures of brain activity from a closely matched neuroimaging study (Woldorff et al., 2004), proposed a temporal cascade of attentional control processes following an instructional cue to covertly shift visual-spatial attention. This cascade begins with activity in the frontal eye fields (FEF), followed shortly later by activity in medial parietal regions, which together lead to the induction and maintenance of pretarget preparatory activity in visual sensory cortex contralateral to the direction of attention. This preparatory contalateral activity was reflected by both the contralateral BRN ERP wave and corresponding increased fMRI signal in low-level visual sensory cortex. In this previous work, we proposed that the pretarget contralateral BRN may reflect preparatory biasing activity in visual sensory cortex in response to control signal activity from frontal and parietal cortex, and thus we termed this negative-polarity electrophysiological activity a "biasing-related" negativity.

In the present study, we directly investigated this hypothesis concerning the role of this pretarget negative-wave activity. In particular, as noted above, we manipulated perceptual difficulty between experiments and found that the magnitude of the swBRN was, as hypothesized, larger when targets were expected to be perceptually more difficult to detect and thus it would be particularly advantageous to evoke sensory biasing. Also, as our ERP-behavior correlational analyses of exp3 suggests, even when detection was relatively easy, participants with stronger swBRN responses tended to show better performance in terms of their percentage of correct detections (higher hit rates). We also tested whether increased pretarget swBRN amplitudes would correlate with the amplitude of posttarget sensory-evoked N1 activity and showed that this indeed was the case. In addition, we compared the topographical distributions of the pretarget swBRN and the target-elicited N1 sensory component and showed that the swBRN distribution was both hemisphere and target-location specific. The results of all these analyses support the view that the BRN is a sensitive marker of sensory biasing and support the hypothesis that a baseline shift in target-location specific sensory cortical areas in advance of an expected target stimulus enhances the early sensory processing of such targets, thereby facilitating their detection.

The interpretation of the BRN as reflecting pretarget biasing activity that facilitates early sensory processing activity of the target fits with reports of baseline shift activity in non-human primate single-cell recordings that results in subsequent modulation of activity in exstrastriate cortex for attended stimuli (Luck et al., 1997; Reynolds et al., 1999). Moreover, it is consistent with the findings that microstimulation of frontal eye fields, at a level below the threshold needed to trigger a saccade, can produce modulation of firing rates in retinotopic visual areas such as V4 that resemble spatial attention effects (Ekstrom et al., 2009; Moore and Armstrong, 2003). The increase in sensory biasing ERP activity shown here with higher levels of expected perceptual task difficulty is comparable to such findings reported by Ress and colleagues with fMRI (Ress et al., 2000). And finally, the fact that the baseline shift interpretation fits the slow-wave BRN, rather than the higher frequency alpha-band power changes, is in line with earlier reports of slow cortical negative-polarity potentials representing increased excitability of underlying cortical areas (Brunia and van Boxtel, 2001), which have been shown to correlate with shifts in sensory thresholds (Devrim et al., 1999).

4.4.2 Functional significance of preparatory desynchronization of alpha-band activity

In the present study there was no comparable correlation for the pretarget preparatory alpha-ERDs with the evoked sensory N1 activity of the target. In addition, alpha-ERD activity was not sensitive to the expected perceptual difficulty of the target stimulus, On the other hand, in contrast to the perceptual-difficulty effects on the swBRN, the manipulation of response instruction in the present study clearly and robustly affected preparatory alpha-ERD activity. In particular, alpha-ERD activity was much stronger when instructions emphasized immediate responding (exp2) compared to when responses were delayed (exp1 and exp3). In addition, only when participants were preparing for possible immediate responses to potential target stimuli (exp2) did their alpha-ERD activity correlate strongly with the subsequently elicited, long-latency, parietal P3b activity to the targets, a correlation that was strongest over the left parietal scalp sites, as compared to the middle or right parietal ones. This combination of results suggests that preparatory alpha-band desynchronization activity in posterior cortex (alpha-ERDs) reflects more than just stimulus-specific preparation. The parietal P3b component has been linked to stimulus-evaluation and decision-making processes (see e.g., Kok, 2001), and thus it might well be that the contralateral alpha-ERD activity reflects the formation and maintenance of an attentional template or task set, containing both stimulus features as well as task-specific features (such as response instructions), which then is implemented for the processing of the target stimulus during the P3 latency window. Note that this interpretation is for contralateral alpha-ERDs only (i.e., alpha power decreases), as the present study did not produce ipsilateral alpha-ERS activity (i.e., alpha power increases) following attend cues, presumably because of a lack of to-be-ignored distractors. Accordingly, we cannot comment on the functional significance of ipsilateral alpha power increases.

Some earlier visual-spatial attention studies have reported correlations between preparatory lateralized alpha activity (greater ERDs or lower alpha power) and improved behavioral detection and/or discrimination performance (Kelly et al., 2009; Thut et al., 2006; Trenner et al., 2008; Yamagishi et al., 2008). In addition, other non-cueing, auditory (Jasiukaitis and Hakerem, 1988; Price, 1997) and visual non-spatial attention studies (Hanslmayr et al., 2007; Min and Herrmann, 2007) have reported correlations between pretarget alpha activity (power) and behavioral performance. In addition, the Hanslmayr et al. (2007) study showed that prestimulus oscillatory alpha activity can correlate differentially with different aspects of cognitive processing and task performance (perception-related versus memory-related in particular).

In the current study, however, no significant correlations between prestimulus alpha-power changes and subsequent behavioral performance were found for either exp2 (hit rate and mean reaction time) or exp3 (hit rate only), the only two experiments here that could be used to investigate such correlations. It should be noted, however, that our tests were necessarily performed across participants, because the low number of available target trials (on average maximally 56 per cue type) did not allow the use of within-subject single-trial correlational analyses. Importantly, however, the earlier reported significant correlations in the literature were of correlations with behavioral performance only, with no relationships with respect to target ERP activity being reported. Unfortunately, a correlation with later behavioral outcome does not delineate the underlying mechanisms that brought about these changes. Improved performance can be explained both by improved early perceptual processing as well as by improved late decision-making processes, or by a combination thereof, or by still other mechanisms. The current study revealed that pretarget alpha-ERD activity correlated with the later target P3b activity, but not with the early target N1 activity (in contrast to the swBRN, which showed the opposite pattern), suggesting that the processes reflected by changes in prestimulus alpha power may bring about their behavioral effects by influencing later decision-making stages of information processing rather than by influencing earlier perceptual processes. Interestingly, the studies cited above all used the more typical instruction of immediate responses to target stimuli, and our current study showed that only under such instructions does prestimulus alpha-ERD activity correlate with the later P3b amplitudes of the targets (but still not with early sensory activity). Accordingly, the current pattern of results suggests that the behavioral improvement observed in those other studies resulted from improved task-set preparation, rather than improved perceptual performance due to a baseline sensory shift. Future studies that include both recordings of electrical brain activity and appropriate behavioral measures could further test this hypothesis .

4.4.3 Topographic distribution of markers of visual cortex preparatory activity

Although in the current study it was not feasible to effectively localize the sources of the preparatory electrophysiological marker activity in the brain, the distribution of the preparatory swBRN distribution did not differ from that of the target N1 sensory component, suggesting similar neural sources, presumably predominantly involved in perceptual processing activity. In contrast, the topography of the alpha-ERD activity differed from both the swBRN and N1 distributions, thus providing evidence for a different functional role than just the biasing of sensory regions to facilitate perceptual processing. In particular, as suggested above, it is possible that alpha-ERD activity reflects the coding and maintenance of an attentional trace (task-set representation) that includes linking of expected sensory and motor aspects of the upcoming task.

An increasing amount of data can be found in the literature supporting the presence of such preparatory sensorimotor activity in posterior brain areas. In the animal literature, for example, the lateral intraparietal lobule (LIP) and the parietal reach area (PPR) in particular have shown increased firing-rates during delay periods (see e.g., Andersen and Buneo, 2002; Platt and Glimcher, 1997), coding both expected target location as well as action intentions (saccades, reaching). Recently, it has been proposed (Bisley and Goldberg, 2010) that these parietal cortical areas code a priority map in which the amount of preparatory activity is proportional to the expected behavioral relevance and value, an idea that fits well with our observation of increased alpha-ERD activity with increasing motor readiness (immediate versus delayed responses). In humans, brain areas in the intra-parietal sulcus (Medendorp et al., 2005) have been shown to code the location for an upcoming saccade, both the direction of the expected target location for prosaccades as well as the opposite direction for antisaccades. In a follow-up study from the same research group (Medendorp et al., 2007), lateralized visual-spatial alpha-ERDs were found during delay periods that could be localized to areas in posterior parietal and occipital cortex, which the authors argued were close to areas V3A and LIP in the monkey that were found to be active during comparable tasks. In sum, our findings suggesting that the alpha-ERDs code both the hemifield of the expected target location as well as action intentions could well reflect activity from a human homologue of the monkey parietal cortex regions that have been proposed to code priority maps during delay periods.

4.4.4 Preparatory top-down attentional control strategies

A perhaps somewhat surprising finding in the current study is the pattern of the effects on brain activity and behavior that the response instruction had. In particular, the data from exp2, in which participants were asked to immediately respond to target stimuli, were clearly qualitatively different from exp1 and exp3, in which responses were delayed. Participants in exp2 also detected more targets than in the other two experiments. Furthermore, their cue-related activity differed from the other two experiments in that it did not contain significant swBRN activity, but, in contrast, contained a much stronger alpha-ERD response with a much earlier onset latency. In addition, in this experiment, preparatory attention affected target processing relatively late (at the level of the longer-latency parietal P3b activity between 350-500 ms post-target onset), not during, or very limited during, the earlier sensory-cortex level of analysis (lateral-occipital P1/N1 activity, before 200 ms). Such a pattern could be explained by differences in induced task strategies. For example, the participants in exp2 may have been using more of an "attention-for-action" strategy, with a stronger focus on the intention to respond as quickly as possible to detected target stimuli, whereas the participants in exp1 and exp3 may have used more of a pure "attention-for-perception" strategy. That is, in the later case the data would appear to show a pretarget location-specific baseline shift for increasing perceptual sensitivity, leading to subsequently enhanced responses in early, sensory cortex activity to the targets.

4.5 Conclusions

In conclusion, the present study adds more in-depth knowledge on the functional significance and relationships between two different electrophysiological markers of sensory-cortex, preparatory activity during the covert allocation of spatial attention, namely the contralateral slow-wave Biasing-Related-Negativity (BRN) and the contralateral alpha-band power decreases (alpha-ERDs). In particular, the swBRN correlates with early location-specific sensory-evoked (N1) responses to the targets, especially under situations of expected perceptually degraded task stimuli, consistent with reflecting a neural activity baseline shift for increasing the perceptual processing of these stimuli. In contrast, alpha-ERD activity correlates with the longer-latency target P3b activity, but only when immediate responses to targets are required. This could point to a role of preparatory alpha oscillations in establishing and maintaining an active task set (representing both stimulus- and response requirements), which then can be used subsequently as an attentional template during final decision-making and task-performance output. Finally, this multi-experiment study clearly shows that key changes in the task paradigm, both in terms of expected perceptual difficulty and behavioural response requirements, can shift participants into different preparatory strategies. Such differential strategies, and the differential attention-related preparatory activation patterns they might lead to, are fundamental factors for understanding the neural processes underlying attentional control.

Chapter 5

Top-down attentional control strategies and susceptibility to crossmodal distraction

Grent-'t-Jong, T., Donohue, S.E., & Woldorff, M.G. (2011). Top-down attentional control strategies and susceptibility to crossmodal distraction. *Preliminary manuscript for publication*.

ABSTRACT

Today's technological advances have increased the amount of cognitive distraction due to conflicting sensory input, potentially triggering impulsive, erroneous, and/or dangerous behaviors. Although much is known about neural activation patterns associated with detecting and helping resolve cognitive conflict during distraction, much less is known about the possible influence of voluntary control strategies on conflict processing. The current EEG study explores the effects of two voluntary task strategies, in a within-subject design, on brain activity and behavior recorded during a cued, crossmodal conflict, letter-discrimination task, a task that revealed conflict-resolution related activity in task-relevant sensory cortices in our previously published fMRI study (Weissman et al., 2004). In one strategic mode ("attention-for-accurate-action", AttAct) preparation was focused strongly on establishing a proper task set, followed by careful implementation thereof to ensure accurate target responses, at the cost of being fast. Under the alternative, "attention-for-speeded-perception", strategy (AttPerc), participants focused more strongly on selectively orienting attentional resources to the task-relevant modality in order to improve subsequent input gain, while emphasizing speed of responding to targets over being accurate. The results showed that the AttAct strategy led to highly accurate, but slower responses, as expected, but which also included large behavioral interference effects that were preceded by weak pre-target preparatory activity and strong post-target conflict-processing activity, even at the fastest trials. The AttPerc strategy, on the other hand, led to faster, but less accurate, responses, preceded by stronger frontocentral preparatory attentional-control activity and reduced target conflict-processing activity. This strategy additionally induced stronger pre-target, modality-selective, sensory-cortex biasing activity, followed by improved post-target early sensory-perceptual target-selection activity. In conclusion, voluntary task strategies strongly influence brain activity and behavior in the face of potential crossmodal distraction. The results indicate that strong attentional control results in enhanced sensory gain and early selection, which subsequently affects interference from task-irrelevant stimuli.

5.1 Introduction

Distraction as a result of goal-conflicting, distracting, sensory input has become the hallmark of daily life in our complex, technology-driven society. While reading this article your phone might start ringing, or a message might pop-up on your computer notifying you of the arrival of a new e-mail. Under many circumstances, immediately responding to such salient, distracting events may be inefficient or perhaps regarded as socially inappropriate behavior. Moreover, if you have a deadline that requires you to finish reading this article within the next 10-15 minutes, it would be important to find a way to ignore such distraction as it conflicts with a prioritized goal of meeting your deadline. More than ever, we are in need of flexible cognitive strategies that can help us cope with the ever increasing onslaught of new information and the associated increase in possible sources of distraction.

During the last two decades, important clues have been uncovered about how flexible control over our behavior can be implemented in the brain. Based on emerging behavioral and functional MRI (fMRI) evidence, one influential neuro-computational model of cognitive control, the conflict-monitoring and conflict-adaptation hypothesis (Botvinick et al., 1999; Botvinick et al., 2001; Botvinick et al., 2004; Botvinick, 2007; Carter et al., 1998) theorizes that the brain is equipped with a set of functionally interrelated regions that monitor ongoing information processing, detect conflict or response errors and subsequently assist in resolving the conflict. More specifically, the theory holds that after conflict is detected by the anterior cingulate cortex, this region rapidly reacts by triggering top-down attentional control, mediated by regions such as the dorsolateral prefrontal cortex (DLPFC), to help resolve the conflict. A substantial amount of converging evidence has supported key aspects of this model in terms of its proposed anatomical substrates and internal functional connectivity within the context of conflict processing (reviewed in e.g.: Carter and van Veen, 2007; Egner, 2007; Egner, 2008; Ridderinkhof et al., 2004; Verguts and Notebaert, 2009). An essential part of the supporting evidence also comes from the study of trial-to-trial sequential effects (Kerns et al., 2004; e.g., Kerns, 2006; Ullsperger et al., 2005), describing the finding that faster and more accurate responses can be provided when the brain very recently (e.g., on the previous trial) detected conflict, compared to when such conflict was not induced recently (a.k.a. conflict-adaptation).

Other clues on how the brain deals with distraction have been provided by models of selective attention, such as, for example, the Biased Competition Model (Desimone and Duncan, 1995), the Load Theory of Selective Attention (Lavie, 1995), and versions of the Sensory Gain Control model (e.g., Hillyard and Mangun, 1987), amongst many others. In contrast to the more conflict-detection triggered control mechanisms that form the core of the conflict-monitoring theory described above, attentional control models suggest that substantial behavioral improvements can be brought about by control mechanisms that are more often imparted voluntarily following an external (instructional) cue or an internal (motivational / intentional) source. The various models of selectively focused attention may differ with respect to postulated exact underlying mechanisms, but they all tend to agree on one basic principle. In particular, this principle holds that a top-down attentional control network coordinates pre-target, stimulus-specific, sensory preparation, which, once the target stimulus is received, aid in selectively enhancing the processing of relevant information in the stimulus and/or inhibiting irrelevant information, and that this tends to begin at a relatively low and early perceptual level of stimulus processing. This selective processing modulation in turn helps to speed-up later stimulus-evaluation and decision-making processes, leading to improved behavioral performance. Translated to the example in the introduction above, selective attention models would argue that rather than waiting for the phone call or email message to automatically trigger late-selection (i.e., post-perceptual) control mechanisms that would help orient you back to your primary task and help resolve the conflict (either now or in the future), one could also decide to strongly focus attentional resources to the task at hand (reading this article) in a more sustained way. This approach could help to reduce possible distractions at the sensory input level in the first place (by promoting early selection through top-down preparatory control).

Recently, a new model of flexible cognitive control has been proposed, termed the "Dual Mechanisms of Control (DMC)" model (see Braver et al., 2009). According to this model, human beings have flexible control over whether they are operating more in, what the authors refer to as, "reactive control mode" or "proactive control mode". In proactive control mode, participants actively maintain the task-goals as well as actively bias attention, perception, and action systems optimally during preparation to promote "early selection" of task-relevant information when the expected stimulus arrives. In contrast, when participants are operating in reactive control mode, the prediction is that attentional control is more likely recruited as a "late correction" mechanism, activated only when needed, such as after the detection of conflicting stimulus input (Braver et al., 2009, page 7351). The predicted effect in this model of a shift from reactive to proactive attentional control on the timing of target selection (late to early) is consistent with predictions from selective attention models. However, evidence for such a shift, for example in the form of task-selective changes in sensory cortex, were not reported in the Braver et al. (2009) study. Note, however, that the low temporal resolution of the fMRI method used in this study would not have been sufficient to extract such information. One would need the higher resolution of, for example, the event-related potential (ERP) method.

If participants indeed have flexible control over the mode in which they are operating, this would lead to some interesting questions to investigate in the current study with the use of high-temporal resolution EEG recordings. First, would a shift in strategy from a more "reactive" (as defined by Braver and colleagues) to a more "proactive" control mode indeed lead to a shift from late to early selection? In the present study, this question will be addressed by looking at strategy dependent changes in the amplitude of early (visual cortex) N1 evoked potential activity under task-relevant and task-irrelevant conditions. In addition, strategy induced changes in sensory cortex biasing activity will be investigated by examining changes in event-related alpha-band activity (esp. alpha desynchronization). Sensory cortex alpha oscillatory activity can be expected to respond to changes in the strength of preparatory attention (Grent-'t-Jong et al., 2011) as well as to respond differentially to attention shifts across modalities (Fu et al., 2001). A second interesting question that will be address in this study is whether a change in strategy and possible shift in the timing of selection would subsequently lead to a change in the amplitude and/or timing of the earliest conflict-detection related N2 ERP component. The N2 difference between the ERP response to congruent and incongruent trials has been shown to be linked to conflict detection (Folstein and Van Petten, 2008), and to be associated with conflict-related anterior cingulate activity seen in fMRI studies (Van Veen and Carter, 2002). Furthermore, strategy dependent changes in the strength of frontal cortex preparatory activity will also be investigated in their relationship with subsequent frontal cortex target conflict processing activity as a function of response speed, following up on the recent findings of a relationship between prestimulus frontal cortex activity and subsequent response speed and conflict-related activity (Weissman et al., 2006). Currently only a few, recently published, ERP studies exist that are somewhat relevant for these questions because of their focus on the comparison between effects of preparatory activity and subsequent conflict-related activity (e.g., Alpay et al., 2009; Correa et al., 2009). These studies, however, did not provide clear answers to the above outlined questions.

In order to better answer the above introduced questions, the current study included a modified, two-strategy version, of a cued crossmodal letter-discrimination conflict paradigm we employed in a previous fMRI study (Weissman et al., 2004). In this paradigm, participants were cued at the beginning of each trial as to which modality was relevant for an upcoming audiovisual target stimulus pair, with the task to determine whether the target letter in the cued modality of the target-distractor pair was an X or an O. The distractor in the irrelevant modality on each trial could be either congruent or incongruent with the target stimulus (equal probability). Participants were trained to use a more reactive control mode with accuracy-over-speed response emphasis ("attention-for-accurate-action" strategy, further abbreviated as "AttAct") in half of the experimental blocks, and to use an alternative more proactive control mode with speed-over-accuracy response emphasis ("attention-for-speeded-perception" strategy, further abbreviated as "AttPerc") in the remaining blocks. A speed-accuracy trade off manipulation was used to ensure that participants would truly use two entirely different task approaches. Speed-accuracy trade off independent estimation of the effects of strategy changes on preparatory activity, early sensory activity and conflict N2 activity were ensured by looking for the interaction between macro-level (between blocks of trials) effects of strategy and micro-level (within-block) effects of response speed (using median-split, reaction-time dependent, averages). We expected that the implementation of the two qualitatively different task-strategies would provide insight into the nature and timing of the selection of task-relevant information in sensory cortex. More specifically, we expected this selection to be earlier with the speeded-perception focused AttPerc strategy than with the more accurate-action focused, AttAct strategy. In addition, we expected that the AttAct strategy, compared to the AttPerc strategy would result in more accurate responses, but likely at the cost of increased conflict-related N2 activity.

5.2 Methods

5.2.1 Participants

Ten healthy adult volunteers (6 female, 7 right-handed) participated in the study (mean age 26.8 yrs, stdev 7.8). Data from seven additional participants were excluded due to either poor behavioral performance (two participants), early withdrawal (two participants), or high contamination of the EEG data with eye and muscle artifacts (three participants). Participants gave written informed consent and were financially compensated for their time. All procedures were approved by the Duke University Health System Institutional Review Board.

5.2.2 Stimuli and task procedures

The current study used a modified two-strategy version of a cued crossmodal letter-discrimination conflict paradigm we employed previously in an fMRI study (Weissman et al., 2004). At the beginning of each 2500-3500 ms trial (Fig. 1), a cue instructed participants to attend to and identify either the visual component or the auditory component of a possibly upcoming audiovisual target-distractor stimulus pair ("attend cues") or to just "wait" until the next cue because no target would occur on that trial ("wait cues"). The visual component of the target-distractor pair consisted of the letter "X" or the letter "O" (1.7° x 1.8° presented at fixation in the middle of a computer screen) and the simultaneously presented auditory component consisted of a spoken letter (also an X or O) presented bilaterally through headphones. On two-thirds of the attend-cue trials, an audiovisual target-distractor pair would follow ("attend-cue-plus-target" trials) but on the remaining one-third of the trials no target-distractor pair would occur (“attend-cue-only trials).

The cue stimuli included two types of attend cues - "LOOK" (attend visual) and "HEAR" (attend auditory) - and one type of control cue ("WAIT", until next cue), which could be presented at fixation either visually (4.5° x 1.1°) or auditorily (bilaterally through the headphones) with equal probability. Auditory stimuli were presented at an intensity level of approx. 65 dB. Participants were instructed to press one button if the target letter in the cued modality was an X and a different button when it was an O, using the index and middle fingers of their right hand. In the attend-cue-plus-target trials, the distractor component of the multisensory target-distractor pair that followed the attend cue was equally likely to be mapped to the same response as the target (a congruent target-distractor pair; Fig. 1 bottom left) or to the competing response (an incongruent target-distractor pair; Fig. 1 bottom right), in which case the distractor conflicted with task goals. Both the unimodal cue stimuli and the multisensory target-distractor stimuli were presented for a duration of 350 ms. Cue-target stimulus onset asynchrony (SOA) was always

1250 ms, whereas the target-to-next-cue SOAs were jittered between 1250-2250 ms. In all trials, the fixation dot (0.22° x 0.22°) changed color from white to red 1250 ms after cue onset (coincident with target presentation in cue-plus-target trials) to signal that no target would occur in cue-only trials (see Corbetta et al., 2002; Weissman et al., 2004). Participants were asked to cease attending when the fixation dot turned red and no target occurred, so they could be ready for the next cue.

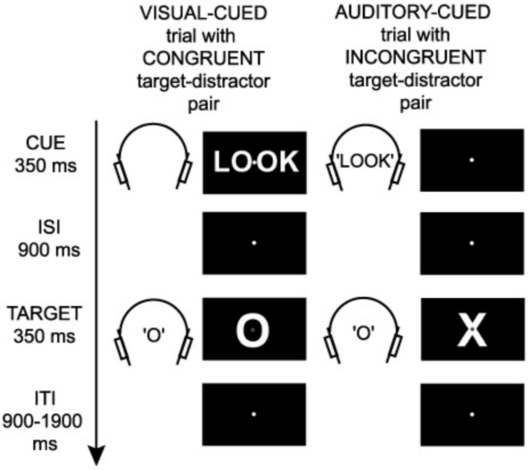


Fig. 1. Schematic illustration of the cued crossmodal distraction paradigm, showing two possible trials. The cue-plus-target trial on the left shows a visually presented cue instructing the participant that the visual part of the upcoming multisensory stimulus is task relevant, followed by a congruent target-distractor pair. The cue-plus-target trial on the right shows an auditorily presented cue with the same instruction (visual modality is task relevant), followed by an incongruent target-distractor pair.

Each experimental block included 14 trial types presented in randomized order: eight "cue-plus-target" trial types and 6 "cue-only" trial types (details below), with a runtime of approx 4.5 minutes for 180 trials. In each block, one-third of the trials were control-cue-only trials (50% visual "WAIT" cues, 50% auditory "WAIT" cues), and the remaining trials consisted of one-third attend cue-only and two-thirds attend cue-plus-target trials (both containing 25% visual "LOOK", 25% visual "HEAR", 25% auditory "LOOK", 25% auditory "HEAR"). Cue-plus-target trials contained either congruent (50% probability: "visX+audX" or "visO+audO", equal probability), or incongruent target-distractor pairs (50% probability: "visX+audO" or "visO+audX", equally likely). Note that, in contrast to some earlier cued conflict studies (e.g., Correa et al., 2009; Luks et al., 2007), congruency of the upcoming target-distractor pairs in a run was unpredictable, and thus participants could not specifically and differentially prepare for the upcoming conflict.

Prior to the EEG recordings, participants were invited to the lab for a training session in order to become familiar with the general paradigm and more specifically with the two different experimental task strategies. One strategy, referred to here as the "attention-for-accurate-action" strategy (AttAct) included an approach in which the participants were asked to emphasize storage and maintenance of the cue information during the cue-target delay interval for later use during the final target stimulus processing (task-set /action oriented), for which they were asked to respond to as accurately as possible and not to worry about responding rapidly (*"Focus on knowing the right answer with the highest degree of certainty, based on the task specifications that you should remember from the cue instruction"*). The other strategy, referred to here as the "attention-for-speeded-perception" (AttPerc) strategy, consisted of an approach in which the participants were asked to translate the task-relevant information from the cue immediately into the action of directing all available attentional resources toward the cued input channel (the computer screen or the headphone input; i.e., perception-oriented), and in addition, to emphasize speed-over-accuracy in their responses (*"Focus on immediately directing all your attention to the cued input channel - eyes or ears - which should help you to reduce the impact of the possible distractor better, allowing for faster responses. Try to prepare so well that you can safely increase your response speed, while still keeping the amount of errors reasonably low*"). The added speed-accuracy trade off switch between the two strategies was motivated by the idea that with a more modality-selective speeded-perception driven preparatory task strategy (AttPerc) participants would be able to base their response decision already on their initial sensory-perceptual analyses (due to attentionally improved signal-to-noise ratio), whereas they would likely have to rely on more late task-set stimulus-response mapping processes under the alternative, more accurate-action driven preparation strategy (AttAct). Manipulating the task instructions this way also ensured that participants would truly use two entirely different task approaches. Participants received 45-60 minutes of training to ensure their proper understanding of these two strategies and how to implement them and the ability to switch strategies between blocks of trials. During the main experiment that included the EEG recordings, participants ran eight blocks of trials in each strategy condition, changing strategy every other set of two runs.

5.2.3 Data acquisition

The EEG was recorded from 64 electrodes mounted in a custom-designed, extended-coverage electrocap (Duke64-cap layout, made by Electro-Cap International Inc, Eaton, Ohio) and referenced to the right mastoid during recording. The 64 channels were equally spaced across the cap and covered the head from above the eyebrows to the lower occiput (slightly past the inion). Vertical eye movements and eye blinks (VEOG) were recorded from two electrodes placed below each eye, referenced to the scalp electrodes above the eye in a bipolar montage. Horizontal eye movements (HEOG) were recorded from two electrodes placed on the outer canthi of the eyes, referenced to each other (bipolar montage). Eye movements were also monitored on-line with a video zoom-lens camera. Electrode impedances were maintained below 2 kΩ for the mastoids, below 10 kΩ for the EOG electrodes, and below 5 kΩ for all remaining electrodes. All EEG and EOG channels were continuously recorded with an online band-pass filter of 0.01 to 100 Hz (Neuroscan SynAmps amplifiers) and digitized with a 500-Hz sampling rate. Recordings took place in an electrically shielded, sound attenuated, dimly lit, experimental chamber. Stimuli were presented using the Presentation software package (Neurobehavioral Systems Inc, Albany, CA).

5.2.4 Behavioral analyses

In the behavioral analyses, mean reaction time and response accuracy measures were determined, separately for each Strategy, for the following target-present conditions: attend-visual-congruent-auditory-distractor, attend-visual-incongruent-auditory-distractor, attend-auditory-congruent-visual-distractor and attend-auditory-incongruent-visual-distractor target trials. Correct reaction times faster than 150 ms post-target onset or slower than twice the standard deviation away from the mean of all reaction times within each condition were removed from the final averages. In order to extract a more speed-accuracy trade off independent estimation of the effect of task strategy on behavioral interference (in accordance with the same approach taken for the analyses of EEG/ERP data), data were also (median) split into the 50% fastest and 50% slowest reaction time trials within each condition for later comparisons. Accuracy was determined by estimating the percentage of incorrect responses (wrong button presses) of the total number of possible correct responses for each of the different conditions. Experimental differences between conditions were assessed by submitting the final averages to rANOVAs, including the within-subject factors STRATEGY (AttAct, AttPerc), CONFLICT (congruent, incongruent), RTSPEED (fast, slow), and task-relevant MODALITY (auditory, visual). Significance was inferred for p-values lower than 0.05.

5.2.5 EEG/ERP analyses

EEG analyses were performed using EEGLAB 7.1.3.14b (Delorme and Makeig, 2004), after down sampling of the raw data to 250 Hz. Final epochs for the different analyses of cue-related activity included data between 200 ms pre-cue and 1250 ms post-cue onset, whereas epochs for target-related activity included data between 100 ms pre-target and 1500 ms post-target onset. Cue and target ERPs were extracted from the same set of preprocessed trials.

Preprocessing started with the removal of trials that contained high-amplitude muscle artefacts or were contaminated by eye blinks or eye movements. Trials with eye blinks were only rejected if the blink occurred near stimulus presentation times (200 ms before and 350 ms after both cue and target onsets). Other blink contamination was subsequently removed using independent components analysis (ICA) in EEGLAB. After these preprocessing steps, the data were divided into three separate analysis pipelines, one for the cue ERPs (for the estimation of preparatory frontal cortex attentional orienting activity), one for target-related ERP activity (estimation of both visual cortex N1 activity as well as frontal cortex conflict-related

N2 activity), and one for the cue-induced changes in preparatory alpha-band (8-13 Hz) power (estimation of visual cortex preparatory, biasing-related, activity).

For the cue ERPs, cue-only and cue-plus-target trials (congruent and incongruent collapsed) were averaged together for attend-visual and attend-auditory conditions within each of the two strategy conditions, collapsed across the modality of cue presentation. Target ERPs were extracted from the cue-plus-target trials (correct trials only), separately for attend-visual, attend-auditory, congruent and incongruent trials. In addition, separate cue- and target-ERP datasets were generated for median-split FAST and SLOW response trials (extracted from cue-plus-target trials) within each condition. All final cue and target ERP averages were imported into ERPSS (ERP analysis software package; UCSD, San Diego, CA) for further analyses. These analyses included re-referencing of the data for all channels to the algebraic mean of the two mastoid electrodes, filtering the cue-ERP data with a low-pass filter of about 56 Hz, filtering the target-locked ERPs with a low-pass filter of about 40 Hz, and finally topographical and statistical analyses.

The analysis pipeline used to extract the induced alpha-band activity started with the computation of averaged Event-Related Spectral Perturbations (ERSPs) over all embedded frequencies (0.01-100 Hz) using the EEGLAB software package, separately for each condition and each channel, using Fast Fourier Transforms (FFTs) of single trials with a frequency resolution of 1.95 Hz. Subsequently, averaged event-related induced alpha-band (8-13 Hz) responses were extracted for all channels from these data, separately for attend-visual and attend-auditory cues from each of the strategy conditions. These data were then further analyzed in ERPSS in the same way as the ERP data.

5.2.6 Statistical EEG/ERP analyses

Statistical analyses of the cue ERPs included the following separate repeated-measures ANOVAs (rANOVAs). Attentional orienting activity was tested on (1) only cue-plus-target trials, separated into cue-plus-fast-RT-target trials (FAST trials) and cue-plus-slow-RT-target trials (SLOW trials), as well as on (2) all cue-plus-target trials and all cue-only trials. The rANOVA analysis for cue-plus-target trials only (first rANOVAs) included the within-subject factors STRATEGY (attend-minus-control activity in AttAct versus AttPerc) and RTSPEED (fast trials versus slow trials). The second rANOVAs for all cue-plus-target and cue-only trial data included the within-subject factors STRATEGY (AttAct, AttPerc) and ORIENTING (attend cues, control cues). Both rANOVAs were repeated for successive 50 ms bins of the extracted ERPs between 250 and 1250 ms post cue onset (relative to a 200 ms pre-cue baseline), on scalp regions of interest (ROIs) encompassing six mid-frontocentral channels, corresponding approximately to the 10-5 system locations (Oostenveld and Praamstra, 2001) of FCz, Cz, FFC1, FFC2, FCC1, and FCC2, respectively[1] (see Fig. 4 for an overview of the location of these ROI channels).

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[1] Channels of our customized cap-design, which deviate from the standard 10-10/5 system, will be referenced with labels corresponding to the closest 10-5 system electrode location.

Statistical analyses for alpha-band preparatory activity included cue-baselined (-200-0 ms) alpha ERSP data from the attend-visual and attend-auditory cue trials (collapsed across cue-only and cue-plus-target trials) averaged between 750-1250 ms post cue (the last 500 ms pre target), extracted from eight lateral occipital-parietal channels (corresponding to the 10-5 system locations O1, O2, PO3, PO4, PPO5, PPO6, CPP3, and CPP4, respectively; see Fig. 5 for an overview of the location of these ROI channels). The rANOVAs used to extract modality-selective alpha-band power modulation effects included the within-subject factors STRATEGY (AttAct, AttPerc) and MODALITY (attend visual, attend auditory).

For target-related activity, the amplitudes of the visual-cortex N1 ERP component (150-180 ms; 100 ms baseline), averaged over the same eight occipital-parietal channels as used for the alpha-band power analyses, were tested for significant differences between modality of task-relevance, within each strategy condition, with rANOVAs, using the within-subject factors RTSPEED (fast trials, slow trials) and MODALITY (attend visual, attend auditory). Finally, conflict-related frontocentral N2 activity was tested in subsequent 20 ms bins of averaged data (100-ms pre-target baseline) between 200-400 ms post-target onset over the same mid frontocentral ROI as used for the attentional orienting activity, using rANOVAs including the within-subject factors STRATEGY (AttAct, AttPerc), CONFLICT (congruent, incongruent) and RTSPEED (fast trials, slow trials). For all statistical tests, in order to reduce type 1 errors, significance for an effect was inferred only if at least three consecutive data bins of 20 ms were significant at p< .05 level.

5.3 Results

5.3.1 Behavioral performance

Figure 2 summarizes grand average (n=10) estimates of behavioral performance, including mean reaction times and response accuracy, separately for the several different experimental conditions. Repeated-measures ANOVAs (rANOVAs), including the factors STRATEGY (AttAct, AttPerc), CONFLICT (congruent, incongruent), RTSPEED (fast, slow trials), and MODALITY (attend visual, attend auditiory), of both mean reaction time and response accuracy data from all conditions revealed the following results. First, the speed-accuracy tradeoff (SAT) manipulation incorporated into the two instructed strategies (emphasizing accuracy under the AttAct strategy and speed under the AttPerc strategy) led, as expected, to the same participants being significantly faster when applying the AttPerc than the AttAct strategy (main effect of STRATEGY, F(1,9)= 76.4, p< 0.0001). However, this overall increase in response speed under the AttPerc strategy, compared to the AttAct strategy, was accompanied by an increase in response errors (main effect of STRATEGY, F(1,9)= 22.3, p= 0.001).

Secondly, participants committed substantially more response errors following auditory than visual targets under the AttPerc strategy, compared to when they applied the AttAct strategy (STRATEGY x MODALITY interaction effect: F(1,9)= 9.6, p= 0.01). Third, independent of strategy, participants were slower and less accurate in responding to auditory targets than to visual targets (main effect of 19.1, p= 0.002), a result consistent with similar findings reported for the previously published corresponding fMRI study (Weissman et al., 2004).

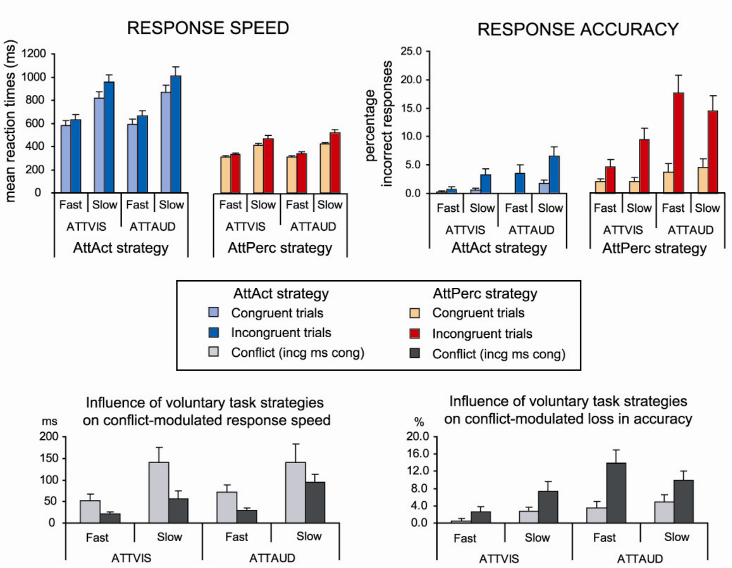

Fig. 2. Overview of grandaverage (n=10) mean reaction times and mean accuracy levels (percentage correct responses) computed for congruent and incongruent target-distractor pairs, separated further for median-split based fast and slow trials within the two different relevant modalities (attend visual [attvis] or attend auditory [attaud]) and strategies (AttAct and AttPerc strategy). Response speed data is displayed on the left, and response accuracy on the right. The top histograms contains the values for each individual condition (error bars represent standard error of the mean), whereas the bottom histograms summarize the interaction effects between strategy and behavioral interference (conflict) effects (incongruent minus congruent conditions) on mean reaction times and percentage of incorrect responses.

With respect to susceptibility to distractor interference, participants responded slower and made more errors on incongruent compared to congruent trials (main effect of CONFLICT on reaction times: F(1,9)= 19.4, p= 0.002; and on accuracy: F(1,9)= 56.0, p< 0.00001). Interestingly, conflict effects for mRT were significantly reduced (STRATEGY x CONFLICT interaction effect for mRTs: F(1,9)= 6.7, p< 0.03) when participants were using the AttPerc strategy (AttPerc: INCG minus CONG mRTs: 51 ms, stderr 10.2 ms) compared to when they were using the AttAct strategy (AttAct: INCG minus CONG mRTs: 101 ms, stderr 25.9 ms), and this effect was independent of modality (i.e., STRATEGY x CONFLICT x MODALITY was not significant). However, across modality and speed, participants made significantly more conflict-related errors in the AttPerc than in the AttAct strategy condition (STRATEGY x CONFLICT interaction effect: F(1,9)= 14.7, p= 0.004). Finally, participants experienced significantly more RT conflict on (median-split) slower trials than on faster trials (CONFLICT x RTSPEED interaction effect:

F(1,9)= 11.6, p= 0.008), averaged across strategy and modality conditions, indicating that, in general, response speed diminishes behavioral interference effects. However, CONFLICT x RTSPEED effects on accuracy were not significant. Finally, STRATEGY x CONFLICT x RTSPEED interaction effects were not found for either reaction time data (p= 0.10) or accuracy data (p= 0.56).

In sum, behavioral performance as reflected in the correct RTs, pointed to a significant decrease in behavioral interference effects (incongruent-minus-congruent RT differences) as a result of both between-block adjustments of long-term task strategies (i.e., macro-level effect), as well as within-block, fast versus slow, adjustments in responding (i.e., micro-level effect). Although no STRATEGY x CONFLICT x RTSPEED effects were found for reaction time and accuracy data, it is possible that increased behavioral interference (conflict) effects still correlated with increased amounts of response errors across the RT distribution. If so, this would mean that the speed-accuracy trade off, embedded in the two strategies, would confound possible strategy-dependent conflict-related effects present in the EEG/ERP data.

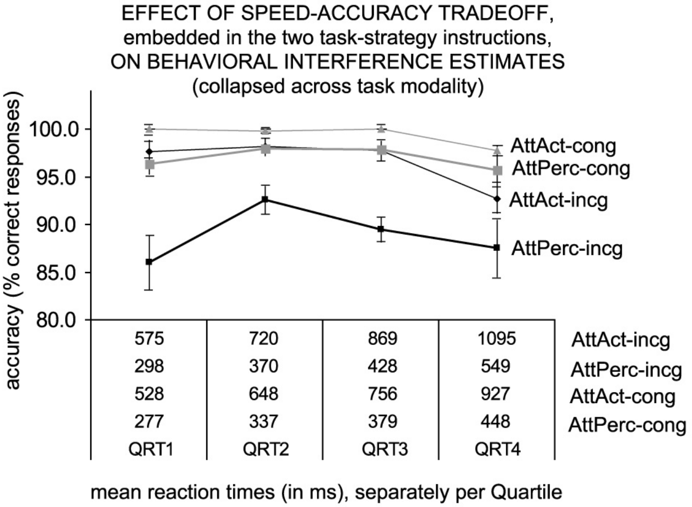

Fig. 3. Grandaverage (n=10) mean reaction times and mean accuracy levels (percentage correct responses) as a function of response speed (quartile-split data), computed separately for congruent and incongruent target-distractor pairs within strategy conditions (averaged across task modalities). Vertical bars indicate standard errors of the means across participants.

In order to rule out this possible confound, quartile-split reaction-time data were plotted against their corresponding quartile-split error rates (see Fig. 3), and the extracted quartile-split accuracy data were submitted to rANOVAs, including the factors STRATEGY (AttAct, AttPerc), CONFLICT (congruent, incongruent), and QUARTILES (1, 2, 3, 4). Consistent with a clear absence of such a correlation in

Figure 3, the rANOVAs did not reveal any significant effect of response speed on error rates (the Greenhouse-Geisser corrected p-value for the STRATEGY x CONFLICT x QUARTILE interaction was 0.46). These results thus validate the approach taken for investigating strategy-induced effects on conflict processing in the EEG and ERP data analyses, as described below.

5.3.2 EEG/ERP data

The analyses of the EEG data focused on answering our two main questions. First we will look at the more general effects voluntary strategies had on frontocentral pre-target preparatory brain activity, as well as on subsequent conflict-related target-response activity for trials containing an incongruent distractor in the irrelevant modality (section 5.3.2.1), as a function of response speed. We will first investigate this relationship at a single-trial level, in subsection 5.3.2.1.1, by examining reaction-time sorted frontocentral single-trial ERP activity across time (including cues and subsequent targets) for our four conditions of interest (congruent and incongruent trials within the two different strategy conditions) with the use of so-called ERP images. Subsequently, in subsections 5.3.2.1.2 and 5.3.2.1.3, extracted target RT-based median-split ERPs are contrasted between strategy and conflict conditions, looking for correlations between preparatory frontocentral ERP activity and subsequent conflict-related N2 ERP activity and behavioral interference estimates. The second question, whether or not a shift in voluntary task strategies can shift participants from late to early selection, will be addressed in section 5.3.2.2. In subsection 5.3.2.2.1, we will investigate changes in preparatory sensory-cortex biasing-related activity by looking at event-related alpha desynchronization patterns over occipital cortical areas. Finally, in subsection 5.3.2.2.2, the effect of strategy-induced changes on early, target-locked, task-related sensory-cortex activity will be examined by contrasting visual-cortex N1 responses between attend visual and attend auditory targets for the two strategy conditions, as a function of response speed.

5.3.2.1 Effects of voluntary control strategies on frontocentral brain activity and behavior

5.3.2.1.1 Trial-by-trial, reaction time dependent, variations and voluntary task strategy influences

As introduced above, as an initial step in the analyses of both preparatory and subsequent target conflict processing activity in relationship to behavioral performance, we examined trial-by-trial (micro-level) variations in activity across a central frontocentral scalp site (FCz), representing the overall pattern seen across large portions of mostly left and central frontocentral scalp areas. For this observational analysis, RT-sorted ERP images (color-coded stacked RT-sorted single-trial activity plotted across time) were used, separately for the four key conditions (congruent and incongruent trials per strategy conditions: see Fig. 4).

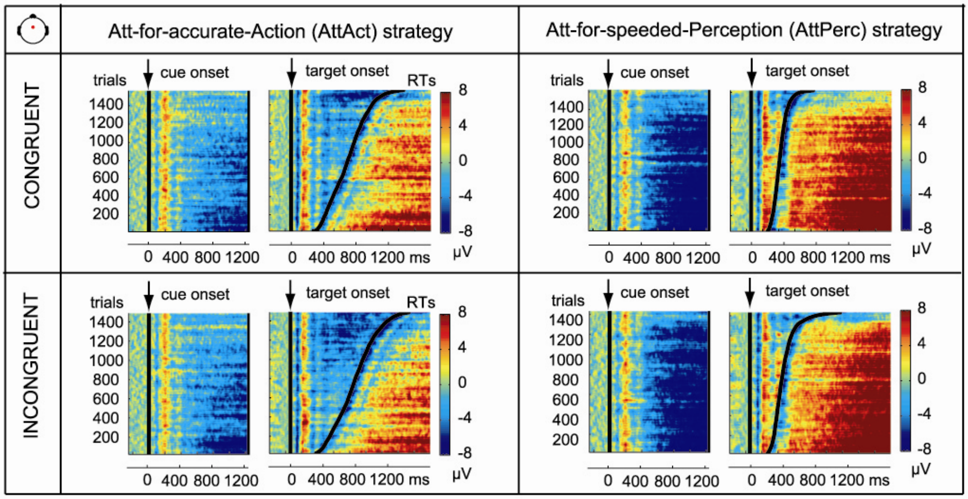

Fig. 4. Single-trial reaction time sorted ERP images (including data from all 10 participants), plotted separately for cue-locked/cue-baselined activity (left ERP images within each cell) and target-locked/target-baselined activity (right ERP images within each cell), with strategy conditions organized in the columns and congruency conditions organized in the rows. Cue-onset and target-onset are indicated by arrows. The solid black line overlaying the target-locked ERP images represents the reaction time distributions.

The RT-sorted ERP images revealed a number of interesting patterns in the data, which can be qualitatively described as follows. First, the two strategies clearly affected the RT distribution (see black S-shaped lines overlaying the target-locked ERP images in Fig. 4). When participants were using the AttAct strategy (left column in Fig. 4), the distribution of reaction times was very wide compared to when they used the alternative AttPerc strategy (right column in Fig. 4), in which case the distribution became not only much narrower (changing in shape), but also shifted to the left. Second, the strength of the cue-locked preparatory attentional-control activity (shown in these plots at channel FCz) showed an inverse relationship across trials with the subsequently triggered, pre-response, target-processing activity (especially in AttAct strategy). More specifically, the weaker the frontal cortex preparatory negative-wave activity, the stronger and longer lasting the post-target, pre-response, negative-wave activity was over the same cortical areas. Lastly, in the AttPerc strategy, participants clearly increased the amount of frontocentral negative-wave brain activity during the cue-target delay period. This appeared to be associated with an almost complete elimination of the later post-target processing negativity (before the responses, indicated by the S-curved black traces) seen when these same participants used the AttAct strategy.

The observed patterns of activity in the ERP images were subsequently quantified (and statistically tested), by extracting mean event-related potential (ERP) data for both cue-locked attentional orienting as well as target-locked conflict-related activity, separately for the 50% fastest-response and 50% slowest-response trials (i.e. median-split) within each condition. An overview of this extracted data is presented in Figure 5 and the results are discussed below, separately for preparatory activity (subsection 5.3.2.1.2) and conflict-related activity (subsection 5.3.2.1.3).

5.3.2.1.2 Strategy and reaction time dependent preparatory ERP activity

Preparatory top-down attentional control / orienting activity was defined by the difference between ERP responses to attend cues ("LOOK" and "HEAR") and control cues ("WAIT"), a contrast that is aimed at removing the contribution of initial cue-processing and cue-interpretation activity which, theoretically speaking, should be very similar in both control and attend cues (see also Grent-'t-Jong and Woldorff, 2007; Woldorff et al., 2004). Attentional orienting activity in the current study (see Fig. 5) started over fronto-central cortex at around 400 ms post cue, after which it became stronger and expanded across the scalp to include more posterior areas, consistent with the results in Grent-‘t-Jong and Woldorff (2007). In addition, this attentional orienting activity differed between both strategy conditions (macro-level effect; more pre-target attentional orienting activity in AttPerc than in AttAct strategy) as well as between fast and slow trials within each strategy condition (micro-level effect; larger preceding fast than slow target-response trials).

Statistical tests of these frontocentral preparatory activity patterns across conditions confirmed these observations. First, rANOVAs, including only the trials presented in Figure 5 (i.e., cue-plus-target trials, separated in FAST and SLOW bins within each condition), revealed that the attentional orienting activity was significantly different between strategies throughout the window between 350-1250 ms post-cue (main effect of STRATEGY for all 50 ms bins: F(1,9)= 8.4-16.6, p’s= 0.02-0.0003). Furthermore, attentional orienting activity was significantly different between FAST and SLOW trials, but only in the later part of the cue-target interval, between 750-1250 ms post-cue (main effect of RTSPEED: F(1,9)= 11.0-33.5, p= 0.009-0.0003), independent of STRATEGY (i.e., there were no STRATEGY x RTSPEED interaction effects found in any of the 50 ms windows). Thus, macro-level (between-block) effects started approximately 400 ms earlier than micro-level (within-block) effects, and the two sets of effects occurred independently of each other.

Second, rANOVAs for the set of all cue-plus-target and cue-only trials (which includes more trials and thus a better signal-to-noise ratio), revealed comparable results: main effects of ORIENTING (F(1,9)= 10.5-64.0, p= 0.01-0.0001) as well as STRATEGY x ORIENTING interaction effects were found within the same window between 350-1250 ms (F(1,9)= 8.5-16.7, p= 0.02-0.003). Post-hoc tests on these trials, separately per Strategy condition, revealed that orienting was not only stronger under the AttPerc strategy but also started slightly earlier (onset between 350-400 ms: F(1,9)= 15.9, p= 0.003) than when the same participants used the AttAct strategy (AttAct onset between 400-450 ms: F(1,9)=7.3, p=0.02).

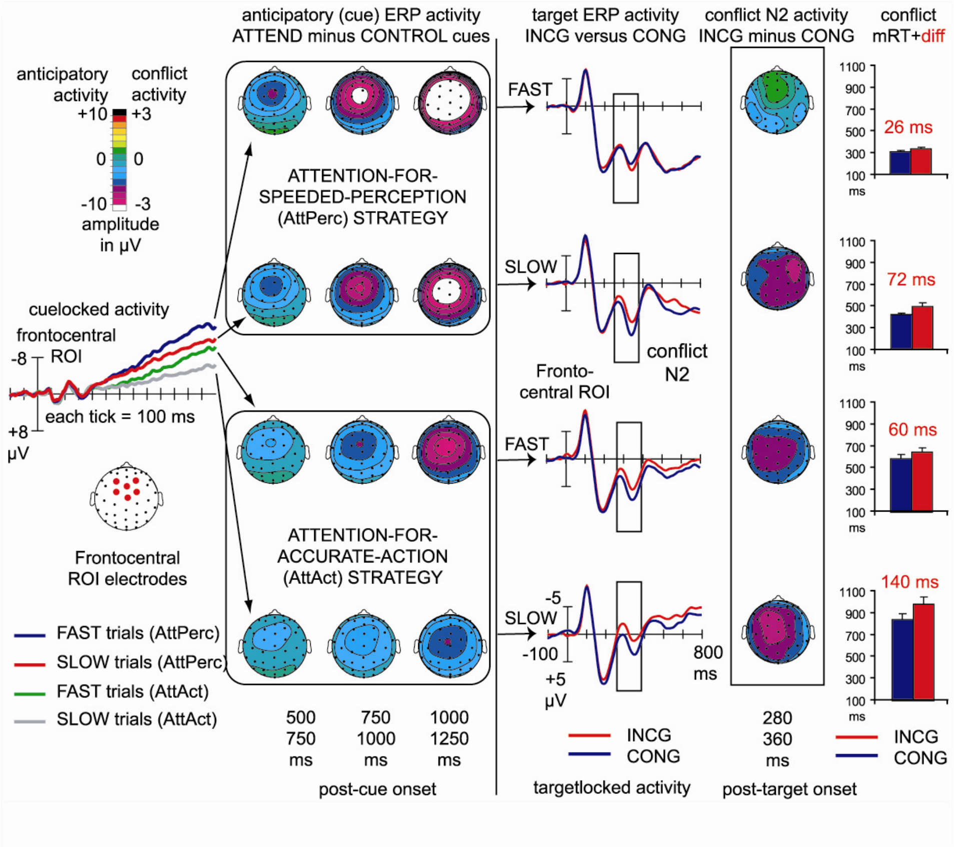

Fig. 5. Grandaverage (n=10) preparatory frontoparietal attentional orienting activity. Left half of figure: Cue-locked ERP activity (traces) and topographical distributions. Right half of figure: Subsequent conflict-related brain activity evoked by targets (ERP traces in the middle and topographic distributions of the conflict-N2 difference), along with their associated behavioral performance values (mean reaction times and conflict-induced RT slowing). ERP traces reflect mean activity across six frontocentral channels (locations shown in red on head on the left), separately for the Strategy (AttAct, AttPerc) and Speed (fast, slow) conditions. Data has been collapsed across modality of task relevance and includes only cue-plus-target trials.

5.3.2.1.3 Strategy effects and reactio- time-dependent conflict-related ERP activity

We also examined electrophysiological correlates of the detection of conflict in the current study and its relationship to the preceding preparatory activity, separated by fast and slow speed of responding. For these analyses, we used the earliest and most reliably reported marker of conflict-related ERP brain activity, namely the frontocentral negative-polarity "N2" difference between incongruent and congruent trials (see review article by Folstein and Van Petten, 2008). Within our analysis windows, rANOVAs (results summarized in Table 1) - including the factors STRATEGY (AttAct, AttPerc), CONFLICT (incongruent, congruent distractor) and

RTSPEED (fast, slow trials) - revealed clear conflict-related N2 activity differences (larger N2 amplitude for incongruent versus congruent trials) between 240-380 ms (p-values < 0.02), averaged across strategy and speed of responding. In addition, between 340-400 ms, these conflict N2 effects were smaller for the AttPerc than for the AttAct strategy (p-values < 0.03). N2 amplitudes in general (i.e., averaged over response speed and conflict) were smaller for the AttPerc than AttAct strategy (between 260-400 ms: p-values < 0.02). N2 amplitudes were also greatly affected by response speed. Averaged across strategy and conflict, larger N2 amplitudes were found for fast than slow trials during the entire test window between 200-400 ms post-target onset (p-values < 0.008).

Table 1. Conflict-related N2 effects. Summary of results of repeated-measures ANOVAs, including the within-subject factors STRATEGY (1, 2), CONFLICT (incongruent, conguent target-distractor pair), and RTSPEED (fast, slow trials), of target-locked ERP data between 200-400 ms, averaged over 20 ms of data from 6 fronto-central ROI channels (n.s. = not significant).

	Strategy		Conflict		RTspeed		Strategy x Conflict		Strategy x RTspeed	
window	**F(1,9)**	**p**	**F(1,9)**	**p**	**F(1,9)**	**p**	**F(1,9)**	**p**	**F(1,9)**	**p**
200-220	n.s.		n.s.		11.4	0.0080	n.s.		n.s.	
220-240	n.s.		n.s.		15.0	0.0040	n.s.		n.s.	
240-260	n.s.		7.4	0.0200	16.5	0.0030	n.s.		n.s.	
260-280	7.4	0.020	20.2	0.0020	23.7	0.0009	n.s.		n.s.	
280-300	12.3	0.007	28.4	0.0010	27.9	0.0005	n.s.		n.s.	
300-320	18.1	0.002	29.6	0.0004	30.2	0.0004	n.s.		n.s.	
320-340	20.1	0.002	34.5	0.0001	30.4	0.0004	n.s.		n.s.	
340-360	17.0	0.003	19.6	0.0020	27.2	0.0006	6.8	0.0300	n.s.	
360-380	12.3	0.007	9.4	0.0100	17.9	0.0020	9.5	0.0100	n.s.	
380-400	9.1	0.010	n.s.		14.4	0.0040	6.6	0.0300	n.s.	

Post-hoc rANOVAs, separately per strategy and response speed condition, revealed that under the AttAct strategy a significant conflict N2 effect was generated in both fast and slow trials: fast trials between 240-400 ms (F(1,9)= 5.2-13.5, all p-values < 0.05) and slow trials between 320-380 ms (F(1,9)= 7.4-11.2, all p-values < 0.02), whereas under the alternative AttPerc strategy, significant conflict N2 differences were only found for the slowest trials between 280-360 ms (F(1,9)= 5.6-11.9, all p-values < 0.04). Interestingly, despite an absence of significant conflict-detection related frontocentral N2 response in the fastest 50% of the trials from the AttPerc strategy, these same trials still showed a significant, although much smaller, behavioral conflict effect of on average 26 ms. In conclusion, conflict effects were substantially affected by both voluntarily adopted task strategies as well as overall speed of responding (note: as indicated in the behavioral analyses, this was independent of an increase in response errors due to the embedded speed-accuracy trade off in the two strategy conditions).

5.3.2.2 Effects of voluntary control strategies on early versus late selection of task-relevant information

Based on predictions from selective attention models we hypothesized that the more modality-selective AttPerc strategy would induce stronger preparatory sensory cortex biasing activity (see subsection 5.3.2.2.1) than the more action focused AttAct strategy. As a result, we expected greater sensory gain control (see subsection 5.3.2.2.2) under the AttPerc than under the AttAct strategy, either in the form of a selective amplification of the relevant modality input or as a selective inhibition of the distractor information (or both).

5.3.2.2.1 Preparatory sensory-cortex biasing activity

Preparatory biasing activity changes between conditions were studied primarily through cue-locked alpha-band (8-13Hz) power changes over posterior scalp sites. These event-related alpha-band power changes have been shown to be a good marker of modality-selective preparatory biasing activity (Fu et al., 2001). In addition, preparatory alpha-band activity has been shown to be highly sensitive to the strength of preparatory stimulus-response mapping or task-set formation, more so than coexisting biasing-related ERP markers, which better reflect baseline shifts under conditions of to-be-expected perceptually hard-to-detect task stimuli (Grent-'t-Jong et al., 2011), which were not present in the current study.

In this study, preparatory alpha-band (8-13 Hz) power, averaged over 500 ms of data before target onset (750-1250 ms post cue; white border outlined boxes in Fig. 6), showed the expected significantly larger decrease when participants directed their attention to the visual modality than when they directed their attention to the auditory modality (main effect of MODALITY: F(1,9)= 15.8, p= 0.003). In addition, there was also a clear effect of STRATEGY (F(1,9)= 6.9, p= 0.03), as well as a STRATEGY x MODALITY interaction (F(1,9)= 8.0, p= 0.02). Post-hoc tests revealed that whereas in both strategy conditions alpha power decreases were significantly different between attended modalities (main effect of MODALITY in AttAct strategy, F(1,9)= 8.8, p= 0.02; and in AttPerc strategy, F(1,9)= 16.4, p= 0.003), alpha power decreases were only significantly different between strategy conditions following attend-visual instructions (main effect of STRATEGY: F(1,9)= 8.7, p= 0.02), and not following attend-auditory instructions. Thus preparatory attention to visual input resulted in significantly stronger visual cortex biasing activity under the speeded-perception, more modality-selective, preparatory control strategy (AttPerc) than under the more accurate-action focused control strategy (AttAct), but attending to auditory input did not.

5.3.2.2.2 Early, target-locked, task related sensory cortex activity

Extracting target-locked modality-selective changes in early sensory cortex activity was somewhat more complicated, because targets were embedded in multisensory target-distractor stimuli. This is problematic mainly because the auditory-cortex-generated auditory N1 component has its maximum over midfrontal cortical areas, which, in the case of an audiovisual multisensory stimulus, then overlaps with activity evoked around the same time by the visual part of this compound stimulus. Because visual-cortex N1 activity is less likely to be contaminated by activity from auditory cortex, we focused our analyses primarily on the visual cortex N1 component. Earlier effects, such as for example visual cortex P1 effects, were not investigated, because of problematically low signal-to-noise ratios for such a low-amplitude component, in addition to a rather low likelihood of such early effects in a non-spatial attention paradigm.

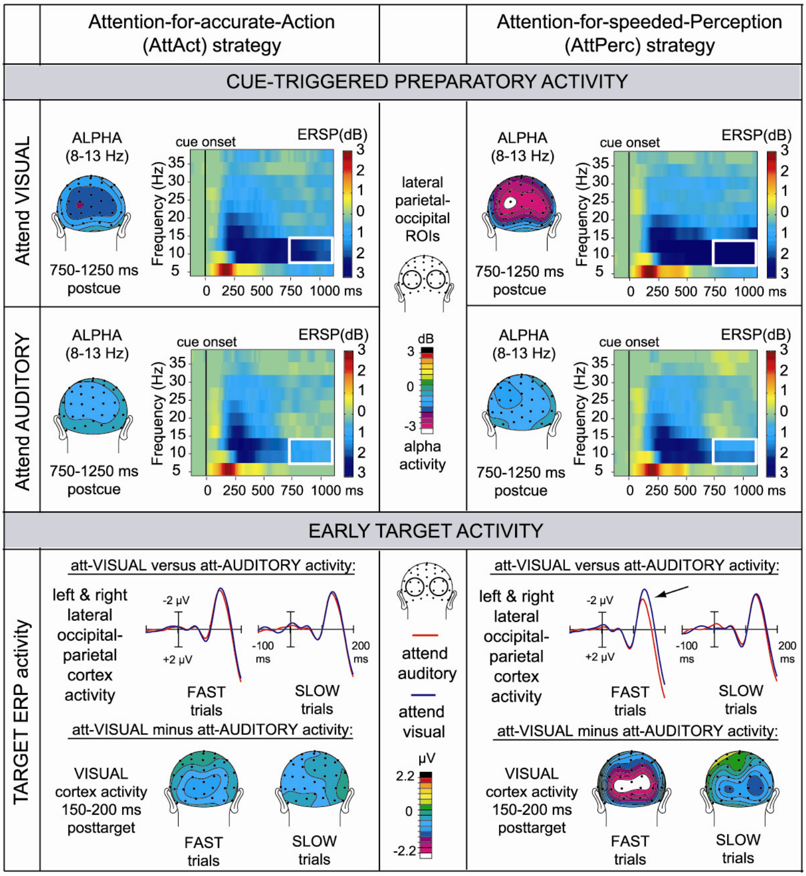

Fig. 6. Overview of grandaverage (n=10) cue-triggered modality-specific posterior cortex biasing activity (upper panels) and subsequently induced target-locked early sensory cortex ERP activity (bottom panels), separately for both strategies (AttAct strategy, left column; AttPerc strategy; right column). Topographic distribution of alpha-band (8-13 Hz) biasing related activity in the upper panels is shown for attend-visual and attend-auditory oscillatory activity (collapsed across all cue-only and cue-plus-target trials) recorded over 8 lateral parietal-occipital scalp sites (circled on the midpanel cartoon head). The activity covered by the white outlined boxes overlayed on the time-frequency (TF) plots corresponds to the plotted scalp-potential distributions displayed to the left of each TF plot. In the bottom panel, early target ERP activity is shown over similar lateral-occipital scalp sites, separately for fast and slow, attend-auditory and attend-visual target-distractor trials. Below those ERP traces, topographical distributions are shown for the corresponding difference-waves (attend-visual minus attend-auditory targets).

The results, summarized in the bottom panels of Figure 6, clearly shows that attending to the visual versus auditory part of the multisensory target-distractor pairs triggered much larger differential N1 activity over visual cortical areas under the AttPerc strategy, in particular on the fastest trials (Fig. 6., right bottom panel, left ERP traces), than under the alternative, more accurate-action focused AttAct strategy. This was confirmed by rANOVAs showing an absence of significant N1 amplitude modulations under the AttAct strategy, but a clear main effect of MODALITY for the AttPerc strategy (150-180 ms: F(1,9)= 11.6, p-value= 0.008), as well as a RTSPEED x MODALITY interaction (F(1,9)= 9.8, p-value= 0.01). Post-hoc tests showed that these results were driven by a particularly strong effect on the fast trials of the AttPerc strategy (main effect of MODALITY: F(1,9)= 21.2, p-value= 0.001). Interestingly, additonal rANOVAs, separately for FAST and SLOW trials, revealed that whereas the N1 amplitudes on slow trials were identical across strategy conditions and attended modality, they were significantly reduced under the AttPerc strategy, compared to the AttAct strategy, when the auditory modality was task relevant (main effect of STRATEGY for attend auditory fast RT trials: F(1,9)= 8.9, p-value= 0.002). In contrast, attending to the visual versus the auditory modality did not enhance the target visual-cortex N1 amplitude in any condition. This suggests that early selection (within the current study), if present, encompasses suppression of irrelevant signals, not amplification of relevant ones.

5.4 Discussion

In this study, we asked whether the type of long-term voluntary task strategies (an attention-for-speeded-perception [AttPerc] and an attention-for-accurate-action [AttAct] strategy) could influence brain activity and behavior in a cued crossmodal conflict paradigm. We expected that the more modality-selective, perceptually related, speeded-perception strategy (AttPerc) would shift participants from late to early selection of task-relevant information, which we hypothesized could theoretically result in faster subsequent decision-making processing and potentially diminish behavioral interference. In contrast, we expected that a strategy that is more directed toward accurate action (AttAct) would result in improved accuracy, but, due to expected weaker early selection and thus subsequently greater need later for more elaborate processing, we hypothesized that this would likely be at the cost of being more susceptible to distractor interference. The results are in line with these predictions and will be further discussed below.

5.4.1 Effects of voluntary strategies on behavioral performance during crossmodal conflict

Behavioral performance was clearly influenced by the manipulation of task strategies within participants. An attention-for-speeded-perception strategy (AttPerc) substantially reduced the amount of behavioral interference, compared to an attention-for-accurate-action based strategy (AttAct), independent of an increase in response errors due to an strategy-embedded speed-accuracy tradeoff.

Modulation of behavioral interference effects have been reported before in cued versions of conflict paradigms. For example, preparing for conflict has been found to reduce behavioral conflict effects in a Stroop like paradigm (Logan and Zbrodoff, 1982) as well as in a spatial version of the Stroop paradigm (Stern et al., 2007; Stern and Mangels, 2006). What is new in the current study, however, is that the amount of behavioral interference reduction strongly depended on "how" participants prepared for the upcoming task. That is, the more optimized and more task-feature selective their long-term task strategy was, the stronger the interference reduction achieved. In addition to strategy-dependent reductions of behavioral interference, the data also revealed that, within strategy (i.e., strategy independent), behavioral interference effects were smaller on faster than slower trials (micro-level effect). Such within-block (micro-level) effects could well correspond to the ongoing, trial-to-trial, adjustments in control activity proposed by the conflict adaptation model. Also interesting in this respect is that increased general slowing across participants has been reported to correlate with significantly increased Stroop interference (Lansbergen et al., 2007), an effect that was suggested to reflect general inefficiency of information processing.

A change in voluntary strategies in the present study also led to changes in the reaction time distributions (see RT-sorted ERP images), including a narrowing of the distribution and a shift toward faster RTs in the AttPerc strategy, compared to the alternative AttAct strategy. Within the context of a conflict paradigm, a shift toward faster RTs as a result of a speed-accuracy trade-off (SAT) manipulation has been reported before (Band et al., 2003; e.g., Osman et al., 2000). The general consensus is that the locus of the speed-accuracy-tradeoff is in brain areas involved in decision-making (mostly frontal areas), rather than in areas concerned with stimulus processing (sensory areas) or motor execution (Bogacz et al., 2010; Forstmann et al., 2008; Ivanoff et al., 2008; van Veen et al., 2008). In the current study, however, we found evidence for input gain control changes in early sensory areas between the AttPerc relative to the AttAct strategy. We also found evidence for less elaborate processing later; the ERP images of the AttPerc strategy revealed less frontocentral pre-response processing negativity during a central processing stage, which can be interpreted as a shortening of the decision-making stage (i.e., less accumulation of evidence being needed for fast and reasonably accurate responses), all which could have caused the changes seen in the RT distributions. From these results we conclude that the behavioral performance and RT distribution changes in the current study were most likely shaped by a combination of the manipulation of SAT and voluntary task strategies.

5.4.2 Effects of voluntary strategies on preparatory brain activity and conflict processing activity

In line with the effects on behavioral performance, voluntary task strategies also strongly influenced preparatory brain activity and subsequent conflict-related neural responses. The AttPerc strategy, compared to the AttAct strategy, resulted in much stronger frontocentral cortex preparatory attentional orienting ERP activity, and also affected subsequent target processing activity differentially. From the assessment of single-trial based cue-target ERP images, for example, it was concluded that voluntary control strategies affected the correlation between the strength of preparatory negative-polarity slow-wave potentials over frontal cortex and the duration and strength of the later target-induced processing negativity over those same areas differentially, with stronger correlations seen in the AttAct than in the AttPerc strategy. The strong results found for the AttAct strategy are mostly in line with our recent study (Weissman et al., 2006) showing that preparatory frontal cortex attentional control activity can covary on a trial-by-trial basis with subsequent brain activity and behavioral responding. It also fits reports of increased frontocentral preparatory CNV activity, correlating with subsequently faster responses to target stimuli, found recently, for example, in a cued conflict paradigm (Fan et al., 2007).

Another major finding in the current study, extracted from subsequent ERP analyses of the same data, is that shifts in voluntary preparatory strategy toward a more perception-than-action driven strategy modulate conflict-related frontocentral N2 activity to the targets, in that it diminished the amplitude of the N2 difference between incongruent and congruent trials, and even eliminated the N2 difference under the condition of most optimal preparation (fastest trials in Strategy 2 condition). The conflict-related N2 effect has been reported as most likely generated in or around the anterior cingulate cortex (Ladouceur et al., 2007; Liotti et al., 2000; van Veen and Carter, 2002) and has thus been argued to be an ERP marker of the detection of stimulus and/or response conflict (which may trigger the subsequent up regulation of attentional control). The current pattern of results seem to argue more for the conflict N2 effect reflecting the initiation of increased attentional control itself, presumably called for primarily because the output of the perceptual stage suggested that more attentional control activity is needed than currently available.

An interpretation of the conflict-N2 effect as being sensitive to available attentional resources at the time of the onset of a conflicting stimulus could partially help resolve some inconsistent findings in the literature, such as the finding that anterior cingulate cortex lesions do not always correlate with impaired cognitive control (Fellows and Farah, 2005). It is possible however, that in the Fellows and Farah study, due to a more general diminished (conflict) processing capacity, lesion patients compensated by switching to a more optimal attentional control mode strategy, compared to control participants. Or in contrast, that their ACC damage hindered adaptive up regulation of attention, rather than the detection of conflict. The current proposed alternative interpretation of the N2 conflict effect might also explain why single- and multi-unit recordings in non-human primates have failed to detect conflict monitoring neuronal populations in anterior cingulate regions (Nakamura et al., 2005). Non-human primates are highly trained before recordings take place and therefore might have already optimized their strategy in order to deal with the task demands. Even in humans, it has been shown, for example, that practice can greatly reduce, and in some cases even eliminate, conflict related behavioral performance decrements (MacLeod, 1998; Raz et al., 2002; Reisberg et al., 1980; Weissman and Compton, 2003). Finally, our interpretation of the conflict-N2 effect also would be in line with recent reports of the frontocentral N2 effect being sensitive to task difficulty (Philiastides et al., 2006; Ratcliff et al., 2009) and to parametric increases in the amount of conflict (Forster et al., 2010), as both these factors can influence long-term strategies. Although the conflict model could predict all these results as well, in the current study the reduced conflict N2 effects went along with increased preparatory activity and more early selection filtering, suggesting that those effects led to the later decreased interference effects, both behaviorally and neurally.

5.4.3 Effects of voluntary strategies on gain control mechanisms and early versus late selection

Consistent with our predictions, the speeded-perception control (AttPerc) strategy induced stronger preparatory modality-specific sensory cortex biasing than the accurate-action control (AttAct) strategy and led to a shift from late to early selection of task-relevant information. First, the AttPerc strategy triggered stronger visual cortex biasing activity, as evident by a stronger pre-target decrease of alpha-band power, than did the alternative AttAct strategy. Second, early selection of task-relevant information with the AttPerc strategy was evidenced by a significant reduction in the visual-cortex N1 amplitude when the auditory modality was relevant, compared to when the visual modality was relevant, which did not occur for the AttAct strategy. With respect to the later N1 effect, unfortunately we could not determine whether such an effect was also present in auditory cortex, primarily because of scalp overlap of such activity with general frontal-parietal attentional control activity and motor-preparatory control activity. If we would have been able to work around this methodological problem, however, it is not unlikely that we would have found much weaker modulation of auditory cortex biasing activity. As the behavioral results indicated, participants experienced more behavioral interference from visual distractor information when the auditory modality was relevant, than from auditory distractor information when the visual modality was relevant, and this was even stronger when they were using the more speeded-perception focused AttPerc strategy. It is possible that this effect was caused primarily by an imbalance in the design parameters (the requirement of visual fixation hinders inhibition of visual input during auditory attention), although an explanation of more difficulty with directing attention to an auditory than a visual event cannot be excluded.

We also found that the recorded early sensory gain control effects were not only strategy dependent - the effects were restricted to the AttPerc strategy - but were also limited to the 50% fastest trials within that strategy condition, suggesting that it requires a highly motivated and optimally prepared participant. As mentioned in the introduction, in the Braver et al. study (Braver et al., 2009) - which argued for shifts in voluntary control strategies causing shifts in timing of selection of task-relevant information - changes in sensory cortex as a result of shifts in strategies were not reported. The reported changes were localized primarily in lateral prefrontal cortex.

It is not unlikely that the dependent measures used in that study - the amount of tonic, sustained, versus phasic, transient, activity during an AX-CPT task, which the authors argued would correspond to pre-target preparatory (tonic) and post-target (phasic) activity - was partly the source of this difference. It is also the case that fMRI is not such a good method for assessing and distinguishing early selection processes, due to its low temporal resolution. That said, it is not unlikely that the frontal cortex results reported in the Braver et al. study (2009) are comparable to our within-block, less strategy-dependent, reaction-time variations in frontal cortex activity.

Finally, the early sensory gain control activity recorded in the current study surprisingly pointed to an underlying mechanism of suppression or inhibition of activity in areas that process task-irrelevant information, rather than enhancement of activity in areas that process task-relevant information. Enhancement of task-relevant activity would have been more consistent with predictions from sensory gain control models (Hillyard et al., 1998) as well as with recent findings from conflict fMRI studies (Egner and Hirsch, 2005; Weissman et al., 2004; Weissman et al., 2005). Inhibition of task-irrelevant activity under more optimized attention conditions, however, (be it in a more indirect way) is more in line with more recent findings of a combination of increased activity in task-modality irrelevant sensory cortical areas and decreased activity in task-modality relevant sensory areas during momentary reductions of attention, found in a comparable design (Weissman et al., 2009). There have also been numerous fMRI studies, showing sensory-cortex suppression of unattended stimuli, or stimulus features, within the same object or spatial location (e.g., Gal et al., 2009; Yi et al., 2004).

A possible solution to the apparent discrepancies with previous fMRI findings of enhancement of task-relevant sensory cortex activity in the context of conflict processing is to assume that, rather than representing early (bottom-up, sensory-perceptual processing related) activity, the activity recorded in these fMRI studies represented longer-latency sensory cortex activity. That is, the activity might have reflected recurrent processing of relevant information during late selection processes, for example those that are recruited as a means to accumulate more information over time needed for a correct decision (within-trial effect). Or, alternatively, they might have reflected an up regulation of activity in task-relevant areas after the response, with the goal to increase performance on the next trial (between-trial effect). With respect to the Weissman et al. (2004) fMRI study, after which the current study was modeled, the reaction time and accuracy patterns in that study were highly similar to the ones described for the AttAct strategy in the current EEG study. In "reactive control mode" here, it was shown that selection of task-relevant information did not occur early (no early sensory differences were found), and the pattern of activity seen in the ERP images of the AttAct strategy was consistent with predictions from sequential sampling (accumulation of evidence) models (Smith et al., 2004; Smith and Ratcliff, 2009). Taken together, it is thus well possible that the fMRI participants in the Weissman et al. (2004) study operated in more of a reactive mode. This then resulted in late selection that took the form of selective enhancement of task-relevant information during the decision-making stage of target processing. This in turn then explains the finding of enhanced visual cortex activity when the visual modality was relevant (without any changes in auditory cortex) and enhanced auditory cortex activity when the auditory modality was relevant (without any changes in visual cortex).

5.5 Conclusions

In the current study we have investigated the effects of a strategic shift in a cued crossmodal conflict paradigm from a more "reactive", attention-for-accurate-action-based strategy to a more "proactive", attention-for-speeded-perception-based strategy. The results showed that when participants operated in the attention-for-speeded-perception mode they were capable of shifting the strength of brain activity in frontocentral attentional control areas from a post-target to a pre-target window and could bias sensory cortical areas in such a way that it would lead to a shift from late to early selection of task-relevant information. In addition, participants in this control mode could diminish (or even eliminate) frontal conflict-related processing activity to the target, as well as strongly diminish their experienced behavioral interference. The results also show that such dramatic changes may require a strongly motivated participant, and perhaps also a release from a strong emphasis on being highly accurate. On the other hand, participants operating in a more reactive, attention-for-accurate-action mode were indeed much more accurate in their responses, but their late selection of task-relevant information and corresponding slower and more careful decision making unfortunately came at the cost of being more sensitive to distractor interference, even when corrected for response slowing. In sum, the current study showed that individuals indeed have control over their cognitive strategies - as suggested by the DMC model – and as reflected by the robust modulation of brain activity and behavior seen in the present findings.

Chapter 6

Summary, discussion and conclusions

SUMMARY

Directing attention selectively to an expected event has already been known for a long time to recruit a network of frontal and parietal brain attentional control areas. In addition, this frontal-parietal control network has been hypothesized to signal stimulus-specific sensory (e.g. visual cortex) areas to increase preparatory (biasing) activity in an attempt to improve subsequent perceptual processing of the expected stimulus. The research presented in this thesis shows that there might actually be multiple, rather than one, frontal-parietal attentional control network, one being more medial-dorsal and the other being more lateral-dorsal in location. In addition, strong evidence was found for a frontal cortex initiation of top-down attentional control, rather than a parietal cortex initiation, as was hypothesized by some selective attention theories. Furthermore, it was found that the subsequently triggered sensory cortex biasing-related activity actually consisted of two different, coexisting, mechanisms: 1) a slow-wave baseline shift mechanism that can lower perceptual stimulus thresholds, and 2) an oscillatory alpha-frequency rhythm that can store an attentional trace (template), including both stimulus and response characteristics and their behavioral relevance. Finally, it was shown that voluntary choices in task strategies could selectively determine which frontal-parietal network would be activated (a more medial-dorsal or a more lateral-dorsal network) and which sensory cortex mechanism would be selectively boosted. In short, an "attention-for-perception" based strategy recruits mostly a medial-dorsal frontal-parietal network and boosts most strongly the baseline shift mechanism, whereas an "attention-for-action" based strategy boosts more strongly the formation of an attentional template in sensory cortical areas. In conclusion, top-down attentional control is not a unitary mechanism, but includes multiple different processes that can be boosted selectively through voluntary choices in top-down task strategy.

DISCUSSION

"The mere formulation of a problem is far more essential than its solution,
which may be merely a matter of mathematical or experimental skills.
To raise new questions, new possibilities, to regard old problems from a new angle
requires creative imagination and marks real advances in science."

A. Einstein & L. Infeld, 1938,
The Evolution of Physics

In the present thesis I have tried to "*regard old problems from a new angle and raise new questions*" in an attempt to avoid the problem of "*transferring old bones to a new grave-yard*". The main goal was to elucidate the functional mechanisms underlying top-down attentional control activity. A relatively "old problem viewed from a new angle" concerned the dominant view of one supramodal frontal-parietal (FEF-IPS) attentional control network in contrast to the high degree of variability of reported attentional control brain areas in the literature. It is still unclear how much of this variability is related to the use of different contrasts, different stimulus-features or modalities, or different recording techniques. These same factors also might have affected some provided answers to the old question of "whether attentional control is more an anterior or posterior brain function". Therefore, some studies in this thesis include manipulations of some of those factors (type of contrast, different modalities) in order to be able to re-evaluate this old question.

One of the "new questions raised" was related to the observation that theoretical models and experimental data were also not always exactly in alignment with each other. I asked, for example, "how the two modes of attentional selection (early versus late selection) are linked to the two hypothesized mechanisms of attentional modulation of sensory cortex activity (i.e., gain modulation and baseline shift), activity that is selective for the attended feature". Such different mechanisms could be expected to have their own representation in sensory cortical activity during preparation, but evidence for this is not available. Another "new question raised" developed during the course of this thesis project and involves the question "what the influence is of voluntary task strategies on attentional control activity and conflict resolution".

In this last chapter, I will summarize the main findings from the presented studies and discuss how these findings answer these questions. Subsequently, I will discuss how these answers might affect our understanding of top-down attentional control.

6.1 Directing attention to spatial frequency patterns

The first study, presented in Chapter 2, involved a manipulation in which participants were asked to either follow the instruction embedded in the word cues on a trial-by-trial basis within a block of trials (experimental condition), or follow the instruction provided prior to a block of trials (control condition). The instruction indicated which of two possible subsequently presented spatial-frequency patterns required a response (low spatial frequency, thick black/white stripe patterns, or high, thin stripes, spatial frequency patterns). Participants used the instruction to optimally prepare for a speeded and most accurate response to the targets.

This particular setup was introduced to equate as much as possible all differences between experimental and control condition that were not related to attentional control activity, differences such as physical differences between cue types used in the contrast, differences in motor preparation, or differences in stimulus features such as perceptual difficulty. In addition to this novel contrast, the paradigm included another new design feature, namely the addition of a behavioral discrimination task to the cue stimuli themselves. This -- until today still unique -- manipulation was introduced to provide behavioral evidence for equal cue interpretation performance across experimental and control condition. The idea behind this manipulation was that it could prevent the methodological problem of potentially misinterpreting early differences in timing, duration, or strength of cue-interpretation activity between conditions as the onset of attentional orienting. Such is often the case when two active cue conditions are contrasted (e.g., attend versus neutral cues) that differ in the amount of processing load. At that moment in time, other studies, using different active cues as contrast, had indicated that directing attention to non-spatial features, such as for example color, gave rise to a posterior onset of attentional orienting activity (Slagter et al., 2005b; Slagter et al., 2005a). This effect was somewhat comparable to the findings of posterior EDAN components in attend-left versus attend-right cue contrasts, used in many older published visual-spatial attentional control studies (see Introduction), as well as in some more recent studies (Green et al., 2005; Talsma et al., 2005). In all these studies, it was unclear how much the claims of posterior onset of attentional orienting activity were affected by the problem of differential cue-interpretation activity. Because the main question addressed in this study was whether top-down attentional control activity would start in anterior or posterior areas, including a control such as behavioral responses to the cues was essential.

The results from our study were in many ways surprising. The first surprising result was that there were no ERP differences between responses to experimental and control cues in the grand average (n=12) ERP waveforms. We argued that such a result could either mean that our contrast had been too tightly controlled, leaving not enough power to find attentional control activity, or alternatively, that we had not included enough participants to gain the power needed to find differences in the first place. Neither of these interpretations appeared to be true. The problem of not finding any experimental effect was related to the fact that 4 out of 12 participants showed a pattern of brain activity that basically cancelled out the pattern of activity seen for the remaining 8 participants. More specifically, the group of 4 participants elicited a fronto-central-parietal "positivity", starting 500 ms after cue onset over frontal and prefrontal areas, later including more central and posterior areas (localized to a lateral and mostly anterior network), whereas the group of 8 participants elicited a "negativity" that started 400 ms after cue onset over central areas and moved only slightly over time to more fronto-central scalp sites (localized to more medial areas in both anterior and posterior regions). The group of 8 also showed weak signs of occipital biasing activity, whereas the other group of 4 did not.

Another surprising finding was that these two groups did not differ in terms of their behavioral responses to both cues and targets, but only in their brain activity. This brain activity difference was not restricted to differences in cue processing, as I've outlined above, but also included remarkable differences in target processing. The group of 4 with the more positive and more anteriorly generated attentional orienting activity elicited earlier and larger Frontal Selection Potentials (FSP) and later parietal P3 components to targets than the group of 8 with the more negativity fronto-parietal attentional orienting activity, who additionally elicited a clear frontocental N2b effect (after the FSP and before the P3b effect).

It was concluded that, in contrast to earlier literature reports, attentional control was initiated in anterior, not posterior areas. This conclusion was supported by the predominantly early frontal distributions of attentional orienting activity under equal discrimination performance to cues in both experimental and control condition for all participants, and by predominant contributions found for frontal, rather than posterior sources in additional source analyses of the data. Furthermore, it was concluded that the striking differences found between two subgroups of participants in this study were likely due to individual differences, rather than strategy differences. However, this conclusion was drawn with caution. First, the source analyses results indicated that both groups might have recruited slightly different networks of brain areas in frontal and parietal cortex, one being more medial frontal-parietal, the other being more lateral and predominantly frontal. And secondly, although both groups responded equally fast and accurate to both cues and targets, the responses were at floor level (i.e., the task was easy), so these results might not have been powerful enough to reveal possible shifts in strategies.

6.2 Directing attention to visual-spatial locations

Like Chapter 2, Chapter 3 also included some novel design features that were introduced to resolve problems detected in earlier studies. The contrast in this study was between "attend cues" and "interpret cues", representing respectively, an active cue instruction to orient attention to a left or right target location and a more passive cue instruction to not orient spatially but remain focused on the central fixation dot in attendance for the next cue (no target or task would follow these cues). Many studies at that time had extracted attentional orienting activity for spatial locations by contrasting "attend left" and "attend right" cue conditions. The problem with such a contrast is that, although being very sensitive to lateralized activity, it does a poor job in detecting activity that is either non-lateralized or identical in strength between cues. Such activity basically will be subtracted out. The contrast used in Chapter 3 avoids this problem.

The paradigm structure in this study was also quite innovative. It had been hard to compare results from fMRI and ERP studies because the paradigms used in these studies were quite different in their stimulus presentation rate. For example, long cue-target intervals (~6-20 seconds) were typically used in fMRI studies in order to avoid overlap of brain responses between subsequently presented stimuli (the peak of the rather sluggish fMRI BOLD response is in the order of 6 seconds). In ERP studies, such intervals were usually less than 1-2 seconds. Longer intervals increase the likelihood of decay of attentional orienting activity over time and stimulates the use of working-memory strategies rather than just attentional orienting during preparation intervals. For this project, the idea was to use cue-target intervals for both an fMRI and a corresponding ERP study that were shorter and importantly, identical, and to develop a paradigm that would help deal with the severe temporal overlap that could be expected in the fMRI recordings if such a fast-rate design would be used. The solution was found in a first order counterbalanced hierarchical design, including "cue-plus-target" trials (attend-right, attend-left), "cue-only" trials (attend-right, attend-left, passive) and "no-cue-no-target (nostim)" trials. As a result of the first-order counterbalancing of trials, the nostim trials capture the same overlap as the other experimental trials and can thus be used to subtract the overlap from the other experimental trials. Another novelty in the paradigm was to delay the response to target stimuli until after a visual response signal, which itself was presented some time after the offset of the target stimuli. Such a setup was needed in order to minimize motor preparation activity in the attend-cue condition that would otherwise introduce an additional (motor preparation) difference between attend and control condition.

The fMRI study was run first and the results were published in 2004, followed somewhat later by the ERP study, presented in this thesis in Chapter 3, which was eventually published in 2007. This thesis only includes the ERP study, but crucially, the ERP study combined the temporal information gathered within the same paradigm (but different participants) with the earlier spatial information (brain areas) extracted from the highly comparable fMRI dataset. This way, we could trace the timing of activity within the different brain areas of the attentional control network, which was predicted to provide answers to the question whether the frontal-parietal control network operated as one highly integrated network, with all subregions activated in sync with each other to perform one function at the time, or, alternatively, as a network with subregions that show different temporal activation patterns, which could point to the different subregions performing different functions.

The results of this attempt to link ERP and fMRI findings overwhelmingly supported not only a frontal onset of attentional orienting activity but at the same time the hypothesis that frontal and parietal areas within the frontal-parietal attentional control network subserve different functions. In summary, independent of the direction of attention, the frontal areas were recruited first around 400 ms post-cue onset and remained highly activated across time. The parietal areas were activated a couple of hundreds of milliseconds later than the frontal areas, namely around 650 ms, and also remained active throughout the cue-target interval. Once both frontal and parietal cortices were activated, together they appeared to be involved in initiating and maintaining activity in sensory cortical areas that was selective for the direction of attention and expected target location. This target-location specific sensory cortex biasing activity started around 850 ms and increased slowly in strength over time. Interestingly, this activity matched in topography with the differential activity of the sensory N1 responses to right and left lower visual field target stimuli, and even continued some time after the estimated onset of target stimuli on cue-only trials, when no target was presented. This clearly biasing-related activity differed, however, in polarity from the more typically reported LDAP (Late Positivity) component, so it was given the new name of Biasing-Related-Negativity (BRN).

In conclusion, both the study reported in Chapter 2 as well as this study provided evidence for a frontal onset of attentional orienting activity. Thus, frontal onset is independent of the attended stimulus features (non-spatial or spatial) of the expected visual target stimulus. This frontal activity is later accompanied by more posterior parietal activity. Together, the frontal-parietal network seems to be involved in initiating and maintaining sensory-cortex biasing related activity in preparation for the expected target stimulus. Note that this model is not inconsistent with the general model of attentional control, although some indication was found in the first study that some participants might have recruited a slightly more lateral and predominantly frontal network, which would be inconsistent (but at the same time could reflect activity in other reported areas, such as the DLPFC). The innovation of especially the second study is that it provided the timing of attentional orienting within the different areas of the dorsal-medial frontal-parietal network. This not only provided evidence for a dominant role of the frontal cortex in initiating control, but at the same time suggested different functional significance of the frontal and parietal areas within the network. What exactly these functions are could only be speculated. It was hypothesized that the frontal cortex most likely is involved in regulatory control over the initiation and maintenance of the orienting of visual-spatial attention, with the aim of keeping track of the task goals and to assist other areas to accomplish these goals. These other areas included the parietal and target-location specific sensory areas (ideas mostly in line with Miller & Cohen's Frontal Executive Control model, 2001). The parietal areas were hypothesized to control the shift towards the expected target location (mostly in line with Posner's model) and the buildup and maintenance of a baseline shift in activity in the relevant sensory cortices (mostly in line with the Biased Competition Model). Finally, it was argued that the function of this baseline shift activity (BRN) was to help increase perceptual sensitivity for the expected hard-to-detect targets.

6.3 Modes and mechanisms of sensory cortex biasing-related activity in the context of visual-spatial attentional control

Leaving the realm of onset latency and functional significance of the frontal-parietal attentional orienting network, the third study presented in Chapter 4 focused on the sensory cortex biasing-related activity. This study included the dataset from the earlier experiment (Chapter 3) as well as two newly collected datasets, from two new sets of participants, who were presented with slightly different versions of the same basic visual-spatial cueing paradigm. Together, these three experiment covered two manipulations: 1) manipulation of perceptual task difficulty (easy versus hard to detect targets), and 2) manipulation of response instructions (immediately after target onset or delayed). In addition, in the two added experiments the passive control cues were also sometimes followed by a target dot, which had to be ignored by the participant. They were used later in the analyses to estimate attentional effects on target processing activity.

With respect to the dependent variable of the expected sensory cortex biasing-related activity, two different components were extracted from the same data, both reported before as reflecting such biasing-related activity. The first component involved our previously discovered slow-wave BRN ERP component. The second component involved changes in power of ongoing alpha-band (8-12 Hz) oscillatory activity. The question addressed in this study was what the functional relationship and significance was of these two different brain responses, recorded over comparable scalp areas, within the context of preparatory biasing-related target-location specific sensory cortical areas.

The results of this multi-experiment study provided strong confirmation of our previous suggestion that the BRN represented a baseline shift mechanism that improves perceptual sensitivity. This component responded clearly to the manipulation of perceptual difficulty, being much more pronounced preceding expected hard-to-detect targets than expected easy-to-detect ones. In addition, its topography correlated with that of the N1 to the targets, and its strength correlated with the amplitude of that same component. In contrast, the alpha responses (in particular, decreased power over sensory areas contralateral to the direction of attention, or alpha-ERDs) were much more sensitive to the manipulation of response instructions, being largest when responses followed targets immediately versus when they were delayed. In addition, these alpha responses did not completely match the location of the target N1 component, nor correlated with this activity like the BRN. In contrast, only in the immediate response experiment, prestimulus alpha responses correlated with post stimulus parietal P3b amplitude.

This pattern of results was interpreted as providing proof of the existence of two different preparatory attention mechanisms in sensory cortex that could bias these areas in advance of an expected target stimulus. The first mechanism includes a (slow-wave) baseline shift (BRN) that is very specifically called for only when needed, namely in situations of expected low contrast gain, likely causing the later increase of the early sensory N1 amplitude. As such, this component could represent the preparatory component of the "Sensory Gain Control" mechanism, increasing signal-to-noise of the targets by changing input gain. It is also consistent with Reynold's mechanisms of attention causing a left-ward shift in the contrast gain function. The second mechanism concerns one that is reflected by the alpha-frequency rhythm. This mechanism more likely includes the formation of a task set, or attentional template, responsive to the target features, stored in sensory areas. This task set was hypothesized to contain both stimulus and response features, information that could be used later, during target processing, to compare the incoming stimulus to in order to improve task performance. As such, this mechanism would be much more consistent with the mechanism proposed by the

Biased Competition Model, namely a tonic shift in baseline firing rates in sensory areas, based on maintenance of the link between stimulus features and behavioral relevance.

Finally, a totally unexpected finding in this study was that by introducing small paradigm changes, participants automatically adopted different strategies. Especially the manipulation of response instructions appeared powerful in this respect. Qualitatively different responses were found in this experiment compared to the other two experiments, that differed from each other only quantitatively. It was concluded that the difference in strategy could be best characterized as "attention-for-action" versus "attention-for-perception".

6.4 Task strategies, top-down attentional control and susceptibility to crossmodal distraction

The last study in this thesis is special in that it incorporates many different aspects of attentional control. First, this study included directing attention to auditory or visual targets, which provides information for our question of generality of attentional orienting activity across sensory domains. Clearly different topographical activation patterns, for example, would argue for modality-selective attentional control, whereas similar distributions would argue for modality-independent control. Second, this study included a target discrimination task in which the task irrelevant information was highly distracting and required strong attentional filtering. Third, like the data in Chapter 3, this study was also accompanied by a highly identical preceding fMRI study (Weissman et al., 2004), so more information about underlying brain networks was available than in typical ERP attentional control studies. Fourth and finally, inspired by observations of the possible influence of voluntary strategies in the earlier studies, this study turned out to be an ideal candidate for a controlled investigation of the possible relationship between voluntary attentional control task strategies and mechanisms of preparatory activity, subsequent timing of selection, and resulting effectiveness of attentional control over later target processing.

The paradigm used in this study included a crossmodal conflict letter-discrimination task. In this crossmodal distraction paradigm, a target letter "X" or "O" was presented simultaneously at the computer screen and through headphones. Both congruent trials (e.g., an auditory "X" coupled to a visual "X") as well as incongruent trials (e.g., an auditory "X" coupled with a visual "O") were presented. Instructional cues were used to inform the participants on a trial-by-trial basis which part of the multisensory letter-distractor-pair was the target ("LOOK" meant visual part is relevant, "HEAR" meant auditory part is relevant). The task for the participants was to prepare to respond to the X or O presented in the cued modality (thus, either the visual or auditory letter), while ignoring the other one presented at the same time in the irrelevant channel, and indicate with one of two buttons whether the target letter was an X or an O.

The fMRI study had revealed some known effects of conflict processing, as well as some novel results. Behaviorally, as expected, participants were slower to respond to incongruent than congruent target-distractor pairs. Another known effect seen again in this study, was the increase in ACC activity in incongruent trials compared to congruent ones. In addition, conflict related activity in areas such as the DLPFC and sensory cortices, that had been indicated in earlier studies, was again found in this study. The leading view is that the ACC detects the conflict and then triggers areas such as the DLPFC to increase top-down control over sensory processing in order to help resolve the conflict (Botvinick et al., 1999; Botvinick et al., 2001; Botvinick et al., 2004; Carter et al., 1998). This then often leads to improvements in behavioral performance on subsequent trials (known as "conflict adaptation"). Novel in this fMRI study were in the first place the finding that the DLPFC was involved in both preparatory orienting activity as well as conflict processing, and that different subregions of the ACC were activated for relevant and irrelevant aspects of the processing of the target-distractor stimulus. Secondly, a double dissociation was found in the pattern of activity in auditory and visual cortices, with activity in the relevant modality being higher when the target letter was presented in the context of an incongruent distracting letter, compared to when it was coupled to a congruent non-distracting letter. Therefore, it was concluded that the sensory cortices, the DLPFC and the ACC all play a role in increasing attention to goal-relevant information in situations of distracting input. An additional interesting finding that is relevant for the current thesis is that attentional-control related brain activity (frontal-parietal network) during the cue-target interval did not differ between attending to the auditory of visual domain. Such a pattern was also found in the ERP data, reported in Chapter 5. Note that this suggests generality in attentional orienting networks across sensory domains.

What remained unclear, however, was the exact timing (early or late) of the sensory cortex effects as well as their underlying mechanisms. The ERP study initially aimed at resolving these questions. The addition of a manipulation of attentional control task strategies, however, proved to be an excellent tool to study the dynamics of both attentional and cognitive control and became the more dominant goal. We tested the possibility that participants can indeed voluntarily change their task strategy in such a way that this substantially influenced their brain activity patterns (both preparatory, pretarget, as well as posttarget responses) and their behavioral performance. The question was if and how it would change both timing of selection of task relevant stimuli (early-versus-late selection) and conflict detection and resolution activity. The hypothesis was that a stronger perceptual focus during preparation could potentially help filtering out the distractor better, allowing for speeded responses on the basis of earlier selection and diminished conflict activity, compared to a more action and task based focus, which could improve behavior through improved late selection in combination with more cautious response decisions. The task strategies were manipulated therefore in such a way that each participant used a more "attention-for-speeded-perception" strategy in one half of the experiment and a more "attention-for-accurate-action" strategy for the remaining half of their task blocks (manipulating both type of attentional preparation as well as speed-accuracy tradeoff during responding).

The results were intriguing. Voluntary strategies not only changed the amount of preparatory and target processing activity, it also changed the relationship between pre- and posttarget responses and the amount of experienced neuronal conflict. The higher accuracy in the "attention-for-accurate-action" strategy was predicted, but not that this resulted in substantially larger conflict-related brain activity, compared to the "attention-for-speeded-perception" strategy. The last strategy clearly increased frontal-parietal preparatory attentional control activity as well as sensory cortex biasing activity, resulting in decreased later conflict-related brain activity. Crucially, the "attention-for-speeded-perception" strategy revealed one of the mechanisms by which sensory biasing can affect later stimulus processing in terms of, for example, the latency of selection of task-relevant information. The stronger general (frontal-parietal) attentional-orienting activity and stronger sensory cortex bias in the form of an improved attentional template (alpha-frequency modulation) resulted in earlier selection: in the "attention-for-speeded-perception" strategy, a decrease in visual cortex N1 activity was found when participants selected the auditory part of the multisensory letter. Thus, participants were better able to filter out the distractor. Such an effect was not seen when the same participants used the alternative, more action/task based, strategy. Furthermore, the fastest trials in the more perception driven approach resulted in the smallest amount of behavioral interference for correct trials and an absence of the expected frontocentral conflict-detection related N2 activity. This was taken as evidence that this N2 response is probably not so much related to the detection of the conflict, which is the dominant view, but rather to the increase of attentional control activity, needed because the earlier perceptual analyses had been inconclusive and thus more elaborated processing was required for proper identification of the target stimulus, although the pattern of results is not inconsistent with the conflict-monitoring interpretation either. Such an N2 response, however, was not needed when preparation already had optimized frontal-parietal cortex activation (fastest trials).

In sum, this study showed that participants can indeed influence their brain activity in ways that have unanticipated consequences for the interpretations of our findings. This aspect will be further discussed in the last subsection below.

CONCLUSIONS

The current collection of studies has provided some interesting answers to our questions. The first question whether there is one supramodal attention control system or multiple systems is the hardest to answer. In the last study, there appeared to be no difference between attending to auditory or visual stimuli, other than sensory cortex biasing related differences. In the first study, however, differences in frontal-parietal activity were seen between participants that pointed to the possible use of different brain areas. Also, the corresponding fMRI studies linked to Chapter 3 and Chapter 5 data revealed different areas. Thus, although not conclusive, we can answer this question in favor of multiple systems. It depends on both the design of the study and the participants' strategy which areas will be recruited and thus show up in our experimental contrast.

The answer to the second question of timing of activity in frontal and parietal attentional control areas can be given with much more certainty: attentional control is initiated in frontal areas. All studies in this dissertation showed frontal cortex initiation. This conclusion, however, contrasts with other more recent claims of posterior onset. In response to our claim of frontal onset, two more recent ERP studies claimed posterior onset, namely a study by Green and McDonald (Green and McDonald, 2008) and one by Brignani and colleagues (Brignani et al., 2009). In the Green and McDonald study (2008), the contrast used was between non-informative and informative (shift-up, shift-left, or shift-right) cues. This difference started 100-200 ms earlier in parietal cortex than in frontal cortex activity, which itself started around 300 ms after cue onset. Thus, the posterior onset effect was found very early within the window of cue-presentation during the time that the cue was still on the screen (cue duration was 300 ms). In addition, the cue instruction embedded in the cues had a strong spatial configuration (with a spatial layout of colored blocks). Such a combination of factors makes interpretation of these early differences in terms of shifting attention to a location of a *future event* very tricky, because it cannot be excluded that the posterior activity reflects top-down attentional control activity over spatial aspects of cue-processing itself. Such early effects could for example also be explained as reflexive orienting to the instructed relevant (color) part of the cue, either as a result of an automatic associate priming mechanisms or through the effect of precue initiated biasing activity for detection of the relevant, instructive, color in the multi-colored cue stimulus. In addition, this study removed all frequency content outside the theta range (4-7 Hz), which is problematic because this might have removed frequency content that was highly informative. We have found attentional orienting activity to be dominated by frequencies lower than 1 Hz. In the Brignani et al. study (2009), early onset of posterior activity (around 330 ms) was claimed between shift and hold cues in a dual stream RSVP task in which the cues were informative about which of the two streams had to be attended (the current one following hold cues, or the other one following shift cues). The problem here is that the demanding RSVP task required a highly alert state of the participants. This decreases the likelihood of finding an onset in frontal areas when comparing two active cues, because these areas are already activated near ceiling level under such conditions. One cannot argue that a process starts in one of two areas if at least one is already activated near ceiling level in a more sustained way.

That said, however, it is true that our contrast between attend-cues and control-cues in the visual spatial attention study in Chapter 3 might have included the confound of differential processing demands between cuetypes, which could possibly explain the early differential frontal activity. However, frontal onset was also clearly found in the study in Chapter 2, in which the experimental and control cues did not differ in any way, not physically and, crucially, also not behaviorally. Such a combination of factors creates a very strong case for frontal onset of attentional control activity. On a final note, one could also argue that the results from the Green and McDonald (2008) and the Brignani et al. (2009) studies are not necessarily inconsistent with our findings. Brignani and colleagues, for example, interpretated the posterior onset as reflecting the onset of "shifting" of visual-spatial attention, whereas we had argued that our frontal onset was related to the onset of "orienting" of visual-spatial attention. Although subtle, there is a crucial difference between these two concepts, namely that orienting includes not only shifting of attention, but also other control aspects such as the top-down regulation of the shift itself. We absolutely agree that shifting of visual spatial attention is under parietal control, but we believe that other areas, most likely frontal (maybe also subcortical structures) control the initation of this shifting. This also better fits other results reported in the literature, such as the fact that microstimulation of FEF regions can trigger attention shifts.

A third and fourth question was related to the link between two theoretically possible sensory cortex attentional control mechanisms and the early-versus-late selection mechanism. Chapter 4 clearly revealed evidence for indeed two different biasing mechanisms that generate different emphasis during subsequent target processing activity. In sum, two mechanisms appear to coexists in sensory areas. One mechanism is recruited in all situations and concerns the establishment of an attentional trace in sensory areas, linking task-relevant stimulus features to the behavioral response and its behavioral valence. This mechanism is reflected by modulation of alpha-frequency oscillatory activity and we have argued that it might be the EEG homologue of the single-cell recorded increase in baseline firing rates indicated by studies supporting the Biased Competition Model. This attentional template mechanism might be accompanied by a second mechanism, one that is reflected by the BRN component, and which is only recruited when needed, in situations of low stimulus contrast. Rather than a change in firing rate, the BRN involves more a change in the threshold for firing, lowering it so that less stimulus energy is needed to trigger a response. Such would be consistent with the attention induced left-ward shift of the contrast-gain function (Contrast-Gain Modulation account, proposed by Reynolds), and would explain Sensory-Gain contrast responses seen in ERP data.

A final question concerned the relationship between these two mechanisms and early versus late selection of task relevant information. The threshold-shift mechanism probably encourages early selection by its enhancing effect on the amplitude of the sensory-cortex N1 component, creating improved early perceptual discrimination. However, we have seen in Chapter 5 that perceptual discrimination can also be boosted by suppression of the response to task irrelevant information without an amplification of the relevant information. Interestingly, this was preceded by an increase in strength of the sensory cortex attentional template (alpha-band responses), and not by a significant threshold shift (although not reported as such in Chapter 5, an extracted BRN-like component, reflecting ERP sensory biasing, did not differ between strategy conditions). In addition, the studies in Chapter 4 showed that the strength of the sensory-cortex stored attentional template is not linked to the N1 amplitude (and thus early selection), but is linked more to late selection mechanisms (enhancement of the later P3, not the earlier N1). This pattern of result across studies could be explained by assuming a possible additional influence of other attentional orienting areas in the regulation of the timing of target selection, areas such as the frontal-parietal network and maybe even subcortical structures. Miller and Cohen's (2001) model suggested that the frontal cortex can also store attentional templates that can guide target processing. It is thus well possible that the early selection results (decreased reponse to task-irrelevant features in visual cortex), reported in Chapter 5, are explained more by the increased frontal-parietal activity than by the increased pre-target visual-cortex alpha desynchronization. The latter could in fact also be explained as an effect of the increased behavioral valence of the expected targets in the attention-for-speeded-perception strategy condition, the condition that required earlier decisions and responses. As Chapter 4 showed, this can strengthen visual-cortex stored attentional templates. Chapter 5 also showed that not only task/paradigm factors can influence the timing of selection (Lavie, 1995), but clearly also voluntary task strategies. More on this issue will be discussed below.

Final remarks

That brings me to some final remarks. First of all, attentional control is clearly *not* a unitary mechanism, rather it includes a number of different mechanisms, such as increasing cortical arousal, shifting of attention, sustaining of attention for a prolonged period of time, establishing and maintaining an attentional template (or maybe multiple), biasing of relevant input areas, and preparing a response. Crucially, this dissertation has shown that which aspects of this set of processes is highlighted appears to be under voluntary control: one can adopt either an "attention-for-perception" strategy or an "attention-for-action" strategy. This is crucial information, because such strategies can be taught and can then provide someone who could benefit from better attentional control abilities with very usefull flexibility in control. For example, if confronted with a highly distracting environment including mostly non-important sources of distraction, an attention-for-perception approach could be adopted in order to better filter out the distraction and focus on the relevant information. However, when distracting information is likely to be more rare and/or might be dangerous to miss and not respond to, adopting an attention-for-accurate-action approach of attentional control would be more appropriate. Thus, flexibility is the key to attentional and cognitive control abilities.

Secondly, if attentional control recruits different areas under different task circumstances and different task strategies, can we then speak of attention as being controlled by some brain area, or a network of areas, by some "little man in the head" (i.e., homunculus)? In other words, what does "control" mean in this context and do we really need it at all? In my view the answer to the last question is both a "yes" and a "no". To start with the "yes" part, yes we do need the concept of control in order to explain how some functions executed in the brain can be boosted by attention, functions such as whether we do or don't perceive a subthreshold stimulus. Perception and perceptual discrimination is clearly not a function of the stimulus alone. Furthermore, other higher-order mechanisms such as working memory and decision making processes are also under regulatory control of attention. The answer is, however, more a "no" if we consider the question from a slightly different angle, namely whether attention is "causal" or not in terms of its controlling function. Here things become much less clear. For example, the variations in activity we have seen between studies, and even within studies, could just as well indicate that we are not looking at a causal agent that we have called "attentional control", but rather that we are looking at the result of the same control of attention in stead. Viewed in this light, attentional control activity is an emerging property of the intention to pay attention and to prepare for the upcoming task, in the sense that it is produced (as a byproduct) by brain activity in certain areas, rather than being localizable itself in those areas. Such an interpretation could also better explain the different brain activation patterns found between studies, between different paradigms, and between different participants. In addition, we have seen that where we observe activity also strongly depends on the experimental contrast used to study attentional control in the brain. Future studies should take these considerations into account when interpreting the results of their investigations.

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Samenvatting, discussie en conclusies

in het Nederlands

SAMENVATTING

De aandacht selectief richten op belangrijke gebeurtenissen in de omgeving is een belangrijk middel om tot betere prestaties te komen. Het was al bekend dat aandacht aangestuurd wordt door een netwerk van frontale (voorkwab) en pariëtale (wandbeenkwab) hersengebieden, die op hun beurt de benodigde sensorische (bv visuele) hersengebieden aktiveren. Uit dit proefschrift blijkt nu dat de frontale gebieden daarbij het voortouw nemen, en niet, zoals sommige theorieën voorspelden, de pariëtale gebieden. Verder werd duidelijk dat het richten van de aandacht op twee (vrijwillige) manieren kan plaatsvinden, namelijk meer perceptie- of meer taakgericht. Deze strategieën versterken vervolgens op een selectieve manier verschillende deelaspecten van de preparatie. De meer perceptie-gerichte aanpak blijkt bijvoorbeeld van nut te zijn bij het waarnemen van slecht zichtbare gebeurtenissen, doordat zij de sensorische hersensignalen, opgeroepen door de vage stimulus, helpt versterken (bv handig in situaties waarin het schemerig is). Daarnaast helpt deze aanpak om onbelangrijke, maar afleidende, gebeurtenissen te doen vervagen (bv andere gesprekken dan die tussen jou en je gesprekspartner). De meer taak-gerichte aanpak echter blijkt beter toepasbaar in situaties waarin het missen van afleidende informatie gevaarlijk zou zijn (bv tijdens het wachten voor een rood stoplicht). Dus, op de juiste wijze je aandacht richten blijkt essentieel voor een goed resultaat.

DISCUSSIE

> *"The mere formulation of a problem is far more essential than its solution,*
> *which may be merely a matter of mathematical or experimental skills.*
> *To raise new questions, new possibilities, to regard old problems from a new angle*
> *requires creative imagination and marks real advances in science."*
>
> *A. Einstein & L. Infeld, 1938,*
> *The Evolution of Physics*

In dit proefschrift is een poging gedaan om oude vraagstukken vanuit een nieuwe invalshoek te bestuderen (*"regard old problems from a new angle"; zie quote Introductie)* en om nieuwe vragen op te roepen (*"to raise new questions"*), waarbij getracht is om daarbij niet in de val te trappen van oude wijn in nieuwe zakken te stoppen ("*transferring old bones to a new grave-yard*"). Het belangrijkste doel van dit proefschrift was om de functionele mechanismes van processen bloot te leggen die betrokken zijn bij het richten van de aandacht (ook wel top-down aandachtscontrole genoemd). Een betrekkelijk oud vraagstuk dat van een nieuwe kant is belicht betreft het alom geaccepteerde idee van het bestaan van één supramodaal en overkoepelend frontaal-parietaal (FEF-IPS) aandachtsnetwerk, in tegenstelling tot het bestaan van meerdere netwerken, iets dat gesuggereerd wordt door de grote variabiliteit van gevonden hersengebieden die betrokken zouden zijn bij dit proces. Het is nog onduidelijk hoeveel van deze variabiliteit mogelijk te maken heeft met verschillende experimentele contrasten, verschillende stimulus kenmerken en/of modaliteiten, of verschillen in gebruikte meetmethoden. Deze factoren kunnen mogelijk ook de antwoorden hebben beinvloed op de oude vraag of aandachtscontrole nu een functie is van frontale (anterieure), voorin het hoofd gelegen hersengebieden of juist meer van posterieure, achterin het hoofd gelegen, gebieden. Daarom zijn in sommige studies van dit proefschrift manipulaties opgenomen van enkele van deze factoren (type contrast, verschillende stimulus modaliteiten) met als doel deze oude vraag opnieuw te kunnen evalueren.

Eén van de nieuw opgeroepen vragen betreft de observatie dat theoretische modellen en experimentele resultaten niet altijd exact met elkaar overeen kwamen. Hierbij is afgevraagd wat bijvoorbeeld de relatie is tussen de twee vormen van attentionele selectie (selectie in een vroeg of laat stadium) en de twee voorgestelde mechanismen van aandachtsmodulatie van activiteit in sensorische gebieden (gain controle en verschuiving van de baseline), activiteit die selectief is voor het geattendeerde stimulus kenmerk. Van zulke verschillende mechanismes kan verwacht worden dat ze hun eigen representatie hebben van preparatoire activiteit in sensorische gebieden, maar bewijs hiervoor was nooit geleverd. Een ander nieuw vraagstuk dat werd aangekaart betreft de vraag wat de invloed is van vrijwillige controle over de gevolgde taak strategieën op attentionele controle activiteit en op het oplossen van conflicterende informatie.

In dit laatste hoofdstuk wordt een samenvatting en discussie gegeven van de belangrijkste resultaten en conclusies uit dit proefschrift en beschreven hoe deze de bovengenoemde vragen beantwoorden. Vervolgens wordt ook beschreven hoe de gevonden antwoorden bijdragen aan ons begrip van aandachtscontrole.

1. Het richten van de aandacht op spatiële frequentie patronen

In de eerste studie, beschreven in Hoofdstuk 2, wordt een manipulatie gebruikt waarbij de proefpersonen gevraagd werden ofwel bij elke trial aanbieding de instructie te volgen die verstopt was in de woord cues tijdens een blok van trials (experimentele conditie), danwel de instructie te volgen zoals die voorafgaand aan het blok van trials gegeven was (controle conditie). De instructie gaf aan op welke van de twee mogelijk getoonde streeppatronen een reactie verwacht werd (dikke zwart/witte streeppatronen [laag spatiële frequentie], of dunne streeppatronen [hoog spatiële frequentie]). De cue instructie diende gebuikt te worden om zich optimaal voor te bereiden op een snelle en meest accurate reactie op de targets.

Deze specifieke taak configuratie is opgenomen om ongewenste verschillen tussen experimentele en controle conditie uit te vlakken, verschillen die niet gerelateerd zijn aan aandachtscontrole (zoals verschillen in de fysieke kenmerken van de cues, verschillen in het motorisch voorbereiden op de response, of verschillen in perceptuele moeilijkheidsgraad). Naast dit nieuwe experimentele contrast bevatte deze studie ook nog een ander nieuw design kenmerk, namelijk een discriminatie taak op de cue stimulus zelf. Deze manipulatie was toegevoegd voor het garanderen van absoluut gelijkwaardige cue-interpretatie processen in de experimentele en de controle conditie. Het idee achter deze manipulatie was dat het mogelijk een methodologisch probleem kon voorkomen, namelijk dat vroege verschillen in de timing, de duur, of in de kracht van cue-interpretatie activiteit tussen condities onterecht gezien kon worden als het begin van het richten van de aandacht. Zoiets gebeurt gemakkelijk als twee actieve cue condities met elkaar vergeleken worden (b.v., aandacht versus neutrale cues) die verschillen in de hoeveelheid informatie die verwerkt wordt. Studies die gebruik hadden gemaakt van actieve cue contrasten hadden bijvoorbeeld laten zien dat het richten van aandacht op een niet-spatiëel kenmerk zoals kleur kan beginnen over posterieure gebieden (Slagter et al., 2005b; Slagter et al., 2005a). Dat effect was min of meer vergelijkbaar met de gevonden vroegste posterieure aandachtsricht effecten in het contrast tussen cues voor het richten van de aandacht naar links of naar rechts in visueel-spatiële aandachtscontrole studies, studies zoals vermeld in de Introductie, maar ook meer recente studies (Green et al., 2005; Talsma et al., 2005). Onduidelijk in deze studies was in hoeverre de claims van een posterieure start van aandachtscontrole activiteit beinvloed waren door het probleem van mogelijk verschillende cue-interpretatie activiteit. Omdat de hoofdvraag in deze studie ging over de vraag naar de start van aandachtsricht activiteit -- anterieur of posterieur -- was de toevoeging van zo'n gedragsmatige controle op de cue interpretatie processen essentieel.

De resultaten van deze studie waren in velerlei opzichten verrassend te noemen. Allereerst bleken er geen ERP (event gerelateerde EEG activiteit) verschillen te zijn tussen de reacties op de experimentele en controle cues (gemiddeld over twaalf proefpersonen). Zo'n resultaat kon betekenen dat we ofwel ons contrast te sterk gecontroleerd hadden waardoor er niet genoeg power meer over was om nog activiteit te vinden die te maken had met alleen het richten van de aandacht, ofwel dat we niet genoeg proefpersonen hadden meegenomen in de studie waardoor we gewoon te weinig experimentele power hadden om in de eerste plaats die verschillen te kunnen vinden. Geen van deze hypotheses klopte echter. Het missen van een experimenteel effect bleek te liggen aan het feit dat 4 van de 12 proefpersonen een patroon van hersenactiviteit lieten zien dat het patroon van activiteit van de overgebleven 8 proefpersonen gewoon had opgeheven. Zo liet de groep van 4 proefpersonen een "positiviteit" zien die begon ongeveer 500 ms na het verschijnen van de cue over frontale and prefrontale gebieden, waarna de activiteit zich uitbreidde over meer centrale and posterieure gebieden (met een focus in een lateraal en vooral anterieur netwerk), terwijl de groep van 8 proefpersonen juist een "negativiteit" liet zien die begon 400 ms na de start van de cue over centrale gebieden, en die zich later iets verplaatste naar meer frontaal-centrale schedel electrodes (met een focus in meer mediale anterieure en posterieure gebieden). De groep van 8 vertoonde ook zwakke biasing activiteit over occipitale gebieden, iets dat niet voorkwam in de groep van 4 proefpersonen.

Een verrassend resultaat was dat deze twee groepen niet verschilden in hun gedragsmatige reacties op de cues en de targets, maar alleen in hun hersenactiviteit. Deze verschillen in hersenactiviteit beperkten zich dus niet alleen tot de verwerking van de cues, maar deden zich ook in sterke mate voor bij het verwerken van de targets. De groep van 4 met de positieve en meer anterieure aandachtsricht activiteit vertoonde zowel vroegere en sterkere Frontale Selectie Potentialen (FSP) als sterkere pariëtale P3b responsen op de targets dan de groep van 8 die weer sterkere negatieve fronto-pariëtale aandachtsricht activiteit lieten zien, en die tussen de FSP en P3b effecten ook nog een duidelijk frontocentraal N2b aandachtseffect vertoonden. Beide groepen verwerkten de targets dus anders, ook al reageerden ze er net zo snel en goed op.

De uiteindelijke conclusie was, dat in tegenstelling tot eerdere bevindingen, het richten van de aandacht dus aanvangt in anterieure, en niet in posterieure, gebieden. Deze conclusie is onderbouwd door het feit dat de vroegste frontale aandachtsricht activiteit werd gevonden bij gelijkblijvende cue interpretatie processen voor alle proefpersonen, en dat bronlocalizatie deze activiteit meer in frontale dan in posterieure gebieden plaatste. Een tweede conclusie betrof de interpretatie dat de enorme verschillen tussen de twee subgroepen proefpersonen hoogstwaarschijnlijk niet veroorzaakt waren door strategische, maar juist door individuele verschillen. Er werd bij deze conclusie echter wel wat kanttekeningen geplaatst. Allereerst lieten de bronlocalizatie resultaten zien dat de twee groepen mogelijk gebruik maakten van verschillende frontale en pariëtale corticale gebieden; de één meer mediaal fronto-pariëtaal, de ander meer lateraal en dominant frontaal. Ten tweede bleken beide groepen gelijk qua gedragsmatige responsen, maar deze resultaten waren niet krachtig genoeg om mogelijke strategie verschillen aan te tonen.

2. Het richten van de aandacht op een visueel spatiële locatie

Het richten van de aandacht op een visuele locatie, anders dan waar de blik op gericht is, werd beschreven in Hoofdstuk 3. In deze studie is een nieuw element toegevoegd in het paradigma om problemen uit eerdere studies op te lossen. Het contrast in deze studie bestond uit een vergelijking tussen meer actieve "aandachtsricht cues" en meer passieve "interpretatie cues". De actieve cue vertelde de proefpersoon dat de aandacht verplaatst diende te worden naar een linker of rechter target locatie. Bij de passieve cue was de instructie juist om dit niet te doen, dus om de aandacht te blijven richten op het centrale fixatiepunt in afwachting van de volgende cue (er volgde toch geen target na deze cues). Vergelijkbare studies in die tijdsperiode hadden activiteit die gerelateerd is aan het richten van de aandacht naar een spatiële locatie gemeten door "verschilgolven" te bekijken tussen "aandacht naar links" en "aandacht naar rechts" cues; d.w.z. de activiteit opgeroepen door die twee cues werd van elkaar afgetrokken. Het probleem met zo'n contrast is dat, alhoewel het erg gevoelig is voor gelateralizeerde activiteit (verschillen tussen linker en rechter hersenhelft activiteit), het niet goed functioneert om activiteit te detecteren die of niet gelateralizeerd is, of gelijk is in sterkte in beide condities. Zulke activiteit wordt door de aftrek procedure namelijk verwijderd. Het contrast dat in Hoofdstuk 3 gebruikt is probeert juist dit probleem te voorkomen.

De structuur van het paradigma in deze studie was ook nieuw. Het was lastig gebleken om de resultaten van fMRI en ERP studies met elkaar te vergelijken, want de paradigma's die in dergelijke studies gebruikt werden verschilden vaak behoorlijk, vooral in de snelheid van de gebruikte stimulus presentatie reeksen. Zo werden in eerdere fMRI studies meestal vrij lange cue-target intervallen gebruikt (~6-20 seconden), met name om overlap van hersenactiviteit, opgeroepen door de stimuli, te voorkomen (de piek van de trage fMRI BOLD response ligt op pakweg 4 tot 6 seconden). In ERP studies zijn zulke intervallen meestal korter, hooguit 1 tot 2 seconden twee stimulus aanbiedingen. Langere intervallen hebben als nadeel dat ze de kans verhogen dat de aandachtsricht activiteit vermindert in de tijd, maar ook dat er geheugenstrategieën gebruikt worden in plaats van juist vooral het richten van de aandacht. Voor dit project werden dezelfde kortere cue-target intervallen gebruikt voor een fMRI en een ERP studie (pakweg 2 seconden). Verder werd het paradigma aangepast op een manier die zou helpen het probleem van temporele overlap in hersenactiviteit tijdens die ongebruikelijk snelle stimulus presentaties in de fMRI studie op te lossen. De oplossing werd gevonden in een "first-order counterbalancing" strategie van "cue-plus-target" trials (aandacht rechts, aandacht links), "cue-alleen" trials (aandacht rechts, aandacht links, en passief) en "geen-cue-geen-target (nostim)" trials. Door deze randomisatie strategie zit er namelijk net zoveel overlap op de nostim trials dan op de andere experimentele trials. De nostim trials konden daardoor gebruikt worden om de overlap uit de experimentele trials te verwijderen. Een ander nieuw aspect van dit paradigma was het uitstellen van de reactie van de proefpersoon op de detectie van de targets tot na een visueel gepresenteerd signaal (de letters REP), dat pas verscheen enige tijd na aanbieding van de targets. Zo'n setup kon de bijdrage van motorpreparatie (ter voorbereiding op de handmatige knopdruk) in de actieve aandachtsricht conditie sterk verminderen.

Dit proefschrift bevat de resultaten van de ERP studie. Relevant in die studie is dat de temporele resultaten (wanneer activiteit plaatsvond) gecombineerd zijn met de spatiële informatie (welke hersengebieden geactiveerd werden), verzameld binnen hetzelfde paradigma dat ook gebruikt werd in de vergelijkbare fMRI studie. Hierdoor kon het exacte tijdstip bepaald worden van de activiteit in de diverse betrokken hersengebieden die te maken hebben met het richten van de aandacht op een spatiële locatie.

De resultaten van deze poging om ERP en fMRI resultaten met elkaar te verenigen leidde niet alleen tot het vaststellen van een frontaal begin van aandachtsricht activiteit, maar ook tot de conclusie dat de verschillende gebieden binnen het frontaal-pariëtale controle netwerk verschillende functies verrichten. Samengevat gold dat, onafhankelijk van de richting van de aandachtsverplaatsing, frontale gebieden het eerst werden geactiveerd, zo ongeveer 400 ms na het verschijnen van de cue, en pariëtale gebieden pas later actief werden, rond 650 ms. Zodra frontale en pariëtale gebieden beide actief waren, leken ze er samen voor te zorgen dat ook de sensorische gebieden geactiveerd werden en dat bleven, precies die gebieden die selectief waren voor de richting van de aandacht en de locatie van de geanticipeerde target stimulus. Deze target-locatie specifieke sensorische cortex activiteit begon rond 850 ms en werd langzaam sterker naarmate de tijd verstreek. Vooral interessant was het feit dat deze activiteit in verdeling over de schedel gelijk was aan die van de sensorische vroege N1 response op de targets en dat deze activiteit zelfs nog even aanhield als die target toch niet verscheen (in cue-alleen trials). Deze duidelijk biasing-gerelateerde activiteit verschilde echter in polariteit van de veel vaker gerapporteerde LDAP (late aandachtsricht positiviteit) component en om die reden hebben we dit effect de nieuwe naam van "Biasing-Related-Negativity (BRN)" gegeven.

Samengevat, de studies uit Hoofdstuk 2 en 3 hebben sterke aanwijzingen opgeleverd voor een frontaal begin van activiteit die te maken heeft met het richten van de aandacht. Verder kon geconcludeerd worden dat deze frontale start onafhankelijk was van het geattendeerde target stimulus kenmerk (spatieel frequentie patroon of locatie). Deze frontale activiteit wordt later vergezeld door meer posterieur pariëtale activiteit. Tesamen leek dit frontaal-pariëtale netwerk dan weer betrokken te zijn bij zowel de initiatie als het aanhouden van sensorische cortex activiteit in voorbereiding op de verwachtte target stimulus. Dit model wijkt op zich niet af van het algemeen geaccepteerde model van aandachtscontrole. Daar staat echter tegenover dat er wel met name in de eerste studie aanwijzingen gevonden werden dat sommige proefpersonen mogelijk een iets meer lateraal en vooral meer uitsluitend frontaal netwerk hadden gebruikt (mogelijk overeenkomend met de in andere studies gerapporteerde bijdrage van de dorsolaterale prefrontale cortex). Daarin wijkt dit resultaat dan weer wel af van het algemene model. Het vernieuwende van met name de tweede studie was dat deze de exacte tijdstippen van de activiteit in de betrokken gebieden openbaarde binnen het dorso-mediale frontaal-pariëtale netwerk. Dit leverde niet alleen bewijskracht op voor een dominante rol van de frontale cortex in het initiëren van aandachtscontrole, maar op hetzelfde moment suggereerde het ook dat de verschillende frontale en pariëtale gebieden verschillende functies uitvoeren. Welke functies dat precies zijn, daarover kon alleen gespeculeerd worden. Zo werd verondersteld dat de frontale cortex het meest waarschijnlijk betrokken is bij het regelen van de verplaatsing van de spatiële aandacht en bij het vasthouden van de aandacht op die nieuwe locatie, met als doel om de taakdoelen in de gaten te houden en andere gebieden, zoals de pariëtale cortex en de target-locatie specifieke gebieden te assisteren om hun doelen te bereiken (ideeën dus die aansluiten bij die van Miller & Cohen: Frontal Executive Control model, 2001). Van de pariëtale gebieden werd verondersteld dat ze hielpen bij het verschuiven van de aandacht naar de target locatie (dat paste weer bij Posner's model) en het opbouwen en volhouden van een verandering in baseline activiteit in de relevante sensorische gebieden (hetgeen paste bij het Biased Competition Model). Tot slot werd voorgesteld dat de functie van de verschuiving van de baseline activiteit (BRN) was dat het zou helpen de detectie van perceptueel moeilijk te detecteren targets te verbeteren.

3. Verschillende vormen en mechanismes van sensory cortex biasing-gerelateerde activiteit tijdens het richten van visueel spatiële aandacht

De studie uit Hoofdstuk 4 beschreef de biasing-gerelateerde activiteit in sensorische gebieden. Deze derde studie bevatte, naast data uit Hoofdstuk 3, twee nieuwe datasets gemeten bij twee nieuwe groepen proefpersonen die een iets gewijzigde variant van hetzelfde visueel-spatiële cueing paradigma kregen aangeboden. De experimenten tesamen omvatte twee experimentele manipulaties: 1) een manipulatie van de perceptuele moeilijkheidsgraad (makkelijk of moeilijk te detecteren targets), en 2) een manipulatie van de response instructies (direct na aanvang van de target of pas veel later).

Voor de afhankelijke variabele van de verwachtte sensorische cortex biasing-gerelateerde activiteit werden twee componenten uit de data gehaald die bekend staan als waarschijnlijk een reflectie van biasing-gerelateerde activiteit. De eerste component betrof de door onszelf gepubliceerde BRN, een trage negatieve ERP component. De tweede component betrof veranderingen in de power van het achtergrond EEG en dan met name de erin voorkomende alfa frequenties (8-12 Hz). De hoofdvraag van deze studie betrof de vraag wat de functionele relatie en de relevantie was van deze twee zo verschillende componenten, geëxtraheerd uit dezelfde data en gemeten over dezelfde hersengebieden, tijdens preparatoire aandacht voor een specifieke target locatie.

De resultaten van deze studie leverde een sterke bevestiging op voor onze eerdere suggestie dat de BRN te maken zou hebben met het baseline shift mechanisme dat perceptuele gevoeligheid verbetert. Deze component reageert namelijk duidelijk op de manipulatie van perceptuele moeilijkheidsgraad, met veel sterkere responsen voorafgaande aan geanticipeerde moeilijk te detecteren targets dan voorafgaande aan de gemakkelijker zichtbare targets. Daarnaast bleek ook dat de topografische verdeling van de BRN activiteit correleerde met die van de target N1 componenten, en dat hoe sterker de BRN des te hoger de N1 amplitude was. In tegenstelling tot deze resultaten bleek de alfa response (met name een verlaging van de power over sensorische gebieden contralateraal aan de richting van de aandacht: alfa-ERDs genoemd) juist weer meer gevoelig was voor de manipulatie van response instructies, waarbij de response veel groter was als proefpersonen gelijk na target aanbieding mochten reageren in plaats van nog even te moeten wachten tot na het response signaal. De schedelverdeling van de alfa responses kwam ook niet precies overeen met de target N1 topografie, en correleerde ook qua activiteit niet met deze target component, zoals wel gevonden was voor de BRN. Daar staat tegenover dat juist de alfa responses voorafgaande aan de target weer correleerden met de latere pariëtale P3b amplitude opgeroepen door de targets, maar alleen als proefpersonen onmiddelijk mochten reageren op de gedetecteerde targets.

Dit patroon van resultaten werd geinterpreteerd als bewijskracht voor het bestaan van twee verschillende preparatoire aandachtscontrole mechanismes in sensorische gebieden die beide "biasing" reflecteren in afwachting van de target stimulus. Het eerste mechanisme ligt ten grondslag aan de trage BRN baseline shift en wordt alleen aangesproken als deze echt nodig is, namelijk in situaties waarin de energie in de stimulus erg laag is (hij moeilijk zichtbaar is) en een verschuiving in de baseline de N1 amplitude kan vergroten. Deze component lijkt dus te passen bij het idee van "Sensory Gain Control" dat de signaal-ruis verhouding van een inkomende stimulus kan veranderen ten gunste van het signaal opgeroepen door die stimulus. Het past ook goed bij Reynold's voorgestelde mechanisme van aandacht waarbij aandacht de contrast-gain functie van een stimulus naar links verschuift. Het tweede mechanisme wordt door het alfa ritme gerepresenteerd. Dit mechanisme draait waarschijnlijk meer om de formatie en het onderhoud van een taak set, of aandachtstemplate, dat ook response kenmerken van de target bevat en opgeslagen wordt in sensorische gebieden. Deze taakset bevat dus zowel stimulus als response kenmerken en deze informatie kan dan ook later gebruikt worden tijdens het evalueren van de binnenkomende target stimulus om zodoende tot een betere beslissing te kunnen komen ten aanzien van de juiste response. Dit mechanisme past dan weer goed bij het mechanisme voorgesteld in het Biased Competition Model, namelijk een langzame shift in het niveau van vuren van neuronen in sensorische gebieden, hetgeen gesuggereerd werd de link tussen stimulus kenmerken en belangrijkheid van de response vast te kunnen houden.

Tot slot bevatte deze studie ook nog een totaal onverwacht resultaat, namelijk dat de kleine wijzigingen in de paradigma's tussen de experimenten hadden geleid tot verschillende automatisch aangenomen taakstrategieën van de proefpersonen. Vooral de manipulatie van response instructies was in dit opzicht effectief. In het enige experiment met directe reacties op de targets waren de BRN en alpha-ERD effecten kwalitatief anders dan in de andere twee experimenten waarbij de proefpersonen langer moesten wachten met hun reactie. Die twee experimenten verschilden alleen kwantitatief van elkaar. De geadopteerde strategieën konden het beste samengevat worden als "taakgerichtte aandachtscontrole" versus "perceptie gerichtte aandachtscontrole".

4. Taak strategieën, top-down attentionele controle en gevoeligheid voor crossmodale afleiding

De laatste studie in dit proefschrift omvat verschillende aspecten van attentionele controle tegelijkertijd. Ten eerste bevatte deze studie zowel het richten van de aandacht op een visuele als op een auditieve target en deze combinatie kan dus antwoord geven op de vraag van generaliteit van aandachtscontrole activiteit over sensorische domeinen heen. Duidelijk verschillende schedelverdelingen in activatie zouden bijvoorbeeld wijzen op modaliteit-specifieke preparatie, terwijl eenzelfde verdeling voor het richten van de aandacht op visuele of auditieve input meer zou wijzen in de richting van modaliteits-onafhankelijke preparatie. Ten tweede bevatte deze studie een target discriminatie taak waarbij de irrelevante informatie een sterke bron van afleiding vormdes en dus een sterke filtering vereistte. Ten derde, net als in de studie beschreven in Hoofdstuk 3, was er voor deze studie ook een fMRI dataset beschikbaar, afgenomen onder sterk vergelijkbare taak omstandigheden (Weissman et al., 2004), met als voordeel dat er dus meer kennis over onderliggende bronnen voor de EEG/ERP studie beschikbaar waren dan normaal gesproken het geval is binnen aandachtscontrole ERP studies. Tenslotte bleek deze studie ook gechikt te zijn om te gebruiken voor een meer gecontrolleerde studie naar de mogelijke invloed van vrijwillige taak strategieën op mechanismes van preparatoire aandacht, en ook op de latere timing van target selectie en de eropvolgende effectiviteit van aandachtscontrole over de verdere verwerking van de target. Deze manipulatie van taak strategieën vormde een logisch vervolg op de observaties van de mogelijke invloed van zulke strategieën in de eerder beschreven studies in dit proefschrift.

Het paradigma dat in deze studie gebruikt is bestond uit een crossmodale conflicterende letter-discriminatie taak. In deze crossmodale afleidingstaak werd op hetzelfde moment een target letter "X" of "O" gepresenteerd op zowel een computerscherm (visueel) als in de koptelefoons (auditief). Er werden zowel congruente trials (b.v. een auditieve "X" tesamen met een visuele "X") aangeboden alswel incongruente trials (b.v. een auditieve "X" tesamen met een visuele "O"). Instructie cues werden gebruikt om de proefpersonen op elke trial te "vertellen" welk gedeelte van dit multisensorische letter+afleider paar de target was ("LOOK" betekende dat de visuele letter relevant was, bij "HEAR" was de auditieve letter relevant). De taak voor de proefpersoon bestond eruit om zich voor te bereiden op het detecteren van de X of de O in de gecuede modaliteit (dus ofwel de visuele danwel de auditieve letter), waarbij de andere letter die op hetzelfde moment in het andere kanaal werd aangeboden moest worden genegeerd. Met een response (twee mogelijkheden) moesten ze aangeven of de target letter een X of een O was.

De fMRI studie had zowel enkele bekende als nieuwe gegevens opgeleverd aangaande het verwerken van conflicterende informatie. Gedragsmatig waren de proefpersonen zoals verwacht trager met reageren op de incongruente dan op de congruente target+afleider paren. Een ander bekend effect dat ook in deze studie naar voren kwam was een toename van activiteit in de ACC op incongruente trials, vergeleken met congruente trials. Daarnaast leverde deze vergelijking ook meer activiteit op in gebieden zoals de DLPFC en sensorische gebieden (in dit geval auditieve en visuele cortex), effecten die ook uit andere studies naar voren waren gekomen. De algemene consensus is dat de ACC het conflict opmerkt en dan gebieden zoals de DLPFC een seintje geeft op de top-down aandachtscontrole processen te versterken in bij voorbeeld de sensorische gebieden om zodanig het conflict op te kunnen lossen (Botvinick et al., 1999; Botvinick et al., 2001; Botvinick et al., 2004; Carter et al., 1998). Dit leidt dan vaak tot een verbeterde prestatie op de eropvolgende trial (daarom wordt het ook wel "conflict adaptatie" genoemd). Nieuw in deze fMRI studie was in de allereerste plaats dat de DLPFC zowel betrokken was bij de attentionele preparatie als bij het verwerken van het latere conflict, en dat verschillende subregio's van de ACC geactiveerd werden voor taak-relevante en irrelevante aspecten van de verwerking van de target+afleider paren. Ten tweede werd er een dubbele dissociatie gevonden in het patroon van activiteit in de auditieve en visuele cortex, waarbij de activiteit in de relevante modaliteit hoger was als de target letter werd gepresenteerd in de context van een incongruente afleider dan in de context van een congruente, niet-afleidende, letter. Daarom werd de conclusie getrokken dat, in situaties waarin er multisensorische afleiding aanwezig is, de sensorische cortex, de DLPFC en de ACC allemaal een rol spelen in het reguleren van de aandacht naar de voor het taakdoel relevante stimulus. Een andere interessante observatie uit deze fMRI studie die van belang is voor dit proefschrift is het gegeven dat de frontopariëtale aandachtsricht activiteit tijdens het cue-target interval niet verschilde tussen de condities van het richten van de aandacht naar een auditieve of visuele stimulus. Zo'n patroon werd ook gevonden voor de vergelijkbare EEG studie, gerapporteerd in Hoofdstuk 5. Dat suggereert dus generaliteit in het aandachtscontrole netwerk over verschillende vormen van sensorische input.

Wat minder duidelijk was echter was de precieze timing (vroeg of laat) van de sensorische cortex effecten alsmede de onderliggende mechanismes. De ERP studie richtte zich dus aanvankelijk op het oplossen van dit vraagstuk. De toevoeging van een manipulatie van aandachtscontrole taakstrategieën echter bleek een uitstekende tool te zijn om de dynamiek van deze controle te bestuderen en dit werd dus uiteindelijk het hoofddoel. Getest werd of proefpersonen inderdaad hun strategie vrijwillig konden veranderen en daarmee invloed konden uitoefenen op hun hersenactiviteit patronen (zowel tijdens de voorbereiding op de target alswel tijdens het verwerken van deze targets). De vraag was of en hoe deze strategie veranderingen de timing van selectie van taak-relevante informatie zou beinvloeden (vroege versus late selectie processen). De hypothese was dat een sterkere perceptuele focus tijdens de preparatie fase mogelijk zou helpen om de afleidende informatie beter uit te filteren, hetgeen dan weer kon leiden tot veel snellere responsen op basis van de vroegere selectie en verminderde afleiding, vergeleken met een meer taak en actie gerichtte strategie, die op haar beurt ervoor kon zorgen dat de accuratesse verhoogd werd onder latere selectie en meer weloverwogen response beslissingen. Om die reden werden de proefpersonen gevraagd om in de ene helft van het experiment een zogenoemde "aandacht-voor-snelle-perceptie" strategie (nadruk of perceptuele filtering en snelle, niet noodzakelijk de meest accurate responsen) te gebruiken en in de andere helft een "aandacht-voor-accurate-taakactie" strategie (nadruk op taakvoorbereiding en accurate, niet noodzakelijk snelle, beslissingen). Kortom, naast de perceptie danwel taakgerichte voorbereidingsstrategie werd er ook een zogenoemde "speed-accuracy tradeoff" voor de uiteindelijk response gebruikt. Dit moest zorgen voor twee absoluut verschillende taakstrategieën.

De vrijwillige strategieën veranderde niet alleen de hoeveelheid preparatoire aandacht en target-verwerkings activiteit, maar veranderde ook de relatie tussen responsen voorafgaand en volgend op de target aanbieding, alsmede de hoeveelheid conflict activiteit. De grotere accuratesse in de "aandacht-voor-accurate-taakactie" strategie conditie was voorspeld, maar niet dat dit ook resulteerde in opmerkelijk meer conflict-gerelateerde hersenactiviteit, vergeleken met de "aandacht-voor-snelle-perceptie" strategie. Die laatste strategie leidde duidelijk tot een toename in frontaal-pariëtale preparatoire aandachts-controle activiteit en tot sterkere biasing van sensorische corticale gebieden, hetgeen dan weer resulteerde in een latere vermindering van conflict-gerelateerde hersenactiviteit. Cruciaal was dat het resultaat dat de "aandacht-voor-snelle-perceptie" strategie liet zien dat één van de twee mechanismes van sensory cortex biasing de timing van selectie van taak-relevante informatie tijdens latere target verwerking kan beinvloeden. De sterkere algemene frontopariëtale aandachtsricht activiteit en de sterkere sensorische cortex biasing in de vorm van een geoptimaliseerde taakset (modulatie van alfa-frequency activiteit) resulteerde in vroegere selectie: in de "aandacht-voor-snelle-perceptie" strategie conditie werd er een afname van de N1 response gevonden over de visuele cortex wanneer de proefpersonen de auditieve letter van de multisensorische letter selecteerden. Dus, proefpersonen waren beter in staat de afleider uit te filteren. Zo'n effect werd niet gemeten als diezelfde proefpersonen de alternatieve, meer taak en actie-gerichtte strategie volgden. Verder bleek dat de trials waarop het snelst gereageerd waren tijdens de meer perceptuele strategie ook de laagste gedragsmatige afleiding lieten zien en, heel interessant, een niet-verwachtte afwezigheid van de frontocentrale conflict-gerelateerde N2 activiteit. Die combinatie van resultaten leidde tot de suggestie dat de N2 response dus niet zo zeer gerelateerd blijkt te zijn aan het detecteren van de conflicting informatie, de algemene consensis op dit moment, maar meer te maken heeft met de toename van aandachtscontrole zelf die nodig blijkt te zijn omdat de eerdere perceptuele analyse geen uitsluiting heeft gegeven over de identiteit van de target en er dus een meer uitgebreidde later analyse nodig is hiervoor, alhoewel de conflict-detectie hypothese hiermee natuurlijk niet gelijk weerlegd is. Zo'n N2 response was echter niet noodzakelijk in de snellere trials van de perceptuele-focus conditie omdat daar de preparatoire frontaal-pariëtale activiteit al optimaal was.

Samengevat laat deze studie dus zien dat proefpersonen wel degelijk invloed uit kunnen oefenen op hun hersenactiviteit op manieren die onverwachtte consequenties kunnen hebben voor onze interpretaties van de resultaten van een studie. Dat aspect zal hieronder verder uitgewerkt worden.

CONCLUSIES

De huidige serie studies heeft een aantal interessante antwoorden opgeleverd op de gestelde onderzoeksvragen. De eerste vraag, of aandachtscontrole een supramodaal systeem betreft of dat er meerdere van zulke systemen zijn, is het lastigste om te beantwoorden. De laatste studie liet geen verschillen zien tussen het richten van de aandacht naar een auditieve danwel visuele stimulus, behalve dan wat verschillen in sensory cortex biasing activiteit. In de allereerste studie echter werden wel verschillen gevonden in frontaal-pariëtale activiteit tussen proefpersonen hetgeen kon duiden op het gebruik van verschillende hersengebieden voor hetzelfde doel. Daarnaast bleken er ook verschillende fronto-pariëtale gebieden gebruikt te zijn tijdens attentionele controle in de corresponderende fMRI studies behorende by Hoofdstuk 3 (meer mediaal-dorsaal) en 5 (meer lateraal-ventraal). Dus, alhoewel niet definitief, we kunnen onze vraag beantwoorden ten gunste van het bestaan van meerdere aandachtscontrole systemen. Het hangt vermoedelijk vooral af van het design van de studie en van de door de proefpersonen gevolgde strategieën welke gebieden precies geactiveerd en dus gemeten worden.

Het antwoord op de tweede vraag aangaande de precieze timing van activiteit in frontale en pariëtale aandachtscontrole gebieden kan met veel meer zekerheid worden beantwoord: aandachtscontrole wordt geinitieerd door de frontale cortex. Alle studies in dit proefschrift lieten een frontale start zien. Deze conclusie echter staat lijnrecht tegenover de meer recente claims van een posterieure start. In reactie op onze publicatie van een frontale start (Grent-'t-Jong and Woldorff, 2007), verschenen er twee ERP studies die een posterieure start claimden, namelijk een studie van Green en McDonald (Green and McDonald, 2008) en één van Brignani en collega's (Brignani et al., 2009). In de Green en McDonald studie (2008) werd een contrast gebruikt tussen niet-informatieve en informatieve cues (verplaats je aandacht naar boven, naar links of naar rechts). Het verschil daartussen begon 100-200 ms vroeger in de pariëtale gebieden dan in de frontale gebieden, die zelf ongeveer geactiveerd werden ~300 ms na het verschijnen van de cue. Aangezien de cue 300 ms lang op het beeldscherm stond, vond deze posterieure onset van aandachtricht gedrag dus heel vroeg plaats, namelijk tijdens het verwerken van de cue. Daarnaast was er een cue gebruikt die was opgebouwd uit vier kleuren blokjes in een spatiële layout (drie naast elkaar en één er midden bovenop). Alleen het blokje met een vooraf aangegeven kleur was relevant voor de proefpersoon, omdat dit blokje de richting bepaalde waarnaar de aandacht verplaatst moest worden. Zo'n combinatie van factoren zorgt ervoor dat de interpretatie van deze vroege effecten in termen van het verplaatsen van de aandacht naar een *toekomstig event* wel erg discutabel is, want het kan niet worden uitgesloten dat de posterieure activiteit vooral top-down aandachtscontrole weerspiegelt over de verwerking van locatie aspecten van de cue-stimulus zelf. Zulke vroegen effecten kunnen ook verklaard worden door bijvoorbeeld reflexmatige shifts naar de geinstrueerde relevant (kleur) informatie in de cue, maar ook door voorafgaande aan de cue gestarte biasing mechanismes voor het detecteren van de relevante kleur. Daarnaast heeft deze studie zich ook beperkt tot theta frequenties (4-7 Hz) in het EEG, hetgeen problematisch is omdat dit mogelijk frequentie informatie heeft verwijderd die wel degelijk informatief was (aandachtsricht activiteit in de studies uit dit proefschrift werd gedomineerd door frequenties lager dan 1 Hz en tussen 8-12 Hz). In de andere studie van Brignani en collega's (2009) werd een vroege posterieure start (~330 ms) geclaimed tussen "shift" en "hold" cues aangeboden in een RSVP taak (een snelle seriële reeks van visuele stimuli) met twee stimulus reeksen waarbij de aandacht gericht moest worden op één van de twee reeksen (de huidige na aanbieding van de "hold" cues, of de andere na aanbieding van de "shift" cues). Het probleem met deze studie is dat zo'n RSVP taak erg veel van een proefpersoon vraagt en dus een hoge staat van alertheid vereist. Dit verkleint dan de kans op het vinden van een vroegere start in frontale gebieden, want deze gebieden zijn al (bijna) op het hoogste niveau geactiveerd in zulke situaties. Het is tevens discutabel om te beargumenteren dat een proces in één van twee gebieden begint als ten minste één van die gebieden al continu actief is.

Het is natuurlijk wel zo dat het contrast tussen aandacht en controle cues zoals gebruikt in de studie beschreven in Hoofdstuk 3 mogelijk het probleem in zich draagt van verschillen in het verwerking van de ongelijke cues. Dit zou ook de vroege frontale verschillen kan verklaren. Een frontale start was echter ook duidelijk aanwezig in de studie uit Hoofdstuk 2 waarin de experimentele en controle cues op geen enkele wijze van elkaar verschilden, niet fysiek, en ook niet gedragsmatig. Zo'n combinatie van factoren zorgt voor een wel erg sterke aanwijzing voor een frontale start van aandachtsricht activiteit. Aan de andere kant kan ook beargumenteerd worden dat de resultaten van de studies van Green en McDonald (2008) en van Brignani en collega's (2009) niet noodzakelijkerwijs inconsistent zijn met de bevindingen uit dit proefschrift. Brignani en collega's, bijvoorbeeld, interpreteerden hun posterieure begin als een reflectie van de start van het "verplaatsen" van de visueel-spatiële aandacht, terwijl wij juist onze frontale start hadden uitgelegd als het begin van de "orientatie" van visueel-spatiële aandacht. Alhoewel erg subtiel, het cruciale verschil tussen deze twee concepten is dat orientatie niet alleen het verplaatsen van de aandacht omvat, maar ook andere controle aspecten zoals de top-down regulatie van de verplaatsing zelf. Het verplaatsen van visueel-spatiële aandacht staat inderdaad onder controle staat van de pariëtale cortex, maar het is aannemelijk dat andere gebieden, meest waarschijnlijk de frontale gebieden (maar wellicht ook subcorticale gebieden) de inititatie van de verplaatsing reguleren. Een duidelijk voorbeeld hiervan is de gevonden effecten van microstimulatie van FEF regio's in de frontale cortex, die ook een aandachtsverplaatsing blijken te kunnen triggeren.

De derde en vierde vraag betrof de link tussen twee theoretisch mogelijke sensorische cortex mechanismes van aandachtscontrole en vroege versus late target selectie mechanismes. De studie uit Hoofdstuk 4 laat duidelijk zien dat er inderdaad twee verschillende biasing mechanismes bestaan die een verschillende effect sorteren op de latere verwerking van de target stimulus. Samengevat zijn er twee mechanismes tegelijkertijd actief in sensorische gebieden. Het ene mechanisme wordt altijd gebruikt en draait om het initiëren en vasthouden van een aandachtscontrole gerelateerd geheugenspoor in sensorische gebieden dat de koppeling tussen taak-relevante stimulus kenmerken bevat tezamen met de verwachte gedragsmatige response en de waarde daarvan. Dit mechanisme komt tot uitdrukking in de modulatie van achtergrond alfa frequenties en we concludeerden dat deze activiteit mogelijk een EEG variant is van de toename in baseline vuurfrequenties gemeten op single-cell niveau in studies die bijgedragen hebben aan de ontwikkeling van het Biased Competition Model. Dit alfa mechanisme kan dan weer vergezeld worden door een tweede mechanisme dat weerspiegeld wordt door de BRN component en alleen aangesproken wordt als dat echt nodig is, namelijk in situaties van lage stimulus contrast. In tegenstelling tot een verandering in de frequentie van neuronaal vuren weerspiegelt de BRN meer de verandering in de neuronale threshold voor vuren, nodig om ervoor te zorgen dat zelfs heel weinig stimulus energie toch nog een response kan opleveren. Zo'n mechanisme is dus consistent met het idee van een door aandacht geinitiëerde shift van de contrast-gain functie naar links (Contrast-Gain Modulatie idee van Reynolds) en dit zou ook de Sensory-Gain contrast responsen in ERP data kunnen verklaren.

Een laatste vraag betrof de relatie tussen deze twee mechanismes en vroege versus late selectie van taak-relevante informatie. Het threshold-shift mechanisme promoot waarschijnlijk vroege selectie door middel van het verhogen van bijvoorbeeld de amplitude van de sensorische N1 component, daarbij zorg dragend voor verbetering van vroege perceptuele discriminatie. Echter, Hoofdstuk 5 liet zien dat perceptuele discriminatie ook versterkt kan worden door het onderdrukken van de response op taak-irrelevante informatie zonder dat dit gepaard gaat met een versterking van de response op relevante informatie. Dit werd voorafgegaan door een toename in de kracht van de sensorische cortex alfa-frequentie activiteit (taakset gerelateerde activiteit) en niet door een shift in de threshold voor vuren (alhoewel niet geraporteerd in Hoofdstuk 5, de "BRN-achtige" ERP activiteit verschilde niet tussen de strategie condities). Daarnaast bleek uit de studie in Hoofdstuk 4 dat de kracht van zo'n visuele-cortex opgeslagen taakset niet correleerde met de N1 amplitude (en dus vroege selectie), maar meer met late selectie mechanismes (verhoging van de latere P3 amplitude). Dit patroon van resultaten over studies heen kan erop wijzen dat er ook nog een mogelijk additieve invloed bestaat vanuit andere aandachtsricht gebieden, zoals het fronto-pariëtale netwerk en mogelijk zelfs ook subcorticale gebieden, op de timing van selectie van taakgerelateerde targets. Miller en Cohen's (2001) model suggereerde dat ook de frontale cortex taaksets kan vasthouden en gebruiken voor target selectie. Het is dus best mogelijk dat de vroege selectie effecten, gerapporteerd in Hoofdstuk 5, meer te maken hebben met de toegenomen frontale preparatoire aandachtsricht activiteit dan met de alfa-power veranderingen die gevonden werden over de sensorische visuele cortex. De alfa effecten kunnen misschien beter verklaard worden vanuit het gegeven dat er in de "aandacht-voor-snelle-perceptie" strategie een grotere nadruk lag op het snel nemen van een beslissing om zo snel mogelijk te kunnen reageren. Zoals de resultaten uit Hoofdstuk 4 lieten zien kan zoiets de taakset, opgeslagen in de visuele gebieden, versterken. Hoofdstuk 5 liet verder duidelijk zien dat de timing van selectie niet alleen beinvloed kan worden door taak/paradigma factoren (Lavie, 1995), maar ook door vrijwillig toegepaste taak strategieën. Hieronder wordt dit punt nog verder uitgewerkt.

Nog wat laatste opmerkingen

Het heeft er alle schijn van dat aandachtscontrole niet een enkel mechanisme omvat, maar eerder een verzameling is van een aantal verschillende mechanismes zoals wellicht het verhogen van corticaal arousal, het verplaatsen van de aandacht, het voor een langere tijd vasthouden van die aandacht, het vastleggen en onderhouden van één of meerdere taakset templates, het aanbrengen van een bias in relevante input gebieden en tot slot het voorbereiden van een response. Dit proefschrift heeft laten zien dat de mate waarin elk van deze processen benadrukt wordt afhankelijk is van vrijwillige controle aspecten: een meer perceptuele ("aandacht-voor-perceptie") strategie levert een andere balans op qua spreiding en kracht van hersenactiviteit dan het volgen van een meer actie en taakdoel gerichtte strategie ("aandacht-voor-taakactie" strategie). Dat is belangrijke informatie, want zulke strategieën kunnen aangeleerd worden om de aandacht meer flexibel te kunnen richten afhankelijk van de situatie waarin men zich bevindt. Bevat een omgeving bijvoorbeeld veel bronnen van niet-belangrijke afleiding dan levert een meer perceptuele aandachtsstrategie betere resultaten op, omdat de afleiding beter wordt uitgefilterd en de concentratie daardoor beter gericht kan worden op wat wel belangrijk is. Is de kans om afgeleid te worden echter klein en is wat af kan leiden mogelijk wel belangrijk en/of gevaarlijk om te missen, dan is het beter om een meer actie en taakgerichtte aandachtscontrole strategie te kiezen. Dus, flexibiliteit is waar het om draait bij het richten van de aandacht.

Ten tweede, als aandachtscontrole verschillende gebieden recruiteert onder verschillende taak omstandigheden en verschillende taak strategieën, kunnen we dan nog wel spreken van aandacht als gecontroleerd door hersengebieden, of een netwerk van gebieden, door "een klein mannetje in ons hoofd" (vaak aangeduid met het begrip "homunculus")? Met andere woorden, wat moeten we verstaan onder het begrip "controle" en hebben we het begrip controle eigenlijk wel nodig binnen deze context? In mijn visie is het antwoord op die laatste vraag zowel "ja" als "nee". Om met het "ja" gedeelte te beginnen, ja we hebben wel degelijk behoefte aan het concept van controle om te verklaren hoe bepaalde functies in de hersenen door aandacht versterkt kunnen worden, functies die bijvoorbeeld bepalen of we nu wel of niet een stimulus waarnemen die aangeboden wordt onder onze grens van waarneming. Perceptie en perceptuele discriminatie zijn duidelijk niet alleen een functie van stimulus kenmerken. Daarnaast zijn ook hogere cognitieve functies zoals werkgeheugen en processen die betrokken zijn bij het nemen van beslissingen afhankelijk van aandachtsregulatie. Het antwoord is echter meer een "nee" als we de vraag vertalen vanuit een iets ander gezichtspunt, namelijk of aandacht "causaal" is of niet in termen van zijn controlerende functie. Hier wordt het allemaal veel minder duidelijk. We hebben bijvoorbeeld veel variatie in hersenactiviteit gezien tussen, en zelfs binnen, studies, en dat kan juist een indicatie zijn van het feit dat we wellicht niet kijken naar aandachtscontrole activiteit als de dirigent, maar eerder naar het resultaat van diezelfde aandachtscontrole. Vanuit dit licht gezien is aandachtscontrole activiteit wellicht meer een algemene eigenschap van hersenactiviteit, in tegenstelling tot aandachtscontrole die een bepaalde locatie heeft. Het kan worden uitgelegd als het gevolg van de intentie om aandacht te schenken en ons voor te bereiden op de toekomstige taak. Zo'n interpretatie kan wellicht verklaren waarom er zoveel verschillende gebieden zijn gevonden tussen de diverse studies, tussen de diverse paradigma's, en zelfs tussen proefpersonen. Daarnaast bleken de gevonden resultaten erg af hangen van het gebruikte experimentele contrast. Toekomstige studies zouden dergelijke bespiegelingen veel meer mee moeten nemen bij de interpretatie van de resultaten van hun onderzoek.

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Curriculum Vitae (in het Nederlands)

Tineke Grent - 't Jong (Tinie 't Jong) werd op 25 oktober 1961 geboren te Apeldoorn. In 1980 behaalde ze haar HAVO diploma, waarna zij twee jaar later de HBO-A opleiding voor klinische chemisch analiste succesvol afsloot. Tussen 1982 en 1989 werkte ze als medisch analiste in het Sint Jans Ziekenhuis (later omgedoopt to West-Fries Gasthuis) te Hoorn. Daarna volgde ze eerst tussen 1989 en 1991 de HBO-J opleiding tot jeugdwelzijnswerker. In 1993 startte ze met de deeltijd opleiding Psychologie aan de Universiteit van Utrecht. De studie Psychologie werd in 2001 succesvol afgerond met een doctoraal diploma in de richting Biologische Psychologie. Al tijdens de laatste fase van deze studie kwam ze in contact met Prof. Marty Woldorff, door een buitenland stage bij professor Ron Mangun in de "Center for Cognitive Neuroscience" (CCN) te Duke University, Durham, North Carolina, VS. Bij Prof. Marty Woldorff heeft ze als onderzoeksassistent en labmanager tussen januari 2002 en mei 2003 gewerkt. Bij terugkomst in Nederland werd ze Assistent in Opleiding (AIO) op een project van Nick Ramsey, nu hoogleraar Cognitieve Wetenschappen in het Universitair Medisch Centrum te Utrecht (UMC), met als eerste promotor Prof. Leon Kenemans van de vakgroep Experimentele Psychologie en Psychofarmacologie aan de Universiteit van Utrecht. Het AIO project verliet ze echter vroegtijdig in het voorjaar van 2005. Vanaf september 2005 tot aan september 2010 heeft ze weer haar oude functie op het lab van Prof. Marty Woldorff op Duke University in de VS vervuld. Tegelijkertijd kreeg ze de mogelijkheid om aan dit nu voor U liggende proefschrift te werken onder de uitstekende dagelijkse begeleiding van haar amerikaanse professor Marty Woldorff en de op afstand beschikbare hollandse professor Leon Kenemans.

Curriculum Vitae (in English)

Tineke Grent - 't Jong (Tinie 't Jong) was born on October 25th 1961 in Apeldoorn, the Netherlands. She received her high-school diploma (HAVO) in Alkmaar in 1980, after which she continued her education at the higher laboratory school (HBO-A) in Beverwijk. She graduated there as a medical technician in 1982. Between 1982 and 1989 she worked full-time as a medical technician in Sint Jans Hospital (later renamed to West-Fries Gasthuis) in Hoorn. From 1989 until 1991 she studied at the higher education school for youth welfare workers (HBO-J). In the fall of 1993, she switched to a (part-time) study Psychology at Utrecht University, where she finally graduated with a Masters degree in Biological Psychology in 2001. During the final year of her study, she visited the Center for Cognitive Neuroscience (CCN) at Duke University, Durham, NC, USA, for an internship with Prof. Ron Mangun. Through her stay in the CCN, she came in contact with Prof. Marty Woldorff, for whom she started working after graduation, from January 2002 to late spring 2003, as an Associate in Research. After moving back to the Netherlands she started a Ph.D. project with Prof. Nick Ramsey from the University Medical Center in Utrecht (UMC) and Prof. Leon Kenemans from the Department of Experimental Psychology and Psychopharmacology at Utrecht University. She resigned, however, from this project prematurely in early spring 2005. In September of that same year she moved back to Duke University, and continued to work as an Associate in Research for her old boss, Prof. Marty Woldorff. In addition, she started working on this dissertation, under the carefull supervision of her American professor Marty Woldorff, and, at the distance, her Dutch professor Leon Kenemans, with the goal to finally graduate with a Ph.D. from Utrecht University.