Beyond ERP's: oscillatory neuronal dynamics

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2.1 Introduction

2.1.1 The discovery of rhythmic EEG oscillations

Since the initial report on the existence of electrical activity stemming from the brain in 1875 by Richard Caton (Caton, 1875), researchers have been intrigued for more than half a century by the strikingly ubiquitousness of rhythmic, oscillatory activity in EEG recordings. In the early reports on EEG, a particularly counterintuitive finding was that the observed oscillations seemed to disappear upon sensory stimulation. Adolf Beck, one of the pioneers of EEG research, struggled with the interpretation of this observation, as evidenced in the following passage from his Ph. D. thesis:

" An important phenomenon which occurred in nearly all experiments (...) was the arrest of the spontaneous oscillations of the action current. The explanation of this phenomenon is not too easy. I would interpret it as an expression of the arrest of the active state at a certain point and a suppression of the changes which occurred spontaneously in the active state. In a word, one can explain it by inhibition. It is nothing new to us that the excitation of some centres causes inhibition of the active state of others ".. Beck, 1891 (Polish thesis, for English translation: Beck, 1973).

Some 20 years later, when the recording equipment was sufficiently powerful, part of the riddle was solved through the identification of two types of rhythmic activities in the EEG of the

dog (Práwdicz-Neminski, 1913). The relatively large-amplitude, low-frequency oscillations described by Caton and Beck did not fully disappear upon sensory stimulation, but shifted to a different pattern of low-amplitude, high-frequency oscillations. These distinct EEG patterns were initially termed waves of the first order and waves of the second order. Later these waves were called A-waves and B-waves, and today they are known as alpha- and beta waves. In 1929 the famous paper by Hans Berger was published (Berger, 1929), which constitutes the first report on human scalp EEG. Berger carefully described the conditions under which the alpha and beta rhythms appear in humans, and noted the inverse relation between amplitude and frequency of EEG rhythms. He is most famous for describing the phenomenon of alpha blocking (also known as the Berger effect), not only upon the opening of the eyes, but also upon the execution of a cognitive task (such as performing arithmetic operations).

2.1.2 From EEG to ERPs

With the development, between the 1930's and 1960's, of better recording devices, more advanced signal analysis techniques and more computational power, EEG became an increasingly popular tool to study the brain in action. As a matter of fact, for almost half a century, i.e. from the early 1960's until present, EEG has been by far the most widely used experimental technique to investigate the relationship between cognitive functions and brain activity (although fMRI might have taken over this position in the last couple of years). Interestingly however, the interest of EEG researchers has moved away from studying oscillatory EEG phenomena to a different approach, that of studying Event-Related Potentials (ERPs). In fact, since the early 1960's the event-related potential (ERP) approach has been the dominant approach to studying the relation between EEG and cognition. As far as we can see, the main

motivation for this shift in focus has been the insight that a large part of the recorded EEG is not related to the processing of the experimental event in question (a stimulus, a response, or a given cognitive process). Therefore, a procedure is needed to extract the truly event-related EEG (the signal) from this so-called background EEG (the noise). An obvious way of extracting the signal from the noise is to average the EEG across a number of epochs that are time-locked to the experimental event. In practice, this means that one typically repeats a given experimental paradigm a number of times (say, 30 times), and then one averages the 30 EEG recordings that are recorded time-locked to the experimental event. The noise (which is assumed to be randomly distributed across trials) diminishes each time a trial is added to the average, while the signal (which is assumed to be stationary across trials), gradually emerges out of the noise as more trials are added to the average.

2.1.3 Phase-locked versus non-phase-locked, or evoked versus induced EEG responses.

The ERP approach has provided a wealth of fine-grained information about the time course, and the neural basis of cognitive processing events. The success of this approach is evidenced, for instance, by the very book you are now reading. However, in the course of the 1980's and 1990's an increasing number of researchers began to realize that an ERP only represents *a certain part* of the event-related EEG signal (we return to that in a minute). Therefore, recent years have seen a renewed interest in another aspect of event-related EEG activity, on which we focus in this chapter. This aspect is related to the event-related fluctuations in rhythmic, oscillatory EEG activity. Indeed, more than 100 years after the initial discovery of EEG oscillations, interest in these phenomena has come back, mainly as a result of the view that they might provide a window on the dynamics of the coupling and uncoupling of functional

networks involved in cognitive processing (see e.g. Singer, 1993, 1999; Varela, Lachaux,

Rodriguez, & Martinerie, 2001), as we explain in more detail later.

In studying oscillatory EEG responses, it is important to realize that any change in

oscillatory activity that is related to an experimental event is time-locked to this event (otherwise

it wouldn't be event-related) but not necessarily phase-locked to the event[1]. The reason for this is

that oscillations are ongoing phenomena, that also live in the absence of any experimental task.

As a result, the phase of the oscillation at the time of occurrence of the event is variable.

Therefore such event-related changes in oscillatory EEG activity are termed non-phase-locked

responses. Note that, although such an oscillatory response may be meaningfully related to the

event in question (for example, the decrease in amplitude of posterior alpha-band activity when a

subject opens his or her eyes – the famous Berger effect), straightforward averaging of a number

of trials in which this response occurs (i.e., using the ERP approach) does not work. As such

non-phase-locked responses are not stationary (because the phase of the response varies from

trial to trial), and therefore they will be severely reduced (and will fully cancel in the long run)

as a result of averaging across trials. The different results of averaging for phase-locked event-

related EEG responses (that is, ERPs) and non-phase-locked responses are illustrated in Figure

2.1

*** Insert Figure 2.1 about here ***

We would like to note in passing that because event-related oscillatory responses are

essentially modulations of ongoing activity, they are often termed induced responses. In contrast,

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[1] The amplitude af an oscillation is, roughly speaking, the size of its (positive or negative) peak deflection relative to some baseline – that is, how 'big' the oscillation is; the phase of an oscillation is, roughly speaking, the slope (or 'direction') of the signal at a given one point in time

the transient, time- and phase-locked activity that is represented by the ERP is often termed evoked activity, because this activity is initially non-existent, and is only driven (evoked) by the experimental event. However, in the remainder of this chapter we prefer to use the more neutrally descriptive (and signal analysis-oriented) terms phase-locked and non-phase-locked activity.

2.1.4 Oscillations, synchronization and functional networks

The distinction between phase-locked and non-phase-locked responses, or between evoked and induced EEG for that matter, is useful in the context of signal analysis. That is, for non-phase-locked EEG responses one needs to use different analysis tools (see section 1.5) than for phase-locked responses, where a simple averaging across trials is sufficient. However, this raises the question of whether there is also a more fundamental difference between the two types of responses.

One thing that has become very clear on the basis of PET and fMRI studies is that a one-to-one mapping between a brain area and a specific component of a cognitive function is very often far too simplistic. Imaging studies often report activations of one and the same area during different tasks or cognitive processes. This indicates that individual cortical areas can be recruited dynamically in more than one functional network (Mesulam, 1998). This raises the question of how, for a given function (e.g. visual perception), the dynamic recruitment of the participating cortical and subcortical areas takes place. Another, yet related question is, how different sources of information (e.g. information about color, shape and movement of an object), that are stored in different parts of the network, are integrated in order to form a coherent neural representation of the object.

An answer to both these questions may be found in the patterns of synchronization and desynchronization of neuronal activity. Over the last fifteen years evidence has accumulated that (de)synchronization is related to the coupling and uncoupling of functional networks in the brain (see e.g. G. Pfurtscheller & Berghold, 1989; G. Pfurtscheller & Lopes da Silva, 1999; G. Pfurtscheller & Neuper, 1997; Singer, 1993, 1999; Varela et al., 2001, and many more). The idea is that synchronous, repetitive firing of neurons facilitates the activation of functional networks because it increases the probability that neurons entrain one another in synchronous firing (e.g. Konig & Schillen, 1991). In addition, elements pertaining to one and the same functional network are identifiable as such by virtue of the fact that they fire synchronously, at a given frequency. This frequency-specificity allows one and the same neuron (or neuronal pool) to participate at different times in different representations. Hence, synchronous oscillations in a wide range of frequencies are considered to play a crucial role in linking areas that are part of one and the same functional network. Importantly, in addition to recruiting all the relevant network elements, oscillatory neuronal synchrony would also serve to bind together the information that is represented in the different elements, as was elegantly demonstrated in a seminal paper by Gray and Singer (Gray, Konig, Engel, & Singer, 1989).

As there is always a substantial level of synchrony in neuronal firing, oscillatory activity dominates raw EEG recordings. Experimental events will occur at random phases of the ongoing oscillations, and will modulate these oscillations, thus resulting in non-phase-locked responses. To cut a long story short, in contrast to phase-locked responses (ERPs) non-phase-locked responses predominantly reflect the extent to which the underlying neuronal activity synchronizes. Since, as we argued, synchronization and desynchronization are indicative of the coupling and uncoupling, respectively, of functional networks, it follows that *event-related, non-*

phase-locked oscillatory EEG responses provide us with a window onto the functional network

dynamics in the brain.

2.1.5 Power and coherence as measures of functional network dynamics

As said, the ERP approach is not adequate for extracting non-phase-locked responses

from the raw EEG. Therefore, methods other than traditional ERP analysis are needed to

optimally capture (de)synchronization phenomena. The question is then, which analysis

procedures would be adequate for studying changes in oscillatory synchrony?

In this context, it is sensible to realize that the neocortex is organised such that at any

place in the cortex, there are very dense connections to adjacent cortical areas. This facilitates

neuronal synchrony at a local scale. In addition, there are long-range connections, albeit much

sparser, to more distant cortical areas, which enable neuronal synchrony across larger distances.

It therefore seems reasonable to assume that distributed functional networks consist of a number

of local 'nodes' that operate in synchrony with each other through long-range synchronization.

As a result, it makes sense also at the level of signal analysis to try and distinguish between local

synchrony, that is, synchronization *within* a node of a functional network on the one hand, and

long-range synchrony, i.e. synchronization *between* different nodes of a network. Let us see how

that works out.

Local synchronous activation of a large number of neurons will, by virtue of the spatial

summation of post-synaptic potentials, result in an increase in amplitude of the resulting field

potential at the recording site. It follows that an increase in local synchronous oscillatory firing

of a neuronal population will lead to an increase in amplitude of the scalp-recorded EEG

oscillations. Such amplitude (or power, i.e. squared amplitude) changes should be studied at the single trial level (although the average amplitude, or power change can subsequently be computed across trials, see Figure 2.1). Different methods for studying event-related power changes have been used in the literature. Widely used are the more traditional event-related band power analyses like Event-related Desynchronization (ERD;G Pfurtscheller & Aranibar, 1979; G. Pfurtscheller & Lopes da Silva, 1999) or Induced Band Power (IBP; Klimesch, Russegger, Doppelmayr, & Pachinger, 1998), the more fashionable single-trial wavelet analysis (Tallon-Baudry, Bertrand, Peronnet, & Pernier, 1998), or the more recently proposed and more sophisticated multitaper analysis (Mitra & Pesaran, 1999).

It should be noted here that the mere presence of power in a given frequency band does not necessarily imply the presence of an oscillation at that frequency. Transients in the EEG signals, such as ERPs, muscle and eye-movement artefacts will yield power in specific frequeny bands, without any oscillations being present. For instance, performing a time-frequency analysis on an averaged ERP (say a succesion of N1/P2/N400 components) will yield power in the alpha (for the N1/P2 complex) and theta (for the N400) frequency ranges, but these ERPs have nothing to do with oscillations. In general, a good indication of the presence of oscillatory activity in a time-frequency decomposition is the presence of narrow-band power increases that last for at least one or two (for low frequencies) or more (for high frequencies) periods of the oscillation (e.g., 400 ms for a 5-Hz oscillation, or 100-200 ms for a 40-Hz oscillation). Short-lasting broadband responses (e.g. a 40-100 Hz increase in power that lasts only for a few tens of ms) are usually indicative of the presence of muscle artefacts, stimulus-related artefacts or other non-brain transients. Moreover, regardless of the exact time-frequency method used, one should realize that the time resolution of a time-frequency decomposition is inherently poor, i.e. in the

order of 1-2 periods of the slowest oscillation under consideration (cf. Knosche & Bastiaansen, 2002 for more details).

Activity in distant neuronal populations is, for the largest part, not picked up by one and the same electrode, but by different electrodes. Therefore the above-mentioned principle of spatial summation, and hence power increase as an indication of local synchrony, does not apply. Here the relevant information lies in the phase relationship between the field potentials recorded from or above different areas. An increase in synchrony will logically lead to an increased stability of the phase difference of two oscillatory field potentials, which is typically termed coherence (see e.g. Varela et al., 2001 for extensive arguments). This can be quantified using methods such as event-related coherence analysis (Andrew & Pfurtscheller, 1996; Nunez et al., 1997) or phase-locking statistics (Lachaux, Rodriguez, Martinerie, & Varela, 1999). In sum, the power of a given frequency band can be used to assess synchronization changes in local neuronal ensembles (i.e., within nodes of the functional network), while the coherence between electrode sites in a given frequency band yields information about synchronization changes between two or more such local ensembles (i.e., between different nodes).

However, although power and coherence are by far the most studied aspects of event-related modulations of oscillatory activity, it is important to realize that there are other aspects (and related measures) of such modulations that may be equally meaningful in better understanding the neural basis of cognitive functions. An excellent overview of potentially relevant phenomena was given by Makeig, Debener, Onton, & Delorme, 2004). For instance, there have been several reports of event-related phase resetting (the phase realignment, across trials, of oscillatory activity with respect to an experimental event, e.g. Braeutigam, Bailey, &

Swithenby, 2001; Rizzuto et al., 2003). Interestingly, because such phase resetting will by definition result in an event-related, phase-locked EEG response (our familiar ERP), it has been proposed (Makeig et al., 2002) that such a phase-resetting mechanism might constitute the basis for many (if not all) ERP-like phenomena. In the next section we discuss this idea in more detail, and we present experimental evidence that disfavors this idea.

2.2 Are ERPs really just oscillations? Phase resetting versus the additive model

Over the past few years, the role of the EEG in cerebral processing has been extensively reconsidered (Makeig et al., 2004; Mazaheri & Jensen, 2006), and ongoing cerebral activity can no longer be though of as just relatively random background noise that must be removed in order to see the event-related responses. However, to date, researchers studying electrophysiological brain activity either concentrate on oscillatory dynamics or on additive effects. Moreover, the relationship between ERPs and oscillatory brain activity has remained elusive. There are currently two different theories which attempt to account for the relationship between stimulus evoked components and the ongoing EEG activity.

One view often referred to as the additive model proposes that the ERPs and EEG are different neural events that are either in the strictest sense completely independent of one another, or in a softer stance potentially modulated by one another. According to the additive model of ERP generation, the stimulus 'evokes' an additive, phase-locked response in each trial, and by averaging, which removes the spontaneous oscillatory activity that is not phase-locked to the onset of the stimulus, this leaves behind the (time- and phase-locked) evoked components. Because the ERP should be seen in the frequency domain as a transient change in amplitude, the

additive model is also often referred to as the amplitude-modulation theory (Makinen, Tiitinen, & May, 2005; Mazaheri & Jensen, 2006; Mazaheri & Picton, 2005; Shah et al., 2004) .

An opposing view, referred to as the phase-resetting view, which of late has started to get some prominence, claims the EEG and ERP to be the same neuronal event. In the phase-resetting view the ERP is generated because of stimulus evoked phase perturbations in the ongoing EEG. According to the phase-resetting view, upon the onset of a stimulus the phases of the ongoing background oscillations become aligned (phase-reset or partially phase-reset) to the stimulus (Gruber & Muller, 2005; Klimesch et al., 2004; Makeig et al., 2002; Penny, Kiebel, Kilner, & Rugg, 2002). By averaging the stimulus-locked trials, the phase-locked oscillatory activity emerges as the evoked component in the average. Figure 2.2 schematically shows how this works. Since alpha oscillations are the predominant oscillatory activity in the EEG/MEG, it is believed that the phase-resetting of these oscillations are particularly relevant for producing the ERP (Gruber, Klimesch, Sauseng, & Doppelmayr, 2005; Klimesch et al., 2004; Makeig et al., 2002). We now critically discuss the validity of arguments for and against phase resetting as a mechanism for ERP generation.

*** Insert Figure 2.2 about here ***

A fundamental feature of the phase-resetting hypothesis is that following the presentation of a stimulus, the phases of ongoing EEG rhythms are shifted to lock to the stimulus. From this it follows that during pre-stimulus intervals, the distribution of the phase at each EEG frequency would be random, whereas upon stimulus presentation, the phases would be set (or reset) to specific values (for each frequency). The resetting of the phases causes an ERP waveform to

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appear in the average (Makeig et al., 2002; Penny et al., 2002). The most commonly cited

evidence for the phase-resetting hypothesis is the fact that the trial-to-trial phase coherence

increases after the onset of the stimulus, suggesting that the phases of the oscillations were

perturbed by the stimulus(W. R. Gruber et al., 2005; Klimesch, Hanslmayr, Sauseng, & Gruber,

2006; Klimesch et al., 2004; Makeig et al., 2002; Penny et al., 2002) . However, as it has

recently been demonstrated by many studies, an increase in trial-to-trial phase coherence can in

no way disambiguate between the additive theory and the phase resetting hypothesis (Mazaheri

& Picton, 2005 Yeung, 2004 #80; Yeung, Bogacz, Holroyd, Nieuwenhuis, & Cohen, 2007)

     This is because adding an ERP waveform (with set phases for each of its component

frequencies) to a randomly phased EEG causes the recorded phases to move toward the phases of

the ERP waveform. The addition of a signal to an unchanging background can therefore look

much the same as a phase locking of the background activity. Thus, phase synchronization

during the ERP is clearly not proof that the ERP is generated by phase-resetting of the EEG (see

Figure 2.3)

                             *** Insert Figure 2.3 about here ***

     Other support for phase-resetting comes from studies reporting no net-power change in

the EEG at the time of the evoked response (accompanied by an increase in phase-

synchronization across trials). However, this too unfortunately cannot disambiguate between the

two theories, since occurrence of a decrease in the amplitude of the EEG (particularly in the

alpha band) at the same time as the evoked potential could mask out any transient evoked

increases (Hanslmayr et al., 2007). In sum, arguments in favor of the phase-resetting hypothesis have remained unconvincing so far.

Now we turn to the arguments favoring the Additive model of ERP generation. Intracortical animal recordings have shown that the visual-evoked ERP can occur when there is little background EEG activity (Shah et al., 2004). This is contradictory to the phase-resetting model since one key requirement of the phase modulation theory is the existence of ongoing EEG rhythms whose phases can be modulated. However, although arguably unlikely it is possible that the visual-evoked ERP of these recordings might have triggered phase locking of EEG rhythms that were not recorded in the multi-electrodes but which might have been visible in the scalp recording. To make matters more complicated, human intracortical recordings of 7–16 Hz rhythms during cognitive processing show clear phase-resetting without any consistent increase in amplitude (Rizzuto et al., 2003).

Using a modeling approach, Makinen et al. (2005) suggested that the amplitude variance across trials could be used as a parameter for distinguishing between two theories of ERP generation. The authors argued that if the oscillations in the EEG are reset as a result of a stimulus then a drop in the variance of the amplitude should be seen at the time of the evoked response. They not only found that the amplitude of the event-related responses were independent of the amplitude of pre-stimulus oscillatory activity, but that the amplitude variance increased across trials (Makinen et al., 2005). Klimesch et al. (2006) were able to counter the claim of amplitude variance serving as an indicator of a phase-reset by integrating event related decreases in alpha amplitude in the model and finding that indeed the variance was unaffected in

a phase-reset (Klimesch, Hanslmayr et al., 2006). Thus, amplitude variance of the oscillatory

activity in the EEG cannot be used to argue against either of the models.

Using a different approach, Mazaheri and Jensen (2006) developed a phase-preservation

index (PPI, see Figure 2.4) which estimates the stability of instantaneous post-stimulus phase

compared with pre-stimulus phase (Mazaheri & Jensen, 2006). The PPI is a variant of the

conventional phase-locking measures in that instead of looking at instantaneous phase-locking

across trials, it looks at the uniformity of difference between a reference phase and an

instantaneous phase. The authors reasoned that to fully disambiguate the two theories it is crucial

to examine the phase of the ongoing oscillations before the stimulus and see if it is preserved

AFTER the event related response. If the phase of the oscillatory activity was perturbed by the

stimulus than there should be no post/pre-stimulus phase relationship. The authors found that

ongoing alpha oscillations (8-13 Hz) after visual stimuli preserve their phase relationship to the

oscillations prior to the stimuli, indicating no phase resetting had taken place. However it must

be noted that even though the PPI is able to assess the stability of phase across time, a break-

down in the PPI (strong evidence AGAINST phase resetting) cannot be used as evidence for

phase-resetting. This is because, like the conventional phase-locking measures, an additive signal

to the ongoing oscillations can bias the measurement of instantaneous phase and cause it to

become uncoupled with the reference phase.

*** Insert Figure 2.4 about here ***

If the evoked potentials are phase-reset EEG oscillations, one would then subsequently expect a

strong relationship between the amplitude of the pre-stimulus oscillations and the amplitude of

evoked potential. Using this premise Becker et al 2008 found that high alpha amplitudes were not able to change the amplitude of visual ERPs and in fact decreased the amount of phase-locking across trials (Becker, Ritter, & Villringer, 2008).

Thus it can safely be said that to date no method has been able to find unequivocal evidence for either of the two theories of ERP generation. Makeig and his colleagues have proposed that the full brain response can be mapped onto a "event-related brain dynamic state" with the dimensions of frequency, power, and phase synchronization (Makeig et al., 2004). This would entail that any cognitive event can both activate a specific pattern of response and reset the phase.

One idea that has been put forward is that the EEG and evoked responses are generated by overlapping generators (Mazaheri & Picton, 2005; Shah et al., 2004). Termed the "shared generator" hypothesis, the idea here is that EEG rhythms share neuronal generators such that neurons in a particular region of cortex are involved in both the generation of EEG rhythms and in stimulus-evoked ERPs. A stimulus may thus cause several changes. First, the stimulus may activate cells that are either relatively quiescent in a precisely time-locked way (yielding a phase-locked response) or are variably time-locked (producing a non-phase-locked response). Second, the stimulus may cause neurons that are already active in producing certain ongoing oscillations to entrain themselves to the stimulus (phase-resetting). This entrainment may result in a power decrease in the frequency of that oscillation and a subsequent power increase in lower or higher frequencies at the time window of the phase entrainment.

After discussing all this, one might be tempted to ask whether trying to establishing a relationship between ERPs and oscillatory dynamics is of any utility? One reason is that neuronal activity measured using electrophysiology exhibits spontaneous variability on time scales of hundreds of milliseconds to seconds, suggesting that the functional state of cortical networks is continuously changing. Yet the ERP alone in principle cannot directly provide any insight into this variability given it reflects the brain's phase-locked response *after* the stimulus. A link between ERP and EEG can provide a unified temporal account (pre-stimulus and post) of how information is processed by the brain. Finally, other imaging modalities can benefit from further insight into this relationship of ERPs. ERPs can provide a critical link between the hemodynamic response indexed by functional MRI and the temporal dynamics of underlying neuronal activity (Murray et al., 2002). If ERPs are just a by-product of phase perpetuation of the EEG, this link would have to be expanded and thoroughly revised. It has been suggested that BOLD responses are likely related to single-trial EEG amplitudes, but not to the phase concentration across trials. In order to gain a deeper understanding of the relation between event-related EEG and fMRI, a separation of amplitude and phase contributions would be a vital and crucial endeavor (Fell, 2007).

2.3 A selective literature review of oscillatory neuronal dynamics in human cognition

Since the early 1990's there has been a true explosion of research efforts directed at investigating the relationship between oscillatory neuronal dynamics on the one hand, and cognitive processes on the other hand. Research has been performed with a variety of experimental tools and a wide range of experimental paradigms, ranging, just to give a few examples, from attentional modulations in spike-field coherence estimates in single-cell

recordings of monkey visual cortex (e.g. Fries, Reynolds, Rorie, & Desimone, 2001), through

subdural recordings of oscillatory EEG activity during spatial navigation tasks in epileptic

patients (e.g. Kahana, Sekuler, Caplan, Kirschen, & Madsen, 1999), to scalp EEG measures of

power and coherence during the processing of semantic violations in sentences in healthy adults

(Hagoort, Hald, Bastiaansen, & Petersson, 2004). Clearly, the amount of work that has been

published is far too large to be reviewed in the context of this chapter (see e.g. Klimesch &

Neuper, 2006 for a much more elaborate sample of research activities). Any literature review we

present here is therefore necessarily limited in nature. In the remainder of this chapter, we

therefore selectively discuss some of the work that has explored the relationship between

oscillatory responses in the scalp EEG or MEG of healthy human adults, and cognitive processes

such as memory encoding/retrieval, working memory and language comprehension, with an

emphasis on our own work.

2.3.1 Working memory and long-term memory

Oscillatory dynamics in the gamma band reflect working memory maintenance

The primary role of the working memory system is to maintain a given stimulus

representation after the stimulus is no longer present. For visual stimuli it has been proposed that

this is achieved by the visuo-spatial sketchpad which serves to maintain the actual memory trace

(Baddeley, 1992). Recent findings in humans point to memory representations being maintained

by sustained oscillatory activity in the gamma band using both MEG and EEG. This has among

others been demonstrated in the visual and auditory domain (Kaiser, Ripper, Birbaumer, &

Lutzenberger, 2003; Tallon-Baudry et al., 1998). In both these working memory paradigms, the

sustained gamma activity was observed in comparison to a control task without a memory

component. In these studies attention demands are a confound since the working memory task is more demanding than the control task. To circumvent this problem, recent studies have aimed at selectively engaging different posterior areas in terms of stimulus specificity. A recent study (see Figure 2.5) relied on subjects maintaining either the identity or the orientation of presented faces (Jokisch & Jensen, 2007). The aim was to engage respectively the ventral and the dorsal stream. When subjects were maintaining the face orientation, induced gamma activity was observed over posterior midline areas. When subjects were maintaining the face identity, posterior midline gamma was not observed. Importantly, the face identity condition was the most demanding of the two conditions. This means that the sustained gamma activity is specific to the working memory conditions with the spatial component (face orientation) and is not explained by general increases in task demands. Source modeling revealed that the posterior gamma activity was produced in occipital areas.

*** Insert Figure 2.5 about here ***

These findings are consistent with a recent MEG study on working memory of saccades (Medendorp et al., 2006). Subjects were cued to prepare a saccade during a 2 s interval either to the left or the right. Gamma activity was observed over the hemisphere contralateral to the saccade direction during the retention period. In summary, these findings suggest that sustained gamma activity produced in the visual system is partly responsible for carrying the working memory traces during maintenance.

Inhibition of visual inputs during working memory maintenance

Successful working memory maintenance relies on the ability to retain the relevant representations. A failure to do so might be due to interference by other incoming stimuli. Thus

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the working memory system might benefit from inhibiting irrelevant sensory input during retention. Recent findings suggest that posterior alpha activity might serve this purpose. Posterior alpha activity has traditionally been interpreted as an idling rhythm (G. Pfurtscheller, Stancak, & Neuper, 1996). This is motivated by the finding that alpha activity emerges strongly when subjects are resting and have their eyes closed. The idling hypothesis has been challenged by findings demonstrating an increase in alpha power during working memory maintenance (Klimesch, Doppelmayr, Schwaiger, Auinger, & Winkler, 1999; Krause, Lang, Laine, Kuusisto, & Porn, 1996). In particular the alpha activity was shown to increase parametrically with working memory load (Jensen, Gelfand, Kounios, & Lisman, 2002). The sources accounting for the parametric increase were localized to the parieto-occipital sulcus, an area typically not associated with working memory maintenance (Tuladhar et al., 2007). On the basis of these findings it has been proposed that posterior alpha activity serves to inhibit incoming visual stimuli which might interfere with the memory maintenance (Jensen et al., 2002; Klimesch, Sauseng, & Hanslmayr, 2006). This interpretation is supported by the study of Jensen and Jokisch (2007) mentioned above in which subjects had to maintain the identity or orientation of presented faces. The alpha activity over dorsal areas was strongest during the face identify condition. In support of the inhibition hypothesis this shows that when the ventral stream is engaged during the retention period, alpha activity in the dorsal stream is increased. This case is further supported by the task on delayed saccades also mentioned above (Medendorp et al., 2006). Alpha activity in the hemisphere contralateral to the saccade was dramatically stronger compared with the ipsilateral hemisphere. The inhibition hypothesis has gained indirect support from studies combining EEG and fMRI demonstrating negative correlation between the BOLD signal and alpha activity produced around the parieto-occipital sulcus (Goldman, Stern, Engel, &

Cohen, 2002; Laufs et al., 2003). Importantly this negative correlation was found to increase with memory load (Scheeringa et al., in preparation)). It should be mentioned that oscillatory activity in the alpha band has been proposed to play an active role in cognitive processing as well (S. Palva & Palva, 2007). This notion is mainly based on studies focusing on the phase relationship between different alpha generators recorded in subjects performing tasks engaging the working memory system (J. M. Palva, Palva, & Kaila, 2005). In conclusion, the power of posterior alpha activity has been proposed to reflect functional inhibition of visual input during working memory maintenance. The main argument is based on findings demonstrating that alpha activity increases in areas not engaged in a given task. This functional inhibition serves to suppress interfering input, thus devoting resources to areas engaged in the actual working memory operations.

Oscillatory gamma activity reflects successful long-term memory operations

In contrast to working memory, long-term memory representations remain stable over longer time periods. It is a strong consensus that synaptic plasticity is responsible for encoding of long-term memories. Long-term potentiation is considered the physiological mechanism responsible for synaptic plasticity. Experimentally it has been demonstrated that the induction of long-term potentiation is modulated by the phase of ongoing gamma oscillations (Wespatat, Tennigkeit, & Singer, 2004). This provides a direct link between gamma oscillations and long-term memory formation. Extensive theoretical work has explored how memory representations can be encoded synaptically in network models of mutually coupled neurons. What these models have in common is that synaptic weights can only be decoded by actually reactivating the initial representations in the network. This activation might be reflected by oscillatory activity in the gamma band. In sum, these considerations motivate the study of oscillatory gamma activity

during long-term memory operations. Both EEG, intracranial EEG and MEG studies have demonstrated that induced gamma activity reflects successful long-term memory operations (T. Gruber, Tsivilis, Montaldi, & Muller, 2004; Osipova et al., 2006; Sederberg et al., 2006). In the study by Osipova et al., 240 pictures of landscapes and buildings were shown during the encoding session. In a subsequent recognition session, these pictures mixed with 240 new pictures were shown. Strong gamma activity produced in occipital areas was observed during the encoding session. Importantly, the gamma activity predicted the encoding of items that later were correctly recalled. During the recall session, gamma activity produced in the same areas correlated with successful long-term memory retrieval. In conclusion, gamma activity reflects successful long-term memory encoding. This might be explained by a stronger feedforward drive due to synchronization in the gamma band promoting synaptic plasticity. The gamma activity during long-term memory recall could reflect a recall process in which the initially encoded memory representations are retrieved.

In conclusion, the findings point to oscillatory brain activity in various frequency bands playing an important role in human memory representations. Activity in the gamma band is likely to reflect neuronal activation of the actual representations. Thus the sustained gamma activity could reflect maintenance of neuronal representations during working memory and/or the activation of the memory representations during recall. Gamma activity during long-term memory encoding is likely to promote synaptic plasticity. On the contrary posterior alpha activity seems to reflect functional inhibition of brain areas not engaged in a given memory task. Future work manipulating oscillatory activity by pharmacological means or trans-cranial magnetic stimulation is required in order to further establish the direct causal role of oscillatory brain responses in human memory.

2.3.2 Language comprehension

In this section we concentrate on the rapid dynamics of the neural processes underlying language comprehension. However, before turning to this, let us first briefly delineate at a very general level what is thought to be the cognitive architecture of language comprehension.

It is generally agreed that during language comprehension, incoming sounds or orthographic patterns trigger a cascade of memory retrieval operations that make available the phonologic, syntactic and semantic properties of individual words. Once available, these different ingredients have to be integrated (unified) at the sentence and/or discourse levels into a meaningful whole, in order to yield a coherent interpretation of the linguistic input (see Hagoort, 2005 for a more detailed elaboration of this framework). Thus, two different cognitive processes, namely memory retrieval operations and unification operations, play a crucial role during language comprehension.

Power and coherence changes in oscillatory neuronal responses during language comprehension have been observed in four different frequency bands: theta (4-7 Hz), alpha (8-12 Hz), lower beta (13-18 Hz), and gamma (above 30 Hz). In (relatively loose) agreement with the cognitive architecture of language comprehension, the observed effects can roughly be subdivided into effects related to memory retrieval operations during language comprehension, and effects related to unification of linguistic information.

Oscillatory neuronal dynamics related to the retrieval of lexical information.

A number of studies suggest that oscillatory neuronal dynamics in the theta frequency range are involved in the retrieval of lexical-semantic information. In an initial study (Bastiaansen, Van der Linden, ter Keurs, Dijkstra, & Hagoort, 2005), we examined EEG power changes in a range of frequencies from 1-30 Hz while subjects read a short story. Power changes were averaged selectively for open-class words (e.g. nouns, verbs and adjectives), which carry most of the semantic information in a sentence, and for closed-class words (e.g. articles, determiners and prepositions), which carry much less semantic information, but rather serve as 'syntactic glue' at the sentence level. As Figure 2.6 shows, open-class words (OC) and closed-class words (CC) both elicited a power increase in the theta frequency range, together with decreases in the alpha and beta frequency ranges, roughly in an interval of 100-600 ms after word onset. The OC words elicited stronger power changes generally. Interestingly however, while the scalp topography of the alpha and beta responses was qualitatively similar, in the theta frequency range we observed a qualitative difference between OC and CC words. Whereas both types elicited a theta power increase over left occipital and midfrontal areas, the OC words additionally elicited a power increase over left temporal areas that was not observed for the CC words (see Figure 2.6). A regression analysis showed that this effect was not dependent upon word length or word frequency. This topographical pattern connects well to existing hemodynamic data. The left occipital power increase may be related to complex visual processing either in Broca's area 18/19 (see e.g. Indefrey et al., 1997; Petersen, Fox, Posner, Mintun, & Raichle, 1988) or in the fusiform gyrus (the putative visual word form area, cf. Cohen et al., 2000; McCandliss, Cohen, & Dehaene, 2003). Most interestingly however, with respect to the differential (OC-specific) theta response over the left temporal cortex, it has been shown that

left temporal areas (more precisely, left posterior superior and/or middle temporal gyrus) are involved in lexical retrieval (see e.g. Indefrey, 2004; Indefrey & Cutler, 2005). Therefore, the qualitative difference between OC and CC words led us to hypothesize that theta-band synchronization of neuronal activity is related to lexical-semantic retrieval.

*** insert Figure 2.6 about here ***

A subsequent experiment (Bastiaansen, Oostenveld, Jensen, & Hagoort, in press) aimed at further testing this hypothesis. Subjects performed a lexical decision task, in which they had to decide whether or not a visually presented string of letters constituted a real word. Non-words could be either pseudowords (phonologically legal, but nonsensical letter strings) or consonant strings. Real words could either be nouns with visual semantic properties (that is, referring to colors and shapes) or nouns with auditory semantic properties (that is, referring to sounds).

Again, both sets of words elicited an increase in theta power and decreases in the alpha and beta frequency ranges. And again, qualitatively different responses were found only in the theta band, where the following double dissociation was found (see Figure 2.7): words with auditory semantic properties showed larger theta power increases in electrodes overlying the left auditory cortex than in electrodes overlying the left visual cortex, while the opposite pattern was found for words with visual semantic properties. Note that, as both sets of words were presented visually, and were matched for length and frequency, they only differed in terms of their semantic properties. We therefore concluded that the results of this study were consistent with the hypothesis that neuronal synchronization in the theta frequency range is involved in the retrieval of lexical semantic information. In addition, our data are in agreement with the

hypothesis that spatially distributed functional networks form the basis of semantic

representations, and that the topographies of these networks reflect the semantic properties of

individual items (for similar hypotheses, see Martin & Chao, 2001; Pulvermueller, 1999, 2001).

*** insert Figure 2.7 about here ***

While the above studies suggest a strong involvement of theta-band synchronization in retrieving

lexical-semantic information, the neuronal dynamics of language comprehension-related

retrieval operations are certainly not restricted to the theta frequency band. Other studies have

related semantic memory operations to power changes in the alpha frequency band (for review,

see Klimesch, 1999). In addition, a few studies have reported effects of memory retrieval in

higher frequency bands (beta/gamma; Pulvermueller, Lutzenberger, & Preissl, 1999; Weiss &

Mueller, 2003).

Oscillatory dynamics related to unification operations in language comprehension

As sentences extend over relatively long time periods, maintaining the working memory

(WM) trace of the linguistic input is a prerequisite to performing unification operations. In

addition to retrieval operations, theta-band changes in neuronal synchrony also appear to play a

role in such WM processes. For example, theta power (Bastiaansen, van Berkum, & Hagoort,

2002a) and coherence (Weiss & Mueller, 2003) linearly increase over the course of correct

sentences. In addition, theta power is larger over the frontocentral midline following words

constituting syntactic (Bastiaansen, van Berkum, & Hagoort, 2002b) and semantic (Hagoort et

al., 2004; Hald, Bastiaansen, & Hagoort, 2006) violations in sentences. These effects were

interpreted to be related to the larger demands that they impose on verbal WM (Hald et al.,

2006). Also, theta coherence is larger following WM-demanding object-relative vs. subject-relative clauses (Weiss et al., 2005). A clear relationship between theta-band oscillations and WM has also been found using intracranial recordings in humans (Raghavachari et al., 2001; Rizzuto et al., 2003).

There is however more to unification than just maintaining the input in WM. Unification requires the active manipulation of phonological, syntactic, semantic and likely also of pragmatic information, resulting in a message-level understanding of the linguistic input. So far, experimental research into the oscillatory neuronal dynamics of unification operations have concentrated on semantic and syntactic unification only.

Semantic unification

Recent we have addressed the oscillatory correlates of semantic unification in the following way (Hagoort et al., 2004; Hald et al., 2006). Subjects read the following three versions of sentences such as: "The Dutch trains are *yellow/white/sour* and very crowded." In fact, Dutch trains are yellow, and therefore the first version of this sentence is the correct sentence condition. However, the linguistic meaning aspects of the alternative color term *white* apply equally well to trains as the predicate *yellow*. It is world knowledge about trains in Holland that make the second version of this sentence false (the world knowledge violation condition). This is different for the third version. The core meaning of *sour* is related to taste and food. Under standard interpretation conditions a predicate requires an argument whose semantic features overlap with that of its predicate. For vehicles such as trains, this is clearly not the case, since semantic features related to taste and food do not apply to the materials that trains are made of. Thus, for semantic-internal reasons the third sentence is an outright semantic violation condition.

The results are presented in Figure 2.8. In the correct sentence condition, where normal semantic unification takes place, we observed a small increase in gamma power relative to baseline in response to the critical word (e.g. yellow). This gamma power increase was much stronger in the world knowledge violation condition, where semantic unification is difficult but not impossible. In the semantic violation condition however, where semantic unification is impossible for the reasons mentioned above, the gamma power increase was absent.

The parametric relation between semantic unification and gamma power described above suggests that gamma oscillations are functionally related to semantic unification operations. Several other studies support this notion. First, gamma coherence is larger for semantically congruous than for incongruous sentence endings (Weiss, Rappelsberger, Schack, & Mueller, 2003). In a different approach, van Berkum et al. (van Berkum, Zwitserlood, Bastiaansen, Brown, & Hagoort, 2004) studied the effects of referential success, referential ambiguity, and referential failure in a sentence, and they found a drop in gamma power following the ambiguous and failing reference conditions, which render semantic unification problematic.

Taken together, the above studies lead us to hypothesize that neuronal synchronization in the gamma frequency range is in some way related to the neuronal implementation of semantic unification.

Syntactic unification

The neuronal dynamics of syntactic unification have been addressed in a number of different experimental paradigms. For instance, Haarmann et al. (Haarmann, Cameron, &

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Ruchkin, 2002) used sentences in which EEG coherence was examined in the interval between the object and the main verb of a sentence (the so-called filler-gap interval). Although this filler-gap interval places a relatively large demand on verbal WM, the gap-filling that the reader has to perform on-line can be seen as a syntactic unification operation. The authors found increased coherence over many scalp areas in the sentences containing a filler-gap interval compared to non-filler sentences, in the lower beta frequency range (roughly 15-18 Hz). This increased coherence is indicative of an increase in long-range neuronal synchronization during the syntactically more demanding filler sentences. A study by the group of Weiss (Weiss et al., 2005) computed EEG coherence during sentences in which the subject of the main clause was also the subject of the relative clause (so-called subject-relative (SR) sentences). This was contrasted with coherence during sentences in which the subject of the main verb was the object of the relative clause (object-relative sentences (OR)). SR sentences are syntactically relatively simple, and have a high frequency of occurrence in everyday language, whereas OR sentences are less frequent, syntactically more demanding, and place a larger load on verbal WM. The authors showed that increased theta and gamma coherences were associated with the higher WM load. The effects of syntactic complexity (which become most evident in the time period just following the relative clause) however were expressed in the lower beta frequency range (13-18 Hz). In a similar type of experiment with Dutch subjects and stimuli, we are currently investigating power changes in the MEG between OR and SR sentences. Preliminary results from this experiment suggest that OR sentences are accompanied with a power decrease in the 13-18 Hz frequency range. Similar results were obtained in a recent study in which syntactic violations occurred in sentences, where violations lead to a relative decrease in power in the same frequency range (Bastiaansen, Magyari, & Hagoort, submitted).

Overall, the experimental data suggest that the two components of language comprehension, namely the retrieval of lexical information from the mental lexicon and the subsequent unification of semantic and syntactic information yield distinct patterns of synchronization in the brain's language network: Retrieval operations are associated with neuronal dynamics in the theta and alpha frequency ranges, whereas unification operations are associated with neuronal synchronization in the beta and gamma frequency ranges. As such, the general pattern of results suggests that at the level of the dynamic neuronal mechanisms by which the brain operates during language comprehension, domain-general processes are operative (that is, the observed mechanisms are not exclusively engaged by linguistic processing, but are also observed in other cognitive domains). This opposes the representational level, where there is a relative domain-specificity for language comprehension (that is, there are brain areas that are partly dedicated to the storage and manipulation of linguistic information, as evidenced by hemodynamic studies).

Thus, it seems that it is possible to capture the dynamics of the brain's language network by a careful analysis of the event-related changes in power and coherence of EEG and MEG data in a wide range of frequencies, in combination with subtle experimental manipulations in a range of language comprehension tasks.

Before ending this chapter with some conclusions, we would like to address one issue that often leads to misconceptions amongst reasearchers that are not familiar with time-frequency analyses of oscillatory EEG/MEG phenomena. This issue relates to the different frequency bands in which experimental effects are reported. One may be tempted to conceive of effects occurring in the same frequency band as being functionally, or neurophysiologically related effects. For

instance, one may think that theta-band power increases reported in one set of studies (on, say, working memory) may be related to theta increases in another set of studies (on, say, error detection). We would like to stress here that such inferences are not warranted. Frequency-band similarity (or dissimilarity) between different event-related responses only means that in both cases neurons are synchronizing at the same (or at a different) rate. This may be due to relatively low-level neurophysiologicsl parameters (such as axonal conductance times, exact connectivity patterns, number of interveining synapses etc.), and as such can hardly be viewed as functionally relevant for the cognitive neuroscientist. Having said this, we should also note that in some special cases there are good reasons to relate oscillation frequency to specific anatomical pathways. For instance, alpha-band responses are often linked to thalamo-cortical interactions (see e.g. Lopes da Silva, 1991; Steriade, Gloor, Llinás, Lopes da Silva, & Mesulam, 1990, whereas theta-band responses are sometimes related to cortico-hippocampal circuits (see e.g. Bastiaansen & Hagoort, 2003; Miller, 1991).

2.4 Conclusion

In our opinion the above experimental data illustrate that there exists a meaningful relationship between oscillatory neuronal dynamics on the one hand, and a wide range of cognitive processes on the other hand. Given that the analysis of oscillatory dynamics extracts information from the EEG/MEG signal that is largely lost with the traditional time-locked averaging of single trials used in the ERP approach, studying the dynamic oscillatory patterns in the EEG/MEG thus proves to be at least a useful addition to the traditional ERP approach.

The analysis methodologies involved in studying oscillatory neuronal dynamics are optimally suited to zoom in on the patterns of synchronization and desynchronization of neuronal activity, and as such they provide one with the necessary means to empirically address issues related to the coupling and uncoupling of functional networks during cognitive processing. Interestingly, there is a clear parallel between the development and rising popularity of EEG/MEG measures of network dynamics on the one hand, and modern fMRI data analysis techniques that focus on network dynamics through measures of functional and effective connectivity (such as studying low-frequency synchronization of BOLD responses, diffusion tensor imaging, or structural equation modeling) on the other hand. These parallel developments are particularly exciting because they essentially demonstrate the growing awareness among cognitive neuroscientists that functional network dynamics are at the core of human cognition.

References

Andrew, C., & Pfurtscheller, G. (1996). Event-related coherence as a tool for studying dynamic interaction of brain regions. *Electroenceph. Clin Neurophysiol, 98*, 144-148.

Baddeley, A. (1992). Working memory. *Science, 255*(5044), 556-559.

Bastiaansen, M. C. M., & Hagoort, P. (2003). Event-induced theta responses as a window on the dynamics of memory. *Cortex, 39*(4-5), 967-992.

Bastiaansen, M. C. M., Magyari, L., & Hagoort, P. (submitted). Dissociation between syntactic and working memory processes in oscillatory dynamics during online sentence comprehension.

Bastiaansen, M. C. M., Oostenveld, R., Jensen, O., & Hagoort, P. (in press). Do you see what I mean: theta power increases are involved in the retrieval of lexical semantic representations. *Brain and Language*.

Bastiaansen, M. C. M., van Berkum, J. J., & Hagoort, P. (2002a). Event-related theta power increases in the human EEG during online sentence processing. *Neurosci Lett, 323*(1), 13-16.

Bastiaansen, M. C. M., van Berkum, J. J., & Hagoort, P. (2002b). Syntactic processing modulates the theta rhythm of the human EEG. *Neuroimage, 17*(3), 1479-1492.

Bastiaansen, M. C. M., Van der Linden, M., ter Keurs, M., Dijkstra, T., & Hagoort, P. (2005). Theta responses are involved in lexico-semantic retrieval during language processing. *Journal of Cognitive Neuroscience, 17*(3), 530-541.

Beck, A. (1891). *Oznaczenie lokalizacyi W Mozgu I rdzeniu za pomoca zjawisk elektrycznych.*, Uniwersytet Jagiellonski, Kraków.

Beck, A. (1973). The determination of localizations in the brain and spinal cord with the aid of electrical phenomena. *Acta Neurobiologiae Experimentalis, Suppl, 3*, 1-55.

Becker, R., Ritter, P., & Villringer, A. (2008). Influence of ongoing alpha rhythm on the visual evoked potential. *Neuroimage, 39*(2), 707-716.

Berger, H. (1929). Über das Elektroencephalogramm des Menschen. *Arch. Psychiat. Nerv.-Krankh., 87*, 527-570.

Braeutigam, S., Bailey, A. J., & Swithenby, S. J. (2001). Phase-locked gamma band responses to semantic violation stimuli. *Brain Res Cogn Brain Res, 10*(3), 365-377.

Caton, R. (1875). The electric currents of the brain. *Br. Med. J, 2*, 278.

Cohen, L., Dehaene, S., Naccache, L., Lehericy, S., Dehaene-Lambertz, G., Henaff, M. A., et al. (2000). The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain, 123 (Pt 2)*, 291-307.

Fell, J. (2007). Cognitive neurophysiology: beyond averaging. *Neuroimage, 37*(4), 1069-1072.

Fries, P., Reynolds, J. H., Rorie, A. E., & Desimone, R. (2001). Modulation of oscillatory neuronal synchronization by selective visual attention. *Science, 291*(5508), 1560-1563.

Goldman, R. I., Stern, J. M., Engel, J., Jr., & Cohen, M. S. (2002). Simultaneous EEG and fMRI of the alpha rhythm. *Neuroreport, 13*(18), 2487-2492.

Gray, C. M., Konig, P., Engel, A. K., & Singer, W. (1989). Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. *Nature, 338*(6213), 334-337.

Gruber, T., & Muller, M. M. (2005). Oscillatory brain activity dissociates between associative stimulus content in a repetition priming task in the human EEG. *Cereb Cortex, 15*(1), 109-116.

Gruber, T., Tsivilis, D., Montaldi, D., & Muller, M. M. (2004). Induced gamma band responses: an early marker of memory encoding and retrieval. *Neuroreport, 15*(11), 1837-1841.

Gruber, W. R., Klimesch, W., Sauseng, P., & Doppelmayr, M. (2005). Alpha phase synchronization predicts P1 and N1 latency and amplitude size. *Cereb Cortex, 15*(4), 371-377.

Haarmann, H. J., Cameron, K. A., & Ruchkin, D. S. (2002). Neural synchronization mediates on-line sentence processing. EEG coherence evidence from filler-gap constructions. *Psychophysiology, 39*, 820-825.

Hagoort, P. (2005). On Broca, brain, and binding: a new framework. *Trends Cogn Sci, 9*(9), 416-423.

Hagoort, P., Hald, L., Bastiaansen, M., & Petersson, K. M. (2004). Integration of word meaning and world knowledge in language comprehension. *Science, 304*(5669), 438-441.

Hald, L. A., Bastiaansen, M. C., & Hagoort, P. (2006). EEG theta and gamma responses to semantic violations in online sentence processing. *Brain Lang, 96*(1), 90-105.

Hanslmayr, S., Klimesch, W., Sauseng, P., Gruber, W., Doppelmayr, M., Freunberger, R., et al. (2007). Alpha phase reset contributes to the generation of ERPs. *Cereb Cortex, 17*(1), 1-8.

Indefrey, P. (2004). Hirnaktivierungen bei syntaktischer Sprachverarbeitung: eine Meta-Analyse. In H. M. Müller & G. Rickheit (Eds.), *Neurokognition der Sprache.* (pp. 31-50). Tübingen: Stauffenburg Verlag.

Indefrey, P., & Cutler, A. (2005). Prelexical and lexical processing in listening. In M. Gazzaniga (Ed.), *The Cognitive Neurosciences III.* Cambridge, MA: MIT Press.

Indefrey, P., Kleinschmidt, A., Merboldt, K. D., Kruger, G., Brown, C., Hagoort, P., et al. (1997). Equivalent responses to lexical and nonlexical visual stimuli in occipital cortex: a functional magnetic resonance imaging study. *Neuroimage, 5*(1), 78-81.

Jensen, O., Gelfand, J., Kounios, J., & Lisman, J. E. (2002). Oscillations in the alpha band (9-12 Hz) increase with memory load during retention in a short-term memory task. *Cereb Cortex, 12*(8), 877-882.

Jokisch, D., & Jensen, O. (2007). Modulation of gamma and alpha activity during a working memory task engaging the dorsal or ventral stream. *J Neurosci, 27*(12), 3244-3251.

Kahana, M. J., Sekuler, R., Caplan, J. B., Kirschen, M., & Madsen, J. R. (1999). Human theta oscillations exhibit task dependence during virtual maze navigation. *Nature, 399*, 781-784.

Kaiser, J., Ripper, B., Birbaumer, N., & Lutzenberger, W. (2003). Dynamics of gamma-band activity in human magnetoencephalogram during auditory pattern working memory. *Neuroimage, 20*(2), 816-827.

Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews, 29*, 169-195.

Klimesch, W., Doppelmayr, M., Schwaiger, J., Auinger, P., & Winkler, T. (1999). 'Paradoxical' alpha synchronization in a memory task. *Brain Res Cogn Brain Res, 7*(4), 493-501.

Klimesch, W., Hanslmayr, S., Sauseng, P., & Gruber, W. R. (2006). Distinguishing the evoked response from phase reset: a comment to Makinen et al. *Neuroimage, 29*(3), 808-811.

Klimesch, W., & Neuper, C. (Eds.). (2006). *Event-related dynamics of brain oscillations* (Vol. 159). Amsterdam: Elsevier.

Klimesch, W., Russegger, H., Doppelmayr, M., & Pachinger, T. (1998). A method for the calculation of induced band power: implications for the significance of brain oscillations. *Electroenceph. Clin Neurophysiol, 108*, 123-130.

Klimesch, W., Sauseng, P., & Hanslmayr, S. (2006). EEG alpha oscillations: The inhibition-timing hypothesis. *Brain Res Brain Res Rev*.

Klimesch, W., Schack, B., Schabus, M., Doppelmayr, M., Gruber, W., & Sauseng, P. (2004). Phase-locked alpha and theta oscillations generate the P1-N1 complex and are related to memory performance. *Brain Res Cogn Brain Res, 19*(3), 302-316.

Knosche, T. R., & Bastiaansen, M. C. M. (2002). On the time resolution of event-related desynchronization: a simulation study. *Clinical Neurophysiology, 113*(5), 754-763.

Konig, P., & Schillen, T. B. (1991). Stimulus-dependent assembly formation of oscillatory responses: I. Synchronization. *Neural Comp, 3*, 155-166.

Krause, C. M., Lang, A. H., Laine, M., Kuusisto, M., & Porn, B. (1996). Event-related EEG desynchronization and synchronization during an auditory memory task. *Electroencephalogr Clin Neurophysiol, 98*(4), 319-326.

Lachaux, J. P., Rodriguez, E., Martinerie, J., & Varela, F. J. (1999). Measuring phase synchrony in brain signals. *Hum Brain Mapp, 8*(4), 194-208.

Laufs, H., Kleinschmidt, A., Beyerle, A., Eger, E., Salek-Haddadi, A., Preibisch, C., et al. (2003). EEG-correlated fMRI of human alpha activity. *Neuroimage, 19*(4), 1463-1476.

Lopes da Silva, F. H. (1991). Neural mechanisms underlying brain waves: from neural membranes to networks. *Electroenceph. Clin Neurophysiol, 79*, 81-93.

Makeig, S., Debener, S., Onton, J., & Delorme, A. (2004). Mining event-related brain dynamics. *Trends Cogn Sci, 8*(5), 204-210.

Makeig, S., Westerfield, M., Jung, T. P., Enghoff, S., Townsend, J., Courchesne, E., et al. (2002). Dynamic brain sources of visual evoked responses. *Science, 295*(5555), 690-694.

Makinen, V., Tiitinen, H., & May, P. (2005). Auditory event-related responses are generated independently of ongoing brain activity. *Neuroimage, 24*(4), 961-968.

Martin, A., & Chao, L. L. (2001). Semantic memory and the brain: structure and processes. *Curr Opin Neurobiol, 11*(2), 194-201.

Mazaheri, A., & Jensen, O. (2006). Posterior alpha activity is not phase-reset by visual stimuli. *Proc Natl Acad Sci U S A, 103*(8), 2948-2952.

Mazaheri, A., & Picton, T. W. (2005). EEG spectral dynamics during discrimination of auditory and visual targets. *Brain Res Cogn Brain Res, 24*(1), 81-96.

McCandliss, B. D., Cohen, L., & Dehaene, S. (2003). The visual word form area: expertise for reading in the fusiform gyrus. *Trends Cogn Sci, 7*(7), 293-299.

Medendorp, W. P., Kramer, G. F., Jensen, O., Oostenveld, R., Schoffelen, J. M., & Fries, P. (2006). Oscillatory Activity in Human Parietal and Occipital Cortex Shows Hemispheric Lateralization and Memory Effects in a Delayed Double-Step Saccade Task. *Cereb Cortex*.

Mesulam, M. M. (1998). From sensation to cognition. *Brain, 121*(Pt 6), 1013-1052.

Miller, R. (1991). *Cortico-hippocampal interplay and the representation of contexts in the brain.* Berlin: Springer.

Mitra, P. P., & Pesaran, B. (1999). Analysis of dynamic brain imaging data. *Biophys J, 76*(2), 691-708.

Murray, M. M., Wylie, G. R., Higgins, B. A., Javitt, D. C., Schroeder, C. E., & Foxe, J. J. (2002). The spatiotemporal dynamics of illusory contour processing: combined high-density electrical mapping, source analysis, and functional magnetic resonance imaging. *J Neurosci, 22*(12), 5055-5073.

Nunez, P. L., Srinivasan, R., Westdorp, A. F., Wijesinghe, R. S., Tucker, D. M., Silberstein, R. B., et al. (1997). EEG coherency. I: Statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at multiple scales. *Electroencephalogr Clin Neurophysiol, 103*(5), 499-515.

Osipova, D., Takashima, A., Oostenveld, R., Fernandez, G., Maris, E., & Jensen, O. (2006). Theta and gamma oscillations predict encoding and retrieval of declarative memory. *J Neurosci, 26*(28), 7523-7531.

Palva, J. M., Palva, S., & Kaila, K. (2005). Phase synchrony among neuronal oscillations in the human cortex. *J Neurosci, 25*(15), 3962-3972.

Palva, S., & Palva, J. M. (2007). New vistas for alpha-frequency band oscillations. *Trends Neurosci, 30*(4), 150-158.

Penny, W. D., Kiebel, S. J., Kilner, J. M., & Rugg, M. D. (2002). Event-related brain dynamics. *Trends Neurosci, 25*(8), 387-389.

Petersen, S. E., Fox, P. T., Posner, M. I., Mintun, M., & Raichle, M. E. (1988). Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature, 331*(6157), 585-589.

Pfurtscheller, G., & Aranibar, A. (1979). Evaluation of event-related desynchronization (ERD) preceding and following voluntary self-paced movements. *Electroenceph. Clin. Neurophysiol, 46*, 138-146.

Pfurtscheller, G., & Berghold, A. (1989). Patterns of cortical activation during planning of voluntary movement. *Electroenceph. clin. Neurophysiol, 72*, 250-258.

Pfurtscheller, G., & Lopes da Silva, F. H. E. (1999). *Event-related desynchronization. Handbook of Electroencephalography and Clinical Neurophysiology, revised series* (Vol. 6). Amsterdam: Elsevier.

Pfurtscheller, G., & Neuper, C. (1997). Motor imagery activates primary sensorimotor area in humans. *Neurosci. Lett, 239*, 65-68.

Pfurtscheller, G., Stancak, A., Jr., & Neuper, C. (1996). Event-related synchronization (ERS) in the alpha band--an electrophysiological correlate of cortical idling: a review. *Int J Psychophysiol, 24*(1-2), 39-46.

Práwdicz-Neminski, W. W. (1913). Ein Versuch der Registrierung der elektrischen Gehirnerscheinungen. *Centralblatt für Physiologie, 27*, 951-960.

Pulvermueller, F. (1999). Words in the brain's language. *Behav Brain Sci, 22*, 253-336.

Pulvermueller, F. (2001). Brain reflections of words and their meaning. *Trends Cogn Sci, 5*(12), 517-524.

Pulvermueller, F., Lutzenberger, W., & Preissl, H. (1999). Nouns and verbs in the intact brain: evidence from event-related potentials and high-frequency cortical responses. *Cereb Cortex, 9*(5), 497-506.

Raghavachari, S., Kahana, M. J., Rizzuto, D. S., Caplan, J. B., Kirschen, M. P., Bourgeois, B., et al. (2001). Gating of human theta oscillations by a working memory task. *J Neurosci, 21*(9), 3175-3183.

Rizzuto, D. S., Madsen, J. R., Bromfield, E. B., Schulze-Bonhage, A., Seelig, D., Aschenbrenner-Scheibe, R., et al. (2003). Reset of human neocortical oscillations during a working memory task. *Proc Natl Acad Sci U S A, 100*(13), 7931-7936.

Scheeringa, R., Bastiaansen, M. C. M., Petersson, K. M., Oostenveld, R., Norris, D. G., & Hagoort, P. (in preparation). BOLD correlates of a WM-related alpha network: a simultaneous EEG/fMRI study.

Sederberg, P. B., Gauthier, L. V., Terushkin, V., Miller, J. F., Barnathan, J. A., & Kahana, M. J. (2006). Oscillatory correlates of the primacy effect in episodic memory. *Neuroimage, 32*(3), 1422-1431.

Shah, A. S., Bressler, S. L., Knuth, K. H., Ding, M., Mehta, A. D., Ulbert, I., et al. (2004). Neural dynamics and the fundamental mechanisms of event-related brain potentials. *Cereb Cortex, 14*(5), 476-483.

Singer, W. (1993). Synchronization of cortical activity and its putative role in information processing and learning. *Ann Rev Physiol, 55*, 349-374.

Singer, W. (1999). Neuronal synchrony: a versatile code for the definition of relations? *Neuron, 24*(1), 49-65, 111-125.

Steriade, M., Gloor, P., Llinás, R. R., Lopes da Silva, F. H., & Mesulam, M. M. (1990). Basic mechanisms of cerebral rhythmic activities. *Electroenceph. Clin Neurophysiol, 76*, 481-508.

Tallon-Baudry, C., Bertrand, O., Peronnet, F., & Pernier, J. (1998). Induced gamma band activity during the delay of a visual short-term memory task in humans. *J. Neurosci, 18*, 4244-4254.

Tuladhar, A. M., Huurne, N. T., Schoffelen, J. M., Maris, E., Oostenveld, R., & Jensen, O. (2007). Parieto-occipital sources account for the increase in alpha activity with working memory load. *Hum Brain Mapp*.

van Berkum, J. J., Zwitserlood, P., Bastiaansen, M., Brown, C., & Hagoort, P. (2004). *So who's "he" anyway? Differential ERP and ERSP effects of referential success, ambiguity and failure during spoken language comprehension.* Paper presented at the Annual Meeting of the Cognitive Neuroscience Society, San Francisco.

Varela, F., Lachaux, J. P., Rodriguez, E., & Martinerie, J. (2001). The brainweb: phase synchronization and large-scale integration. *Nat Rev Neurosci, 2*(4), 229-239.

Weiss, S., & Mueller, H. M. (2003). The contribution of EEG coherence to the investigation of language. *Brain Lang, 85*(2), 325-343.

Weiss, S., Mueller, H. M., Schack, B., King, J. W., Kutas, M., & Rappelsberger, P. (2005). Increased neuronal communication accompanying sentence comprehension. *Int J Psychophysiol, 57*(2), 129-141.

Weiss, S., Rappelsberger, P., Schack, B., & Mueller, H. M. (2003). Koharenz- und Phasenuntersuchungen und ihre Bedeutung fur die Untersuchung von Sprachprozessen. In G. R. H.M. Mueller (Ed.), *Neurokognition der Sprache*. Tubingen: Stauffenburg.

Wespatat, V., Tennigkeit, F., & Singer, W. (2004). Phase sensitivity of synaptic modifications in oscillating cells of rat visual cortex. *J Neurosci, 24*(41), 9067-9075.

Yeung, N., Bogacz, R., Holroyd, C. B., Nieuwenhuis, S., & Cohen, J. D. (2007). Theta phase resetting and the error-related negativity. *Psychophysiology, 44*(1), 39-49.

Figure Captions

Figure 2.1. Simulated EEG data illustrating the difference between phase-locked (evoked) activity and non-phase-locked (induced) activity. The left-hand side of the figure shows single-trial EEG time courses that show two consecutive event-related responses (an amplitude increase at 10 Hz). The first response is phase-locked with respect to the reference timepoint (t=0), and as a result this evoked response is adequately represented in the average ERP. The second response is time-locked, but not phase-locked to t=0, and as a result this induced response is largely lost in the average ERP. The right-hand side of the figure shows time-frequency (TF) representations of each single trial, with red colors coding for the amplitude increase at 10 Hz. Crucially, the average TF representation contains both the phase-locked and the non-phase-locked responses.

Figure 2.2. Simulated data illustrating the principle of phase resetting. Three single trials are shown whose phases are not aligned initally. Red arrows indicate the point in time at which an event-induced phase reset occurs. The bottom trace shows what the average ERP would look like if a sufficient number of such trials (in practice > 30 trials) are averaged.

Figure 2.3. The upper left of the figure shows 20 superimposed trials of a model evoked potential consisting of a single cycle of activity added to ongoing activity of the same frequency with variable phase and amplitude. Below is given the average evoked potential over 100 trials. At the upper right are the polar plots showing the phase distributions and the frequency of the evoked potential (and background activity) during the baseline and at the middle of the evoked potential. Adapted from Mazaheri and Picton (2005) Cognitive Brain Research.

Figure 2.4 The Phase Preservation Index (PPI)of the α oscillations. (*A*) The temporal evolution of the PPI averaged over eight subjects for the α frequency identified in individual subjects. Error bars indicate the SEM. The reference phase was determined at −0.25 s. The PPI decays slowly, showing that the poststimulus phases are preserved with respect to the prestimulus phase, up to approximately 0.3 s poststimulus. PPI values above the red line are considered statistically significant ($P < 0.01$; see *Methods*). The dashed line indicates the PPI for trials shuffled in time (temporally uncorrelated). (*B*) The PPI for the unstimulated trials. The PPI values between the stimulated and unstimulated trials were not significantly different across time. (*t* test, $P < 0.05$). Reproduced from Mazaheri and Jensen (2006) PNAS.

Figure 2.5. A working memory task showing sustained alpha and gamma. (A) Subjects were requested to maintain either the identity (ID) or orientation (OR) of a presented face. After a 3 s retention period, a sample item was presented and the subject had to indicate a match or non-match by means of a button press. (B) Only in the OR condition, which engaged the dorsal stream, sustained gamma activity (60-90 s) was present centrally during the retention interval. Sources accounting for the gamma activity were identified within occipital cortex. (C) Only in the ID condition, which engaged the ventral stream, sustained alpha activity was present centrally during the retention interval. Sources accounting for the alpha activity were identified around the parieto-occipital sulcus. Reproduced from Jensen and Jokisch (2007) J. Neuroscience.

Figure 2.6 Results of a time-frequency analysis of power changes, for open-class words and closed-class words separately. Left- and right-hand parts of the figure show a time-frequency

representation of the percentage power change at one frontal channel (Fz). Words are presented at t=0. The middle part of the figure shows the topographical distribution of three time-frequency components, indicated by the black tiles in the time-frequency respresentations. Note the qualitative difference in scalp topography of the theta power increase.

Figure 2.7 Topographical distribution (a) and region-of-interest time courses (b) of percentage theta power changes induced by visually presented words with auditory semantic properties (AUD) and visual semantic properties (VIS). The regions of interest are indicated by the black ellipses in (a). Shaded areas in (b) indicate the time interval used for the statistical analyses.

Figure 2.8 Time-frequency analysis of the power changes elicited by the critical words in correct sentences, sentences containing violations of world knowledge, and sentences containing semantic violations. The middle part shows the time-frequency representations, the left- and right-hand parts show the topographical distribution of gamma and theta power changes, respectively. Note the small but significant increase in gamma power over lateral frontal areas in the correct condition, the strong gamma power increase following a world knowledge violation, and the absence of gamma power increase after a semantic violation.