Anticipatory Attention

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Anticipatory Attention

an Event-Related Desynchronization approach

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Stellingen

behorend bij het proefschrift:
Anticipatory Attention, an Event-Related Desynchronization approach
door M. C. M. Bastiaansen.

1. Anticipatoire aandacht in de visuele modaliteit gaat gepaard met een event-related desynchronisatie van het EEG en het MEG, die maximaal is boven de occipitale hersengebieden (dit proefschrift).
2. a. Anticipatoire aandacht in de auditieve modaliteit gaat bij sommige proefpersonen gepaard met een desynchronisatie van het MEG, die maximaal is boven de temporale hersengebieden (dit proefschrift).
   b. Deze desynchronisatie treedt niet op in het EEG van dezelfde proefpersonen (dit proefschrift).
3. Anticipatoire aandacht in de somatosensorische modaliteit gaat gepaard met een desynchronisatie van het EEG, die maximaal is boven de postcentrale hersengebieden (dit proefschrift).
4. Wanneer men de topografie wil bestuderen van de ERD van MEG data gemeten met axiale gradiometers is het wenselijk om de ERD te berekenen op de tangentiele afgeleide van het ruwe signaal (dit proefschrift).
5. Het is mogelijk om door middel van het analyseren van de Event-Related Desynchronisatie van het EEG of MEG, cognitieve processen in kaart te brengen die met de meer traditionele Event-Related Potential benadering niet zouden worden opgemerkt (dit proefschrift).
6. a. Doordat wetenschappers beoordeeld worden op basis van *output* is het voor een beginnend wetenschapper tegenwoordig van groot belang om vroeg in zijn/haar carriere opvallende onderzoeksresultaten te verkrijgen.
   b. Hierdoor is het behalen van academisch succes in zekere zin een loterij geworden.
7. De –op zijn zachtst gezegd nogal merkwaardige- vraag van de kant van universitaire bestuurders en subsidieorganen naar de maatschappelijke relevantie van fundamenteel wetenschappelijk onderzoek getuigt niet van veel inzicht in hoe wetenschappelijke progressie tot stand komt.
8. De laatste stelling van een proefschrift is doorgaans de meest oninteressante.

ANTICIPATORY ATTENTION
AN EVENT-RELATED DESYNCHRONIZATION APPROACH

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ANTICIPATORY ATTENTION

AN EVENT-RELATED DESYNCHRONIZATION APPROACH

(Anticipatoire aandacht: een Event-Related Desynchronisatie benadering)

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Katholieke Universiteit Brabant, op gezag van de rector magnificus,
prof. dr. F.A. van der Duyn Schouten, in het openbaar te verdedigen
ten overstaan van een door het college voor promoties aangewezen commissie
in de aula van de Universiteit
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door

Marinus Cornelis Maria Bastiaansen

geboren op 26 augustus 1970 te Breda

Promotor: prof. dr. C.H.M. Brunia
Copromotor: dr. ir. P.J.M. Cluitmans

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Part I:
Theoretical part.

Chapter 1: General Introduction.

In the research described in this thesis anticipatory behavior, and more specifically a component hereof, namely anticipatory attention, has been studied with psychophysiological methods. In this introductory chapter anticipatory behavior and anticipatory attention are introduced at a conceptual level. I first describe what is meant with the term anticipatory attention, and address the behavioral functions of it. Next it is argued that physiological measures are well suited to study anticipatory attention, and I formulate the central research question of this thesis. Finally, an outline of the thesis is provided in order for the reader to have a clear insight into its structure.

1.1 Anticipatory behavior.

It is difficult to imagine a world in which everything happens unexpectedly. One would be ceaselessly taken by surprise, and every intention, every plan would be made impossible by our inability to foresee what will happen in the near future. Clearly, this must be a rather unpleasant world, and one would most probably not survive very long in such an environment. Fortunately however, most of the events that we experience everyday do not happen unexpectedly. This enables us to anticipate events that can be expected to happen in the near future. Anticipatory behavior plays a ubiquitous role in everyday life. As Requin et al.(1991, pp. 360) state it, *" at any moment a large part of the present activity of an organism is devoted to preparing for subsequent behavior "*.

In order to illustrate the effects of anticipation upon subsequent behavior, imagine two men who have an argument, and decide to solve their dispute by challenging each other for a 100 meters dash (see Figure 1.1). As the umpire gives them the signal to get ready for the start, the first man takes the starting position. His feet meet the starting blocks. He holds his breath, and concentrates on the upcoming sound of the starting pistol. The other man is still thinking about the argument that led to the challenge, and his thoughts dwell over the long history of friendship the two men have had together. As he is still in doubt whether he should wish his friend good luck, the starting pistol is fired. The starting shot takes him completely by surprise, and once he realizes that this sound indicates the beginning of the race, he sees his friend some 20 meters in front of him running towards a sure victory

This example illustrates two points about anticipatory behavior. First, the mere fact that the first man in the previous example was anticipating the race increased the speed of his reaction to the starting shot. In the psychological laboratory, the task our two athletes were engaged in is usually called a forewarned reaction time task. The signal to get ready is called a Warning Stimulus (WS), while the starting shot is termed the Reaction Stimulus (RS) or imperative stimulus. The experimental finding that reaction time (RT) is shorter when a RS is preceded by a WS which has a fixed temporal relation to the RS, as compared to a situation in which no WS is presented, has been reported as early as 1914 (Woodrow, 1914). One can infer from this general and well-documented experimental finding that anticipating an event provokes a change, or several changes, in the state of the organism, which leads to a faster, and/or more efficient information processing once the anticipated event occurs. At a general level, the goal of this thesis is to contribute to a better understanding of the nature of these changes.

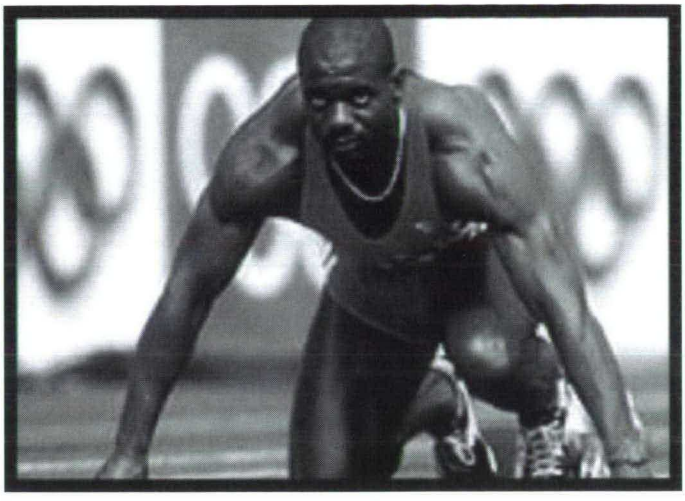

Figure 1.1: Anticipatory Behavior

Second, our clever athlete did not only anticipate the actual running, which most probably affected the readiness of his motor system to rapidly perform a sequence of movements. In addition, he also anticipated an auditory stimulus, that is, the sound of the starting shot, which increased the readiness of his auditory system to rapidly process the upcoming stimulus. Thus, our example illustrates that anticipatory behavior has two components, a perceptual component that enhances the processes at the input side of the organism, and a motor component that ameliorates the processes at the output side of the organism. Note that the distinction between the perceptual and motor aspects of anticipatory behavior is not new. In 1890, Lange, a student in Wundt's laboratory, distinguished between 'extreme muscular' and 'extreme sensorial' attention (described in James, 1890, pp. 92). Throughout this thesis, I shall use the term motor preparation to refer to anticipatory behavior that is directed at the motor system, and I shall reserve the term anticipatory attention for anticipatory behavior that is directed at one of the sensory systems. The term anticipatory behavior will be used to refer both to motor preparation and to anticipatory attention. This thesis is devoted to investigating the perceptual component of anticipatory behavior, i.e. anticipatory attention.

1.2 How to study anticipatory behavior?

The study of anticipatory behavior can be traced back to 1890. In his influential book entitled *Principles of Psychology*, William James (1890) describes an experiment for which he credits Wundt. In this experiment, strong and weak sounds were presented to a subject under two conditions. In the first condition the weak and strong sounds were presented in an alternating sequence, which allowed for a successful prediction (anticipation) of the upcoming stimulus, while in a second condition the sounds were presented in an irregular manner. The subject was asked to react as quickly as possible to either sound. In the alternating condition, the RTs to strong and weak sounds were 116 and 127 ms, respectively, while in the irregular sequence the RTs were 189 and 289 ms, respectively. Thus, the subject benefited from the predictability of the upcoming sequence. From this and other experiments, James concluded:

> *" Concentrated attention accelerates perception, so, conversely perception of a stimulus is retarded by anything which either baffles or distracts the attention with which we await it ".* James (1890, pp. 429).

However, traditional psychological research methods, which focus on the analysis of behavioral measures such as RT or error scores, are not particularly suited to study the process of anticipatory behavior *itself*. These measures can only yield information about the behavioral *outcome* of anticipatory behavior (e.g., a decrease in RT, or a reduction in error percentage). However, timing is one of the inherent properties of anticipatory behavior. By definition it occurs exclusively *prior to* an event. In order to gain insight in the temporal dynamics of anticipatory behavior, continuous measures are needed that reflect the ongoing process of anticipation itself. Physiological signals such as the electroencephalogram (EEG) or the magnetoencephalogram (MEG) are continuous, and are therefore well suited for the task at hand. Other physiological signals, such as the amplitudes of the Achilles tendon reflex (or T-reflex) and eyeblink reflex, or the amplitude of the evoked EEG response to probe stimuli (the evoked potential), are not continuous. However, when a subject performs a certain task a number of times (i.e., on different *trials*), evoking these signals, in different trials, at different points in time relative to an anticipated event, allows for the study of the temporal dynamics of anticipatory behavior.
Psychophysiological measures can yield information about the state of the Central Nervous System (CNS) in relation to the execution of a certain task. Different measures can be used to assess the state of the CNS at different levels. For example, the T-reflex, which is evoked by applying a tap on the Achilles tendon, has a relatively stable amplitude when a subject is comfortably seated and in a relaxed state. During motor preparation, the amplitude of the T-reflex is modulated because of changes in the excitability of motoneurons in the spinal chord (cf. Brunia and Boelhouwer, 1988 for a review). Therefore T-reflexes can be used to assess the state of the CNS at the spinal level. Similarly, eyeblink reflexes have been used to assess the state of the CNS at the brainstem level (e.g. Boelhouwer, 1984; Brunia and Boelhouwer, 1988). EEG and MEG mainly reflect activity of the cortex cerebri; therefore, these measures can be used to assess the state of the cortex during anticipatory behavior. The latter approach will be followed in the research described in the experimental part of this thesis.

1.3 Central question of the thesis.

The RT studies described by James demonstrate that anticipatory behavior serves the goal of a faster and/or more efficient information processing of the anticipated event. Today, more than a hundred years later, the mechanisms that mediate this enhancement of information processing are still poorly understood. It has been proposed that anticipating an event is accompanied by a reduction of the firing thresholds of neurons that are involved in the processing of the upcoming, anticipated event (e.g. Birbaumer et al., 1990). This may be accomplished by a subthreshold depolarization of the cell membranes of these neurons, which increases the readiness of the cells to fire. The result then would be a faster processing of the anticipated event once it occurs. Alternatively, it has been proposed that the thalamus, an assembly of nuclei in the diencephalon, serves as a gate in the transmission of information to the cortex (e.g. Skinner and Yingling, 1977; Brunia, 1993). In this view, the transmission of information through the thalamus to cortical structures that are not involved in the processing of the anticipated event is blocked, while the thalamic gate to the relevant cortical area(s) is open. The neurophysiological models on which these propositions are based will be described in detail in Chapter 4.
It should be made clear from the start that to *directly* test the thalamocortical gating model is clearly beyond the scope of this thesis. Such a direct test could only be accomplished through

intracerebral recordings simultaneously in different thalamic nuclei and their corresponding cortical projection areas. Since the research described in this thesis is based on scalp-recorded EEG and MEG, the data do only allow for statements about *cortical* activity. However, the thalamocortical gating model predicts that during anticipatory attention for an upcoming stimulus of a known modality, there will be an increase in activity in the sensory cortex corresponding to the modality of that stimulus. This increase in activity would be a reflection of the fact that the thalamic gate to that particular cortical area is open. The data presented in this thesis *do* allow for statements about cortical activity. Therefore, if the EEG and MEG data are found to be in accordance with the prediction that anticipatory attention for an upcoming stimulus leads to an increase in activity in the corresponding sensory cortex, then the present data will provide at least *indirect* support for the thalamocortical gating model. Thus, one of the major goals of this thesis is to test this prediction. The issues of exactly what kind of activity is to be expected, and how information about this activity can be extracted from the measured EEG or MEG, are subordinate goals of the thesis, and will be dealt with in later chapters. For the present I will restrict myself to stating the central question that this thesis addresses:

> *Is anticipatory attention for an upcoming stimulus realized at the neurophysiological level as a prestimulus activation of the sensory cortex corresponding to the modality of the anticipated stimulus?*

1.4 Outline of the thesis.

This thesis is divided into two parts, a theoretical part and an experimental part. In the *Theoretical Part*, I will present reviews of the psychophysiological literature in as far as it is relevant to the central question of the thesis. This will set the stage for the *Experimental Part*, in which I will describe the results of the experiments that have been performed in order to provide an answer to the central question. It should be noted that as a result of the choice of presenting the Experimental Part in the form of a compilation of research articles, there will be some overlap between the Theoretical Part and the introductory sections of the chapters of the Experimental Part. Below I will describe the contents of the Theoretical and Experimental Parts in some detail. Finally, in the final chapter entitled *Summary and conclusions*, the results of the different experiments will be integrated and I will discuss to which extent the results answer the central research question.

A large part of the data analyses performed in this thesis address the modulation, or reactivity, of rhythmic EEG/MEG activity, which I will study with a technique known as Event-Related Desynchronization (ERD; Pfurtscheller and Aranibar, 1977). In order to set up a theoretical framework for these analyses, *Chapter 2* will address the neurophysiological basis of EEG/MEG rhythms, with a special emphasis on rhythmic activity with a frequency of about 10 Hz. In *Chapter 3*, the functional significance of the reactivity of EEG/MEG rhythms will be discussed, and several techniques for analyzing this reactivity will be considered. In *Chapter 4*, I will present a number of models that make propositions about the neurophysiological basis of anticipatory behavior, and I will review the available experimental evidence for these models. In *Chapter 5* I will first integrate the foregoing chapters. Next I will account for the general research methods that will be used to investigate the aforementioned processes. Finally, I will operationalize the central research question of this thesis by formulating specific hypotheses that allow for an experimental evaluation.

Next, *Chapters 6, 7, 9 and 10* describe the experiments that have been carried out in order to test these hypotheses. *Chapter 8* is devoted to an important methodological issue in the computation of ERD on MEG data recorded with axial gradiometers. In the different

experiments three sensory modalities have been addressed: the auditory, visual and somatosensory modalities. The remaining two sensory modalities, olfaction and taste, have not been used for the following reasons. Taste stimuli have not been used primarily because they are difficult to standardize; at least, standardization of such stimuli would require highly specialized equipment. Furthermore, if taste stimuli are applied to the tongue, there would be an inherent interaction of the taste with the somatosensory modality. The olfactory modality has not been used because it has a neurophysiological organization that differs from the other modalities, in the sense that the afferent inputs from this modality do not flow through the thalamus on the way to the cortex.

Chapter 2: Neural mechanisms underlying the generation of 10-Hz rhythms.

In this chapter I will first present a brief historic overview of the early investigations into rhythmic EEG/MEG activity (section 2.1), which is partly based on a paper by Coenen et al. (1998). Subsequently the current thinking on neural mechanisms involved in the generation of 10-Hz activity will be outlined in a number of steps. First, a neurophysiological model will be presented that describes the neural basis of sleep spindles, and that may also partly account for the generation of the occipital alpha rhythm (section 2.2). Next, essential differences between sleep spindles and the occipital alpha rhythm will be discussed (section 2.3), and the existence of other 10-Hz rhythms will be considered. Finally a short description will be given of rhythmic EEG/MEG activity in other frequency ranges, and where possible the current thinking on their generator mechanisms will be reviewed (section 2.4).

2.1 A historic perspective.

The first report of (rhythmic) EEG activity can be traced back to 1875 (Caton, 1875). In a brief abstract, Caton described the spontaneous waxing and waning of the electrical activity recorded from the brains of rabbits and monkeys:

> *" Feeble currents of varying direction pass through the multiplier when the electrodes are placed on two points of the external surface (...). The electric currents of the gray matter appear to have a relation to its function " (Caton, 1875).*

Two years later, Caton (1877) described identical results for a larger number of animals. It is accepted nowadays that Caton's convincing and indisputable claim is the first description of the electroencephalogram, and of rhythmic activity of the EEG. It was however only some years later that considerable attention was drawn to this phenomenon through a Ph. D. thesis and a number of related publications by Adolf Beck (1890a, 1890b; Beck and Cybulski, 1890; Beck, 1891 (Russian thesis, for English translation: Beck, 1973)). Beck explored the electrical brain activity in greater detail than Caton did. Together with Cybulski he described the localization of sensory modalities on the cerebral cortex by electrical or sensory stimulation. In doing this they discovered spontaneous oscillations of the brain potentials and showed that these were not related to heart and breathing rhythms. Moreover, they described a cessation of the spontaneous fluctuations of the electrical waves. This potential *decrease* following sensory stimulation was a counterintuitive finding, and difficult to interpret, as is evidenced by Beck's remarks about this phenomenon:

> *" 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).*

It was only some 20 years later that the recording equipment was sufficiently powerful to identify two types of rhythmic activities in the EEG of the dog (Práwdicz-Neminski, 1913), that 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 they are nowadays denoted as alpha- and beta waves. The same researcher also coined the term elektrocerebrogramm (Práwdicz-Neminski, 1925), which was later changed to elektrenkephalogramm by Hans Berger. In 1929 the famous paper by Hans Berger was published, which is the first report of electrical activity from the intact human skull (Berger, 1929). 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. The famous neurophysiologists Adrian and Matthews (1934) started to replicate his findings, and only after some positive replications Berger's results were seriously considered. The systematic scientific study of the desynchronization of the electroencephalogram was born.

2.2 Sleep spindles.

Rhythmic activity of the EEG or MEG dominates the human EEG during natural sleep. Basically two rhythms can be identified in the EEG of a sleeping individual, delta waves and sleep spindles. Sleep spindles can be defined as waxing and waning waves within the frequency range of 7-14 Hz, grouped in sequences that last for 1.5-2 seconds and that recur periodically with a frequency of 0.1-0.2 Hz (Steriade et al., 1990). Spindles are the epitome of EEG synchronization during the early stage of sleep. They represent the electrographic landmark of the transition from waking to sleep. Although sleep spindles are not the main focus of the present text, I will discuss in some detail the neural mechanisms underlying their generation. The reason for this is that it is thought that to some extent the mechanisms responsible for the generation of sleep spindles are similar to those responsible for the generation of 10-Hz rhythmic activity (Steriade et al., 1990). The main differences between both types of phenomena probably lie in the dynamics of the two types of rhythmic activities. At least, barbiturate-induced spindles are considered to be an acceptable experimental animal model of the occipital alpha rhythm (Andersen and Andersson, 1968). There are however a number of obvious differences between the two phenomena that will be discussed in the next paragraph.

In the past two decades much effort has been devoted to the study of sleep spindles. This has led to a good understanding of their neural basis. Evidence for an integrative view of the generation of sleep spindles has accumulated basically at two levels. At the cellular level, evidence has been gathered that certain types of neurons have intrinsic oscillatory properties. At the network level, new insights have been gained into the main circuits responsible for the generation and modulation of rhythmic activity in neuronal populations; it is currently thought that the thalamo-cortical circuits are mainly responsible for generating sleep spindles. Below I will present the existing evidence for these new insights.

2.2.1 Oscillatory properties at the level of single cells.

The question of whether EEG rhythms are initially generated by single cells with pacemaker properties has been an important issue in the study of the mechanisms underlying the generation of sleep spindles. Besides thalamically projecting brain stem neurons, that will not be discussed here, three types of cells are of major importance in this discussion, namely cortically projecting thalamic neurons, thalamically projecting cortical neurons and reticular thalamic neurons. The cell properties of each of these neurons are becoming understood, and will be discussed below. Note that only the main aspects will be presented that are relevant for understanding how rhythmic activity may be generated at the level of single cells. For a

comprehensive account of the properties of the different cell types, the reader is referred to the extensive reviews by Steriade and Llinás (1988) and Steriade et al., (1990).

Cortically projecting thalamic neurons.

Two studies by Jahnsen and Llinas (1984a, 1984b) have led to significant advances in the understanding of the functioning of thalamocortical neurons. Jahnsen and Llinas demonstrated that by virtue of their ionic conductance properties (described in Steriade et al., 1990) thalamic neurons display oscillatory behavior within the frequency range of 6-10 Hz in vitro. It is probable that this oscillatory behavior plays a role in shaping the rhythmic behavior of the networks to which they belong. It appears however that in addition to these oscillatory properties, the thalamocortical neurons are also capable of functioning as relay elements, when their cell membranes are depolarized (Deschênes et al., 1984; Jahnsen and Llinás, 1984a, b). Thus, this type of cell can operate in two modes, a burst mode and a tonic mode (Steriade and Llinás, 1988). In burst mode, which occurs when the membrane potential is hyperpolarized (that is, more negative than –70 mV), thalamocortical neurons generate oscillatory activity that leads to the occurrence of spindles. In tonic mode, which occurs when the membrane potential is depolarized to a level of -60 mV or more, these cells show repetitive activity that may correspond to the transmission of afferent activity to the cortex (Deschênes et al., 1984; Jahnsen and Llinás, 1984a, b).

Thalamically projecting cortical neurons.

Although the ionic conductance properties that lead thalamocortical cells to oscillate are less sizeable in corticothalamic neurons (cf. Steriade et al., 1990), these cells are also capable of repetitive firing. In section 2.2.2 we will see that these corticothalamic cells, by virtue of their influence upon thalamocortical cells, may play a role in the synchronization of oscillatory spindle activity over large areas of the thalamus and neocortex.

Thalamic reticular neurons.

The thalamic reticular neurons, which constitute the reticular nucleus (RN), form a thin sheet of GABA-ergic neurons which covers the entire lateral and anterior part of the thalamus. It was found that when cortically projecting thalamic neurons are disconnected from the input of RN cells, the rhythmic behavior of the TCR cells disappears (Steriade et al., 1985; cf. Steriade and Llinás, 1988; Lopes da Silva, 1991 for reviews), although in vitro they may preserve their oscillatory properties (Jahnsen and Llinás, 1984a, b). The thalamic reticular neurons have ionic conductance properties that are similar to those of cortically projecting thalamic cells, but in addition they possess other conductance properties that allow them to oscillate more readily than the thalamic neurons themselves (Llinás and Geijo-Barrientos, 1988). As will be discussed later, it appears then that the real pacemaker of sleep spindles resides not in the cortically projecting thalamic nuclei, but in the RN nucleus.

2.2.2 From single cells to networks.

In order to understand how oscillatory behavior emerges in thalamocortical circuits from the intrinsic oscillatory properties of the membranes of single cells, the basic structure of these neuronal networks has to be considered.

The RN neurons synaptically interact with the thalamocortical relay (TCR) neurons, upon which they have an inhibitory influence. The dendrites of the RN neurons have synaptic contacts with the axons of the TCR cells. Thus, the TCR and RN nuclei are interconnected by means of a feedback loop. In addition, thalamic nuclei also contain local interneurons, which inhibit the TCR cells and receive inhibitory input from the RN nucleus. In this way, a number of feedback circuits can be identified between TCR and RN neurons (cf. Figure 2.1). It has been shown by Steriade et al. (1985) that TCR nuclei are incapable of generating spindle

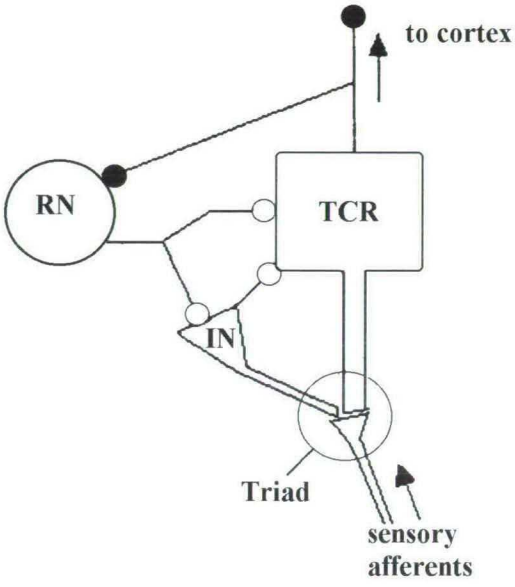

Figure 2.1. Schematic representation of the thalamic feedback circuit involved in the generation of oscillatory activity. Open circles indicate inhibitory (GABAergic) synapses, filled circles indicate excitatory synapses. TCR: Thalamocortical relay nucleus; RN: Reticular thalamic nucleus; IN: interneuron. Adapted from Lopes da Silva, 1991, with permission from the author.

oscillations when deprived from input of the RN. Therefore the existence of such feedback circuits is necessary for spindling to occur under normal, in vivo conditions. Steriade and Deschênes (1984, 1988) have described how the intrinsic oscillatory depolarizations in RN neurons described in the previous section jointly occur as oscillatory hyperpolarizations in TCR neurons. These hyperpolarizations are due to sequences of long-lasting inhibitory post-synaptic potentials (IPSP's), generated by the inhibitory synapses formed by RN neurons on TCR cells. The hyperpolarization of TCR cells leads to the generation of burst mode action potentials that produce a feedback activation of the RN cells by means of their axon collaterals (cf. Figure 2.1). This again leads to a hyperpolarization of the TCR cells, and in this way the oscillatory state is established. As an aside, this implies that while the mean membrane potential of the TCR cells is hyperpolarized during spindling, at the same time that of the RN cells is depolarized. This thalamic feedback system, which is responsible for the generation of rhythmic activity, gets its input from specific sensory afferents (see Figure 2.1). In addition, it receives input from two main, aspecific systems, which may modulate the oscillatory activity that generates spindling (not displayed in Figure 2.1): a cholinergic thalamopetal brain stem projection, and monoaminergic projections arising from locus coeruleus and the raphe nuclei. First the influence of the cholinergic brain stem projections will be discussed. It has been shown that approximately 1 second before the transition from wakefulness to sleep, i.e. just before the emergence of sleep spindles, there is a decrease in the firing rate of the cholinergic brain stem neurons. This leads to a decrease (mediated through nicotinic receptors) in the depolarizing effect of the cholinergic afferents on the TCR cells, while at the same time the inhibitory effect of the acetylcholine on RN cells is removed.

The co-occurrence of both effects probably conditions the emergence of sleep spindles. On the other hand, stimulation of the cholinergic brain stem neurons leads to a blocking of the sleep spindles, probably through inhibition of RN cells (Sillito et al., 1983).
The monoaminergic inputs to the thalamic feedback system consist mainly of noradrenergic fibers originating in the locus coeruleus and of serotonergic fibers arising in the raphe nuclei. Pape and McCormick (1989) have provided evidence for the notion that these afferent inputs result in a reduction of the responsiveness of the TCR cells to a hyperpolarizing input. Since hyperpolarization is a necessary condition for spindles to occur, it is probable that the monoaminergic inputs to the thalamic feedback system tend to decrease the occurrence of spindling.
Recently, evidence has been gathered for the notion that corticothalamic projections play an important role in synchronizing the oscillatory behavior in large portions of the thalamus and cortex (Contreras and Steriade, 1996, 1997; Steriade, 1997; Destexhe et al., 1999). A slow cortical oscillation , with a frequency below 1 Hz, has been described (Steriade et al., 1993a), that is thought to contribute to the regulation of this synchrony. Contreras and Steriade (1997) argued that, since this slow oscillation survives extensive thalamic lesions, but is disrupted by the disconnection of intracortical synaptic linkages, its origin appears to be cortical. It has been shown that sleep spindles generated by the interplay between thalamus and reticular nucleus, are grouped in sequences recurring periodically within the frequency range of the slow cortical oscillation (Steriade et al., 1993b, 1994). These data suggest that the slow cortical oscillation guides the synchrony of thalamic oscillations, and thus that thalamically projecting cortical neurons may play a role in the synchronization of the oscillations generated at the thalamic level.

2.3 The alpha rhythm and other 10-Hz rhythms.

The alpha rhythm can be defined as spontaneous waxing and waning waves within the frequency range of 8-12 Hz, that are most pronounced during relaxed wakefulness, particularly during eyes closure, and that show the largest amplitudes over the occipito-parietal cortex. Before discussing the experimental results that have been obtained in the study of the neurophysiological basis of alpha rhythms, it should be noted that 'the' alpha rhythm is most probably not a unitary phenomenon. Even within a relatively confined cortical area such as the occipital cortex there exist a variety of rhythms, possibly reflecting activity of different thalamo-cortical circuits (e.g. Walter, 1969).
Rhythms with a frequency of approximately 10 Hz are present over the entire human neocortex. Since there are good reasons to believe that 10-Hz rhythms can be grouped on the basis of their reactivity to experimental manipulations (this will be discussed in section 3.3.1), the use of the term alpha rhythm will be restricted throughout this thesis to that subcategory of 10-Hz rhythms which is maximal over the occipital cortex, and which reacts to visual stimuli in some way. However, although there are obviously a large number of functionally different, parallel thalamocortical circuits that generate 10-Hz rhythms, it appears reasonable to think that the neural mechanisms involved in the generation of different 10-Hz rhythms are the same. Therefore it makes sense to discuss the common neural basis of 10-Hz rhythms as if they were a unitary phenomenon. It should be noted that almost all of the research into the relationship between sleep spindles and spontaneous 10-Hz rhythms has been performed with the occipital alpha rhythm. Therefore I will use the term alpha rhythm rather than the more general term 10-Hz rhythm in the following paragraph.
In order to study experimentally the mechanisms of generation of 10-Hz rhythms, it is necessary to have available experimental models of this type of rhythmic EEG activity. Two types of models have been used in this respect: (1) the induction of spindles in experimental animals by means of barbiturate anesthesia, since sleep spindles and alpha activity bear a

remarkable resemblance, and (2) recordings by means of chronically indwelling electrodes in experimental animals in the awake state, under conditions that resemble as much as possible those known to be necessary for alpha activity to occur in humans. Results obtained by means of the former experimental model have been discussed in some detail in the previous paragraph; the present paragraph will address the main results obtained by latter type of model, which will reveal a number of basic differences between the dynamics of sleep spindles and of the alpha rhythm.

Recordings from chronically indwelling electrodes in awake animals have been performed mainly in cat (Lanoir and Cordeau, 1970; Rougeul et al., 1974), in dog (Storm van Leeuwen et al., 1967; Lopes da Silva et al., 1970, 1973a, b, 1974, 1976, 1980; Lopes da Silva and Storm van Leeuwen, 1977, 1978) and in monkey (Jurko and Andry, 1967). A number of features characteristic of the alpha rhythm that differentiate between this type of rhythmic activity and sleep spindles have been thus established, and will be summarized here. First, the alpha rhythm is different from sleep spindles in spectral content and topographic distribution (Lopes da Silva et al., 1973a, b). These researchers compared the alpha rhythm with barbiturate-induced spindles, recorded from intracortical and intrathalamic electrodes in the same dogs. They found that differences in peak frequency between different electrode sites were larger for alpha activity than for spindles. Moreover, the alpha rhythm was found to be largest over posterior areas, in particular over the occipital part of the marginal gyrus, and over the mesial part of the occipital cortex. In contrast, barbiturate spindles showed a widespread distribution. In addition, they reported much larger thalamo-cortical coherences for spindles than for alpha activity. The latter suggests that under the natural conditions during which alpha activity occurs, thalamic and cortical structures act more independently than during barbiturate anesthesia. Further evidence for this notion stems from studies that demonstrated that in most cases coherences between adjacent cortical areas are larger than thalamo-cortical coherences during alpha activity (Storm van Leeuwen et al., 1967; Lopes da Silva and Storm van Leeuwen, 1977). Lopes da Silva et al. (1980) used partial coherence analysis in order to establish which part of the cortical alpha rhythm (recorded from the dog's visual cortex) can be explained by cortico-cortical propagation, and which part is produced by thalamic oscillations (recorded from the lateral geniculate nucleus (LGN) and the pulvinar). They found that removing the influence of the LGN signals resulted only in a small reduction of cortico-cortical coherences, and removing the influence of the pulvinar resulted in a much larger reduction of the intracortical coherences. In some cases, the cortico-cortical coherences remained significant after partialization, while in other cases these coherences were not significantly different from zero. They concluded that although the thalamic nuclei had a clear effect on the degree of coherence of cortico-cortical signals, there must be cortico-cortical processes involved in the propagation of the cortical alpha rhythm. Since the alpha rhythm has been shown to have a cortical source (they originate in layers IV and V of the visual cortex (Lopes da Silva and Storm van Leeuwen, 1977, 1978), the hypothesis has been put forward that functionally different (thalamo-) cortical networks may generate cortical epicenters of alpha activity, and that by cortico-cortical propagation of the alpha activity these networks may influence neighboring networks in such a way that the basic alpha oscillation of each network is modulated by the activity of other networks (Lopes da Silva et al., 1997).

In conclusion, it can be hypothesized that the neuronal elements and networks responsible for the generation of sleep spindles, that is, the thalamic feedback system involving the RN and TCR nuclei also account for the generation of the alpha rhythm, and more generally of 10 Hz rhythms. However, there is an additional cortical propagation of the epicenters of 10-Hz activity generated by this mechanism. The main differences between both types of

phenomena then appears to lie in the dynamics and functional significance of the two types of rhythmic activities (see also section 3.3.1).

2.4 Rhythmic activities outside the alpha frequency range.

Rhythmic activity with a frequency of about 10 Hz, that is, sleep spindles and 10-Hz rhythms, are by far the most investigated EEG/MEG rhythms. However, there exist a variety of other oscillatory phenomena, that are not only characterized by different resonant frequencies, but that most probably are generated by different neural mechanisms, both at the single cell level and at the level of neuronal networks. Although a thorough discussion of the neural basis of the different types of rhythmic activity outside the 10-Hz range are beyond the scope of this thesis, for the sake of completeness I will very briefly discuss the current state of the art on the generator mechanisms of the other prominent EEG rhythms: the delta and theta rhythms, and the fast EEG rhythms in the beta / gamma range.

2.4.1 The delta rhythm.

The delta rhythm can be defined as slow waves between 0.5 and 4 Hz that prevail during the deep stage of normal, EEG synchronized sleep. It is probable that the generator mechanisms of delta waves are different from those underlying sleep spindles and 10-Hz rhythms, since experimental animal studies have shown that spindles are abolished in athalamic cats, whereas the delta rhythm persists at the cortical level (Villablanca, 1974). It has been demonstrated by animal studies in cat and rabbit that delta waves are generated in the cortex, between layers II-III and layer IV (Calvet et al., 1964; Petsche et al., 1984). Ball et al. (1977) studied the extracellular microphysiological properties of delta waves produced by lesions of the subcortical white matter, the thalamus or the reticular formation. He demonstrated that cortical delta waves exhibit a dipolar profile across cortical layers. Tangential recording of delta activity over distances of the cortex comparable to its thickness did not show any evidence for a tangential component in the current flow underlying delta waves. These findings indicate that delta waves are generated by vertically arranged dipole layers lying parallel to each other. This makes the pyramidal neurons in the cortex the most likely candidates for the generation of delta activity.

2.4.2 The theta rhythm.

The theta rhythm is an EEG rhythm with a frequency between 4-7 Hz. It dominates the electrical activity recorded from the hippocampus in most mammals, but is most prominent in rodents. Because in lower mammals there is quite some interspecies variation in the exact theta frequency (with frequencies ranging from 3-4 Hz up to 10-12 Hz), the phenomenon is often termed rhythmic slow activity (RSA). It has been a matter of some debate whether theta waves occur exclusively in lower mammals or also in humans (cf. Arnolds et al., 1980; Halgren et al., 1985). A possible explanation of the relative difficulty in recording theta activity from the human hippocampus, may be that its amplitude is reduced and its pattern is more irregular in higher primates (Lopes da Silva, 1992).
Although the theta rhythm is commonly associated with the hippocampus, rhythmic activity with the same characteristics has been reported in the entorhinal and cingular cortices, and the septum as well (Petsche et al., 1962). It is generally agreed that an intact septum is a necessary condition for the occurrence of the hippocampal theta rhythm, while destruction of the medial septum results in a disappearance of theta from the hippocampus and other limbic cortical areas (Petsche et al., 1962; Vinogradova et al., 1980). This suggests that the septum serves as a pacemaker for the theta rhythm to occur in other structures. However, Konopacki et al. (1988) have shown that hippocampal networks are capable of producing theta activity when isolated from septal input. Furthermore, it has been established that the hippocampal

theta rhythm is not primarily determined by intrinsic membrane conductance properties, but rather by local synaptic interactions within the hippocampus, entorhinal cortex, and cingulate cortex (for reviews see e.g. Steriade et al., 1990; Lopes da Silva, 1992). For comprehensive reviews of the literature on the theta rhythm, the reader is referred to reviews by e.g. Robinson (1980), VanderWolf and Robinson (1981) and Lopes da Silva (1992). In section 3.3.3 I will discuss some studies that have addressed the functional significance of the reactivity of the theta rhythm.

2.4.3 Rhythmic activity in the beta and gamma ranges.

Rhythmic EEG activity in the high frequency range (14-30 Hz) is usually called beta activity, while rhythms with even higher frequencies (30-50) Hz are mostly referred to as gamma activity (Bressler, 1990). It should be noted that some authors do not support the distinction between beta and gamma activity (e.g. Steriade, 1997). Penfield and Jasper (1954), using intraoperative epicortical recordings, have demonstrated blocking of beta activity over the precentral hand areas prior to and during voluntary hand movements. More recent studies (e.g. Pfurtscheller, 1992; Salmelin and Hari) support the interpretation of beta activity as an intrinsic rhythm of the motor system (see also section 3.3.1). Gamma activity dominates the local EEG recorded from olfactory areas in the basal forebrain (Bressler and Freeman, 1980), from the entorhinal cortex in cat (Boeijinga and Lopes da Silva, 1988), from the central and parietal cortex from the alert cat (Rougeul-Buser et al., 1983) and is clearly seen in the visual cortex (e.g. Gray et al., 1988; Eckhorn et al., 1989). De France and Sheer (1988) have reported gamma activity related to the performance of a motor task, and following movements an increase in gamma activity has repeatedly been reported (e.g. Pfurtscheller, 1992). In general, both the beta and gamma rhythms are associated with behavioral conditions in which one is alert and focussing attention.
Little is known about the neural mechanisms underlying beta and gamma oscillations. Whereas 10-Hz activity is evident both in the cortex and thalamus, beta and gamma rhythms appear only in the cortex. Furthermore, it has been suggested that, at least in cat, these rhythms are dependent on an intact system of cortically projecting dopaminergic fibers arising from the ventral tegmental areas (Montaron et al., 1982). In general however, it can be stated that the origins, cellular basis and to a large extent also the functional significance of the beta and gamma rhythms remain to be elucidated (cf. Steriade et al., 1990).

Chapter 3: Functional significance of rhythmic EEG/MEG activity.

The previous chapter has mainly dealt with the neurophysiological basis of rhythmic activity in the 10-Hz frequency range. I reviewed the existing evidence for the notion that 10-Hz rhythms are mainly generated in thalamic feedback circuits, and that cortico-cortical processes play an important role in the propagation of 10-Hz rhythms. The present chapter tries to bridge the gap between neurophysiology and psycho(physio)logy in this respect. That is, I will address the issue of the functional significance of fluctuations in oscillatory activity, in as far as such fluctuations are related to -internal or external – events, such as the presentation of stimuli, the preparation and production of movements, and higher-order cognitive / psychological processes such as memory or attention. In the first section I will discuss in general terms the functional significance of synchronization and desynchronization of EEG/MEG rhythms. In section 3.2 I will discuss different methodological approaches that can be used to study these phenomena. Finally, in section 3.3 I will review the literature on synchronization and desynchronization as far as it bears relevance to one of the central questions in this thesis: is it possible to use event-related desynchronization as a tool for studying anticipatory behavior.

3.1 Synchronization and desynchronization.

3.1.1 Functional significance of (de)synchronization in the 10-Hz frequency range.

In chapter 2, it was described that cortically projecting thalamic neurons, also termed Thalamo-Cortical Relay (TCR) neurons, can operate in two modes, burst and tonic modes, depending upon the voltage level of their membrane potential. In burst mode, which occurs when thalamocortical cell membranes are hyperpolarized, the transfer of inputs to the cortex is disengaged. Thus, the cortex is deprived of the relevant input, and will not be engaged in active processing. Concurrently, as was pointed out in the previous chapter, burst mode firing in thalamocortical neurons leads to the occurrence of synchronized oscillatory activity at the level of the cortex. These synchronized oscillations correspond to a state that may be termed cortical idling (e.g. Pfurtscheller, 1992), or cortical inactivity. Whether or not these synchronous oscillations are detected at the scalp depends on various antecedent conditions: the topology of the cortical area displaying synchronous oscillatory activity, the distance and angle of the area relative to the recording sensors at the scalp, and the extent of the cortical area (cf. Lopes da Silva and Pfurtscheller, 1999a). With respect to the latter, it is interesting to note that synchronicity is a crucial factor in whether or not oscillatory activity is detectable at the scalp. Nunez (1995) has addressed the question of how many neurons within a given neural mass make a detectable contribution to the local EEG or MEG. Nunez estimated that the contribution of a number of synchronously active neural sources (represented by M) relative to the number of asynchronous generators (represented by N) to a local EEG signal can be expressed by the general formula M / square root (N). As an example, let us assume that in a cortical area containing 10^5 neurons, 20% of these neurons fire synchronously, while 80% is firing asynchronously. Applying the general rule reveals that these 20 % contribute approximately 70 times more to the local EEG than the 80 % asynchronously firing neurons! As a general rule, it is estimated that a high degree of synchrony in an area of 100 mm^2 is required for oscillatory activity to result in a clear peak in the frequency spectrum of the

scalp-recorded signal (cf. Lopes da Silva and Pfurtscheller, 1999a for a discussion). If these antecedent conditions for synchronous oscillations to be detected at the scalp are met, then there is a clear relationship between scalp-recorded high-amplitude, low-frequency EEG and cortical idling.
In tonic mode, which occurs when the membrane potential of cortically projecting thalamic cells is depolarized, these cells show repetitive activity that corresponds to the transmission of afferent activity to the cortex. Thus, in this case the cortex is provided with the relevant input, and will engage in active processing of the incoming information. This is accompanied by a disruption of synchronous oscillatory activity, or desynchronization. Assuming that the oscillations were initially detectable in the scalp EEG, this disruption will be reflected at the scalp by a shift from high-amplitude, low-frequency EEG to low-amplitude, high-frequency EEG.
These insights have far-reaching implications for psychophysiological research. Scalp-recorded high-amplitude, low-frequency EEG reflects cortical idling, whereas a shift in spectral content to low-amplitude, high-frequency oscillations at the scalp reflects cortical activity. The important point here is that by studying changes in the spectral content of the EEG or MEG trace at a particular location at the scalp, inferences can be made about the state of the underlying cortical area. If a sufficiently large number of sensors is used, and frequency spectra are computed over relatively short periods of time (e.g. some hundreds of milliseconds), spatiotemporal patterns of cortical activity can thus be distinguished, which is very useful in the study of the relationship between brain activity and behavior in general. In section 3.3, I will review the existing literature in which this approach has been followed, as far as it is relevant for the present purpose. However, in order to fully appreciate the experimental evidence presented in section 3.3, it is important to have insight in the different methodological approaches that have been used to quantify event-related fluctuations in EEG / MEG rhythms. Therefore I will first give an overview of the available methods, and discuss the advantages and disadvantages of the different approaches.

3.1.2 Functional significance of (de)synchronization in other frequency bands.

It is of crucial importance that one realizes that the relationships described in the previous section between synchronization and cortical idling on the one hand, and between desynchronization and cortical activity on the other hand, only hold for oscillatory activity in the 10-Hz frequency range. As outlined in the previous chapter, there is now consensus about the notion that oscillatory activities in other frequency ranges are based on different neural generator mechanisms, although the exact neural mechanisms for most of the oscillatory activities outside the 10-Hz band are only poorly understood. As a consequence, the interpretation of event-related fluctuations in these oscillations differs depending on the frequency band studied. Although the functional significance of different oscillatory activities outside the 10-Hz frequency range is much less straightforward than for 10-Hz rhythms, the past decade has seen an enormous increase in the understanding of how to interpret the different phenomena. It is now -more or less- generally agreed that oscillatory activity in the theta frequency range relates to memory processes, while higher beta band oscillations around 40 Hz (often also termed gamma band oscillations) are in some way related to specific attentional states.

3.2 Desynchronization quantified.

Studying changes in the spectral content of the EEG or MEG can be accomplished in various ways. However, a method for studying the spectral content of the EEG or MEG that has gained popularity during the last two decades is the computation of a measure known as Event-Related Desynchronization (ERD), a term that has been coined by Pfurtscheller and

Aranibar (1977). Since this early report on ERD a number of variants have been introduced on the 'classical' ERD. Below an overview will be given of the different methods, and the rationales for their use will be considered.

3.2.1 'Classical' ERD.

Computation.

The classical method used for ERD computation involves the following steps: (1) applying a bandpass filter to single EEG epochs that are timelocked to an -internal or external- event, leaving intact the frequency band of interest (e.g. 8-12 Hz); (2) squaring the amplitudes of the filtered EEG epochs, in order to obtain an estimate of the power in that particular frequency band; (3) integrating the power over short time intervals (e.g. 250 ms) in order to obtain a more reliable estimate of the power; (4) averaging the power in each time interval over epochs; (5) expressing the power in each time interval as a percentage of the power in a reference interval or baseline computed e.g. in 1-second intervals prior to each epoch, in which no task, stimulus or response was present. The resulting measure is the average power increase (Event-Related Synchronization, ERS) or decrease (Event-Related Desynchronization, ERD[1]) in a particular frequency band, in a particular time interval, relative to the level of the power in the baseline. This procedure can be repeated for each channel, and topographic maps can be constructed of the power in- and decrease. Following the reasoning outlined in section 3.1, it is generally agreed upon that if an ERS is found at a certain area of the scalp, the underlying cortical area is inactive, while ERD corresponds to cortical activity, at least when the 10-Hz frequency range is considered.

A slightly different procedure, termed Temporal-Spectral Evolution (TSE) has been proposed by Salmelin and Hari (1994). Instead of squaring the amplitudes of single EEG epochs (as in step 2 of the procedure described above), these researchers use the absolute values of the EEG amplitude. Although the TSE method produces results that are identical to the ERD method, an advantage of TSE may be that the resulting measure is expressed in the same units as the original responses, and can be directly compared to the single epoch data or to the Event-Related Potentials (ERPs).

Topographic mapping.

When topographic mapping is desirable, it is common practice to compute the second spatial derivative, or surface laplacian, of the EEG prior to ERD computation. The reason for this is twofold: first, it eliminates ERD effects at the reference electrodes, which can strongly influence the topography of the ERD (cf. Pfurtscheller, 1991); second, this procedure increases the spatial resolution of ERD mapping, since an inherent property of the surface laplacian is that it acts as a spatial highpass filter. For obvious reasons (MEG is inherently reference-free) this step is omitted when ERD is computed on MEG data. The surface laplacian can be computed in a variety of ways, partly depending upon the phenomenon under investigation, and partly depending upon the number and montage of the electrodes (e.g. Pfurtscheller, 1991). Two methods are widely accepted: source derivations (Hjorth, 1975) and spline-based scalp current density (SCD) fields (e.g. Perrin et al., 1987, 1989; Babiloni et al., 1996). Currently other methods for enhancing the spatial resolution of ERD are being developed, such as cortical imaging based on linear estimation (e.g. Edlinger et al.,

[1] Throughout this thesis, the terms ERD and ERS will be used to refer to a power decrease and a power increase, respectively. Additionally however, I will use the term ERD to denote the ERD technique itself, that is, the quantification of synchronization and desynchronization, whereas some authors use the compound term ERD/ERS to indicate the technique. For example, I will use the term ERD mapping to refer to the construction of topographic maps of ERD *and* ERS.

1998; van Burik et al., 1998). These methods have the theoretical advantage of offering the possibility to integrate the complementary information contained in EEG and MEG into one topography, although there are as yet some problems to be solved in order to accomplish this (e.g. Edlinger et al., 1999). For an excellent and comprehensive review of the advantages and disadvantages of the different methods that are currently available the reader is referred to van Burik et al. (1999). Finally it should be noted that the considerations regarding the topographic mapping of ERD apply not only to the classical method for ERD computation, but they apply equally to all the different ERD methods presented below.

3.2.2 ERD based on intertrial variance.

Induced, evoked and spontaneous rhythms.

In order to understand the rationale behind the computation of ERD based on intertrial variance, it is important to distinguish between three types of rhythmic oscillations in the EEG or MEG: induced rhythms, evoked rhythms and spontaneous rhythms. Induced rhythms may be defined as '*oscillations caused or modulated by stimuli or state changes that do not directly drive successive cycles of the rhythm*' (Bullock, 1992, pp.1). Evoked rhythms on the other hand are directly driven by stimuli or state changes. In contrast to induced and evoked rhythms, spontaneous rhythms have by definition no direct relation to an -internal or external- event, and therefore are of limited use in the study of the relationship between brain activity and psychological processes. In neurophysiology, an example of an induced rhythmic response is the blocking of the occipital alpha rhythm by the opening of the eyes (Berger, 1929), while an example of an evoked rhythmic response is the Steady-State Response to 40 Hz stimulation (e.g. Rockstroh et al., 1996).

ERD vs. ERPs.

From a signal-analytic point of view, the main difference between induced and evoked activity is that the latter is both time-and phase-locked to a certain event, whereas the former is time- , but not necessarily phase-locked to the event. Evoked activity can be extracted from the ongoing EEG by a straightforward averaging of the event-related EEG epochs. The resulting average is a traditional Event-Related Potential (ERP). However, the activity that is time-, but not phase-locked cancels as a result of the averaging procedure used in ERP computation. When computing the classical ERD on the other hand, the activity that is not phase-locked is retained, by virtue of the fact that the power is computed (i.e., amplitudes are squared) before averaging over single EEG epochs. An important implication here is that the classical ERD contains information about the event-related EEG epochs that is not present in the ERP (i.e., the non-phase-locked activity). However, there is also some overlap in the classical ERD and the ERP, in that both contain the phase-locked activity (cf. Figure 3.1). This means that to some extent, it is not possible with the classical ERD method to differentiate between induced and evoked power changes. However, such a differentiation is important when it can be expected that the evoked activity (i.e., the ERP power) is in the same frequency range as the induced activity. In this case, the ERD is contaminated by the ERP. As an example, imagine that one is interested in the induced changes in the 10-Hz rhythm as a result of auditory stimulation. It is known that the presentation of auditory stimuli evokes a negative deflection in the EEG with a latency of 100 ms (the N100). Because of its shape, a significant portion of the power of this ERP component is concentrated within the 10-Hz frequency range. Since the N100 will be present in every event-related EEG epoch, computing the ERD in the first 250 ms interval following auditory stimulation will result in an increase in 10-Hz power because of the N100. Now let us assume that the true effect of auditory stimulation on the induced 10-Hz rhythm is a power decrease. The net effect then

will be that the ERD reveals no significant change in 10-Hz power because the ERD (power decrease) is contaminated by the ERP (power increase).

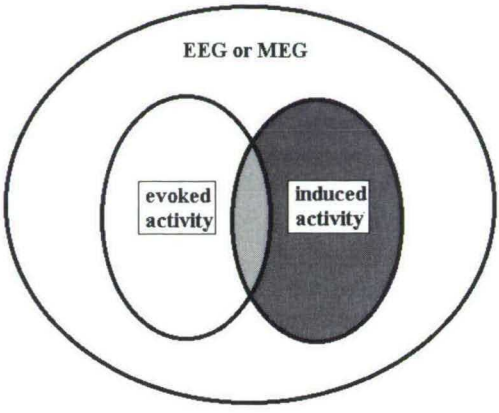

Figure 3.1 The EEG or MEG contains two classes of event-related activity: evoked activity, which is contained in the traditional ERP, and which is both time- and phase-locked to an event; induced activity, which is time- but not necessarily phase-locked to an event. With the induced band power method only the non-phase-locked part of the signal (depicted in dark gray) is retained. The classical ERD method additionally includes the phase-locked part of the signal (the ERP) insofar as it falls inside the selected frequency band (depicted in light gray).

Separating non-phase-locked activity from phase-locked activity.

ERD based on intertrial variance offers a solution to this problem, by separating the non-phase-locked activity from the phase-locked activity. This method has been first proposed by Kalcher and Pfurtscheller (1995). The procedure for calculating this ERD variant is the following: (1) single EEG epochs are bandpass filtered; (2) these filtered epochs are averaged, thus yielding a bandpass filtered ERP that corresponds to the pure phase-locked activity in that frequency band; (3) from each single, bandpass filtered EEG epoch the bandpass filtered ERP is subtracted, thereby removing the phase-locked activity from the non-phase-locked activity. (4) squaring the amplitudes of the subtracted data, which yields the intertrial variance (Kaufman et al., 1989). The subsequent steps are the same as for the computation of the classical ERD, that is integrating over time intervals, averaging over epochs and expressing the induced band power in a particular time interval as a percentage of the power in the baseline interval. Applications of this method by e.g. Kalcher and Pfurtscheller (1995) and Klimesch et al. (1998a) have shown that changes in induced rhythms thus quantified may be considered a phenomenon that is largely independent from the occurrence of ERPs.

For the present purpose it should be noted that for the experiments performed in the context of this thesis, we could exclude beforehand the possibility that the ERPs elicited in our experimental paradigm contaminate the ERD. In all the experiments performed, we computed the ERD in the 10-Hz frequency range, in a paradigm that evokes ERPs which have a spectral power that is concentrated below 1 Hz (i.e., slow negative potential shifts that extend over

periods longer than one second). Therefore we did not make use of the ERD based on intertrial variance.

3.2.3 Increasing the temporal resolution: amplitude envelope analysis.

As discussed in the previous sections, there are two good reasons for analyzing the ERD in addition to the ERP: first, ERD focuses on a part of the signal that is not used when only ERPs are analyzed, thus it yields different information; second, ERD has a good spatial resolution, in some cases better than that obtained with ERPs (see also section 3.3.2). However, the time resolution of ERD, in the order of a few hundred milliseconds, is poor compared to ERPs. This seriously limits the applicability of ERD analyses to phasic EEG phenomena that extend over short periods of time, which is often the case in psychophysiological research. To overcome this limitation, a method has been proposed in which desynchronization can be computed with a time resolution only limited by the sampling frequency. This method is based on measuring the amplitude modulation of the EEG. This is accomplished by estimating the envelope of bandpass filtered EEG data using a Hilbert transform (Bhansali and Potter, 1986). Clochon et al. (1996) have compared this method, referred to as AM-EEG (Amplitude Modulation of the EEG), to the classical ERD. They demonstrated that the ERD is effectively a time integration of amplitude modulation, and showed that AM-EEG responses produce statistically significant results that are very similar to ERD, but with a much better time resolution (Clochon et al., 1996). Although this method is not widely applied yet, it is a promising development since it allows for studying the short-lasting, non-phase-locked changes in induced EEG/MEG rhythms that can be expected to accompany many psychological processes.

3.2.4 On the determination of frequency bands.

As I pointed out in section 3.1, the interpretation of ERD depends on the frequency band considered. Although there is general agreement about the nomenclature used to designate different frequency ranges, e.g. 4-7 Hz for the theta band and 8-13 Hz for the alpha band (see e.g. Noachtar et al., 1999 for a glossary of terms most commonly used in EEG research). However, for two reasons it may be useful in ERD computation to deviate from these fixed, predefined frequency bands: (1) within the predefined frequency bands different components may reflect functionally different processes. For example, for several reasons (discussed in section 3.3) some researchers differentiate between the upper and lower alpha frequency bands. (2) The use of fixed frequency bands may in some cases obscure the effects one is looking for, due to the rather large intra-individual variability in the exact location of EEG/MEG spectral peaks. In ERD computation, four methods for determining appropriate frequency bands are used. Below I will shortly describe the different methods and the rationales for their use.

Fixed, predefined frequency bands.

This method involves the straightforward use of fixed, predefined frequency bands. Examples are 4-7 Hz and 8-12 Hz for the lower and upper alpha bands, respectively (cf. Noachtar et al., 1999). The main advantage of this method is that it is simple; its use may be warranted in purely explorative research, in which case no special hypotheses exist about which frequency bands will be reactive to the experimental manipulations.

Determination of frequency bands relative to the individual alpha peak frequency.

It has repeatedly been reported that there exist large differences in individual alpha peak frequencies (IAF; Köpruner et al., 1984; Klimesch et al., 1990, 1993; see Klimesch, 1999 for a discussion). Young normal adults of about 30 years have a IAF of about 10 Hz, with a

standard deviation of 1 Hz. This implies that within a group of subjects of the same age an inter-individual difference in alpha peak of 2 Hz is quite common. In addition, IAF is negatively correlated with age. Köpruner et al. (1984) have found a linear relationship between IAF and age, that is expressed in the formula IAF = 11.95 – 0.053 * age. Clinical evidence further demonstrates that a variety of brain diseases result in a lower IAF (e.g. Sheridan et al., 1988).

These findings imply that in some cases the use of fixed, predefined frequency bands is undesirable and may lead to a blurring of the results, because large portions of alpha power may fall outside of the predefined frequency band(s). An alternative has been proposed by Klimesch and coworkers (see for example Klimesch, 1999). They suggest the use of the IAF as an anchorpoint to adjust alpha frequency bands individually. They have defined four frequency bands with a width of 2 Hz that cover the traditional range of theta and alpha frequencies as follows: theta = (IAF – 6 Hz) to IAF – 4 Hz); lower-1 alpha = (IAF - 4 Hz) to (IAF – 2 Hz); lower-2 alpha = (IAF – 2 Hz) to IAF; and upper alpha = IAF to (IAF + 2 Hz). ERD is then calculated individually in these frequency bands and subsequently averaged over subjects. It should be noted that although this procedure is well-defined for the theta and alpha frequency bands, there is no clear definition of beta/gamma bands based on individual spectral peaks.

Determination of most reactive frequency bands based on the comparison of power spectra.

Determining frequency bands on the basis of spectral peaks in the EEG or MEG is in some cases problematic. It may be, for instance, that large differences in spectral peak exist between different recording sites, which may be reflections of different rhythmic activities (for example, the central mu rhythm and the occipital alpha rhythm, cf. section 3.3.1, that have comparable but not entirely identical frequency ranges). In this case the decision of which channels to use in the determination of the spectral peak may be rather subjective. Alternatively, it may be that frequency ranges that are strongly affected by the performance of a certain task do not coincide with spectral peaks, in which case this induced activity will be overlooked if frequency bands are determined exclusively on the basis of these peaks. In other cases, very large inter-individual differences in maximally reactive frequencies can be expected. This occurs, for example, in the post-movement ERS in the beta frequency ranges that can be observed following the offset of self-paced voluntary movements (e.g. Pfurtscheller, 1992, cf. section 3.3.1 of this thesis).

In cases when the spectral peak is not a very adequate anchorpoint for determining frequency bands, another approach can be used to select frequency bands. In this approach, the idea is to determine which frequency bands are maximally reactive to a given experimental manipulation. It is based on the comparison of two short-time power spectra calculated over a number of event-related EEG epochs. One spectrum is calculated for the reference interval or baseline, chosen some seconds before an event occurs; the other is calculated in a period when the subject is actively engaged in the performance of an experimental task. The difference of these two power spectra can be used to determine those frequency components that most react to the experimental manipulation.

There is one important caveat when frequency bands are selected on the basis of this method. The calculation of frequency spectra results in a number of peaks that are harmonically related. Bandpass filtering of the basic and first harmonic frequencies can therefore result in similar band power time courses, which may thereby misleadingly suggest that e.g. the mu and beta rhythms behave identically in a movement experiment. Examples of this problem, and a solution for it, are discussed amongst others in Pfurtscheller et al., 1997a; Pfurtscheller, 1999).

3.3 ERD as a psychophysiological research tool.

Since the first report on ERD by Pfurtscheller and Aranibar (1977), the method has been applied to a wide variety of psychophysiological phenomena. It is clearly beyond the scope of this thesis to provide a detailed and comprehensive literature review of ERD research. Such a review is provided by a recently published book on ERD edited by Pfurtscheller and Lopes da Silva (1999). In this section I will only discuss those topics that bear relevance to the research questions that will be addressed in the present thesis. In chapter 1 it was noted that the central question of this thesis is whether anticipatory attention manifest itself as a modality-specific cortical activation preceding the presentation of stimuli in one of the main sensory modalities (auditory, visual, somatosensory). Since in the experimental part of this thesis I will use ERD as a tool for studying this modality-specificity, it is most important to establish whether it is in principle possible to demonstrate modality-specificity with ERD, in section 3.3.1 I will summarize the evidence, that has accumulated over the past 50 years, for the notion that each modality has its own 10-Hz rhythm.
Traditionally, ERD has been used as a tool to study motor behavior. The extensive work on movement-related ERD has yielded a clear and robust picture of the ERD elicited by movements. Since all of the experiments that were performed in the context of this thesis required motor responses from the subjects, it is important to have insight in the movement-related ERD. This issue is addressed in section 3.3.2. Finally, the work on ERD related to memory processes has incidentally provided some data on the relationship between ERD in the 10-Hz frequency range and attention. Obviously it is important to be aware of these findings, since they bear relevance to the central question of this thesis. Section 3.3.3 therefore discusses the results of these studies as far as they are related to attentional processes.

3.3.1 Alpha, mu and tau: modality-specific 10-Hz rhythms.

Recently it has been proposed that next to a global cortical 10-Hz rhythm, there are several local cortical 10-Hz rhythms (Nunez, 1995) that can be functionally distinguished from each other on the basis of differences both in scalp distribution and in reactivity to experimental manipulations. In the following we would like to propose a functional classification of local cortical rhythms, and to forward the notion that every sensory modality has its own (class of) rhythm(s).

The alpha rhythm.

When a healthy individual is in a relaxed state, with his eyes closed, one can record rhythmic activity of around 10 Hz from occipito-parietal leads both in the EEG and in the MEG. As early as 1929, Berger (1929) observed the reactivity of the occipital alpha rhythm to opening or closing of the eyes. It should be noted here that the occipital alpha rhythm is not a unitary phenomenon. Even within this relatively confined cortical area there exist a variety of rhythms, possibly reflecting activity of different thalamo-cortical loops. As Grey Walter observed on the basis of intracerebral recordings:

> *" ... (occipital-parietal) alpha rhythms are plural and complex in every sense (...) In regions that are practically adjacent and almost congruent one finds a great variety of alpha rhythms, some of which are blocked by opening and closing eyes, some are not, some are driven by flicker, some are not, some respond in some way to mental activity, some do not."* (Grey Walter in Mulholland, 1969, pp. 115).

However, it seems likely that the majority of occipital 10-Hz oscillations originates from the visual cortex, and is closely linked to the visual system. Animal studies have demonstrated an important contribution of the visual cortex to the generation of occipital alpha (cf. the literature review in section 2.3), and human studies that have tried to localize the generators of the occipital alpha rhythm have consistently found at least a subcluster of generators in the visual cortex (e.g. Salenius et al., 1995).

The mu and beta rhythms.

The mu rhythm is a rhythm with a frequency of approximately 7-11 Hz, and is most prominent over the pre-and postcentral areas. A number of early studies (e.g. Jasper and Andrews, 1938; Jasper and Penfield, 1949; Gastaut, 1952; Kuhlman, 1978) already provided evidence that the mu rhythm is generated by neuronal structures in the pre- and postcentral gyri. Furthermore, the mu rhythm is attenuated by passive and self-paced movements (Chatrian, 1959), and during planning or imagining of a self-paced movement (see for example Pfurtscheller and Klimesch, 1991 and Pfurtscheller and Neuper, 1997, respectively). It appears however that the mu rhythm is not a unitary phenomenon. Its arch-like shape indicates that it is built up of a 10-Hz component and a 20-Hz component. Results of recent experiments suggest that there may be a qualitative difference between these two components: source analysis of the 10- and 20-Hz components (Salmelin and Hari, 1994; Salmelin et al., 1995) has demonstrated that the 20-Hz component has generators mainly in the precentral gyrus (and a few in the post-central gyrus as well), while generators of the 10-Hz component are confined to the post-central gyrus. It should be noted that decades ago, Penfield and Jasper (1954), using intraoperative epicortical recordings, have already demonstrated blocking of 20-Hz activity over the precentral hand areas prior to and during voluntary hand movements, a finding that supports the notion that the 20-Hz component of the mu rhythm is a motor rhythm.

One cannot, however, speak of "the" motor rhythm or "the" somatosensory rhythm. A number of studies have demonstrated that the reactivity of the 20-Hz component of the mu rhythm to different types of movement has a somatotopic (or rather a "motorotopic", as Salmelin et al. (1995) termed it) organization, and other studies have demonstrated a somatotopical organization of the 10-Hz component. Salmelin et al. (1995) studied the reactivity of the magnetoencephalographic 10-Hz and 20-Hz components during and following voluntary movements of the fingers, toes and tongue. They found that the sites of maximal suppression and subsequent rebound of the 20-Hz component followed the somatotopic representation of fingers, toes and tongue over the motor cortex, while reactivity of the 10-Hz component did not vary with the type of movement. Similar results have been reported using EEG (Pfurtscheller et al., 1998). On the other hand, subdural EEG recordings have demonstrated that the 10-Hz reactivity also follows a somatotopic organization (Arroyo et al., 1993; Toro et al., 1994). Toro et al. (1994) further reported that the 10-Hz somatotopy was not present in the simultaneously recorded scalp EEG. These data suggest that, as with the occipital alpha rhythms, there exist a number of mu and beta rhythms that may subserve slightly different functions within the somatosensory modality and within the motor system, respectively.

Taken together, the available data suggest that the two frequency components are functionally different, the precentral 20-Hz component being a motor rhythm, and the 10-Hz component being a rhythm that is somatosensory in nature. It should be added that for two reasons it appears unlikely that there is a strict, 100% separation between these two rhythms. First, there is a strong, intrinsic coupling between the motor system and the somatosensory system, as obviated by the simple fact that every movement generates (proprioceptive and reafferent) activity in the somatosensory system. Second, the robust findings on movement-

related ERD (see section 3.3.2) in the 10-Hz range are very difficult to interpret strictly in terms of somatosensory activity.

The tau rhythm.

The existence of the posterior alpha rhythm and the central mu rhythm has been established decades ago, and their discovery has initiated a great deal of research. It is not until recently however, that the existence of still another rhythm has been demonstrated. In 1990, Niedermeyer reported the existence of rhythmical activity originating in the temporal lobe. By means of epidural and intracortical EEG recordings, he was able to demonstrate rhythmic activity around 10 Hz that could not be picked up by simultaneously recorded scalp EEG (Niedermeyer, 1990, 1991). This indicates that normal, scalp-recorded EEG is blind to this kind of rhythmic activity, at least when there are no abnormal holes in the skull overlying the temporal cortex. Niedermeyer termed it the "third rhythm", and showed that it could be functionally differentiated from alpha and mu activity on the basis of the observation that it did neither display any reactivity to opening or closing of the eyes, nor to activity of the somato-motor system.

At about the same time, Tiihonen et al. (1991) reported the existence of a magnetoencephalographic rhythm probably originating from the supratemporal auditory cortex, which was later termed the tau rhythm (Hari, 1993). Again, this rhythm was not affected by clenching the fist, or opening and losing the eyes. Tiihonen et al. (1991) demonstrated that the tau rhythm was most of the time clearly attenuated following auditory stimuli. This, together with the fact that source analyses demonstrated that the sources of the tau rhythm were spatially very similar to the sources of auditory evoked responses, namely in the supratemporal plane, strongly suggests that the tau rhythm is an intrinsic rhythm of the auditory cortex. These results were replicated by Lehtelä et al. (1997). The latter study further indicates that not every subject is 'tau-responsive', since only in 8 out of the 9 subjects studied the tau rhythm was suppressed by the auditory stimuli. The authors suggested that the absolute level (that is, the average amplitude or power) of the tau rhythm may be in part related to the level of vigilance of the subject, higher vigilance leading to less prominent tau. This is supported by data of Lu et al. (1992) suggesting that the tau rhythm is most prominent during drowsiness. The relation with vigilance may partly explain the fact the remarkably large inter-individual differences in tau reactivity that was found in the study of Lehtelä et al. (1997): very low baseline levels might prohibit a further suppression.

It is unclear at present whether the (electric) third rhythm of Niedermeyer and the (magnetic) tau rhythm of Tiihonen et al. (1991) are reflections of one and the same phenomenon, since the electric rhythm is not affected by auditory stimulation (see Hari et al., 1997 and Niedermeyer, 1997, for discussions).

In sum, the available evidence indicates that on the basis of scalp topography and functional reactivity, local 10-Hz rhythms can be identified that are specific to the three main sensory modalities: an alpha rhythm corresponding to the visual modality, a mu rhythm corresponding to the somatosensory modality (and partly to the motor system) and a tau rhythm corresponding to the auditory modality. These findings are important with respect to the question of whether ERD can be used as a tool to investigate a possible modality-specificity in prestimulus cortical activation that may form the basis of anticipatory attention. The existence of local, modality-specific 10-Hz rhythms makes it likely that if such a process exists, ERD may be an adequate tool for demonstrating it.

3.3.2 ERD and movement.

Pre-movement ERD.

The preparation for and execution of a voluntary movement is accompanied by a circumscribed ERD in the 10-Hz (alpha) and 20-Hz (beta) frequency bands, localized close to the sensorimotor areas (e.g. Pfurtscheller and Aranibar, 1979; Pfurtscheller and Berghold, 1989; Derambure et al., 1993; Toro et al., 1993). This desynchronization starts about 2 s prior to movement onset over the contralateral central cortex, and becomes bilaterally symmetrical immediately prior to movement execution. Interestingly, the spatial characteristics of the premovement ERD in the 10-Hz and 20-Hz bands differ in two respects. First, the premovement ERD in the 10-Hz range is relatively independent of movement parameters, such as brisk vs. slow movements (e.g. Stancak and Pfurtscheller, 1995) or moving body part (e.g. finger, thumb or hand, cf. Pfurtscheller et al., 1998). It should be noted however that the premovement ERD in the 10-Hz band preceding foot movements deviates from this general rule. In this case, Pfurtscheller and Neuper (1994) and Pfurtscheller et al. (1997) reported a mu ERD over the frontocentral midline, corresponding to the cortical foot representation area together with a mu ERS over the cortical hand representation area, while the opposite pattern was found preceding hand movements. On the other hand, electrocorticographic recordings have demonstrated that the premovement ERD in the 20-Hz band is more somatotopically specific than that of mu ERD (Crone et al., 1998). Second, a further difference in premovement ERD between the 10-Hz and 20-Hz frequency bands is that the localization of 20-Hz ERD is slightly more anterior than that of 10-Hz ERD. This has been found both in the EEG (Pfurtscheller et al., 1994) and in the MEG (Salmelin et al., 1995). A possible explanation of the spatial differences in premovement ERD in the mu and beta bands has been put forward by Salmelin et al. (1995). These authors suggested that the mu rhythm originates from the primary somatosensory area, while the beta rhythm originates from the primary motor cortex (cf. section 3.3.1).

Post-movement ERS.

Following movement offset one can generally identify an ERS (Pfurtscheller, 1992; Pfurtscheller et al., 1996), which is mostly found in the beta band, where it is most prominent, but which has also been reported in the 10-Hz band (e.g. Pfurtscheller et al., 1996; Bastiaansen et al., 1999a). The induced beta oscillations are found in the first second after movement offset, when the mu rhythm still displays a desynchronized pattern of low amplitude. The low amplitudes of the mu rhythm at this moment in time result in a relatively good signal-to-noise ratio for the beta oscillations. The ERS in the alpha band occurs much later in time: it develops 1 to 2 s post-movement, and may reach its peak even later (e.g. Pfurtscheller et al., 1996). Special care must be taken to identify beta rhythms that are harmonically unrelated to the mu rhythm (see section 3.2.4 on the determination of frequency bands), but bicoherence analysis (cf. Pfurtscheller et al., 1997b) can demonstrate that this is the case.

The post-movement beta ERS is characterized by the following features. (1) It is somatotopically organized, its maximum corresponding to the cortical representation of the moving body part (Salmelin et al., 1995; Neuper and Pfurtscheller, 1996). (2) It is significantly larger following wrist movements as compared to finger movements (Pfurtscheller et al., 1998), and (3) it can be found not only following movements that are actually executed, but also following the imagination of movements, in the absence of EMG activity (Neuper and Pfurtscheller, 1999, Leocani et al., 1999). (4) The frequency band showing the largest post-movement beta ERS is highly subject-specific.

Synchronization in the beta frequency band cannot be straightforwardly interpreted to reflect cortical idling, since it cannot be assumed that beta activity is based on the same neurophysiological generator mechanisms as 10-Hz activity. However, the generally accepted interpretation of postmovement beta ERS as reflecting cortical idling, or de-activation (Pfurtscheller, 1992) has recently found strong support through a study by Chen et al. (1998). These authors investigated the corticospinal excitability related to movement execution by means of transcranial magnetic stimulation of the motor cortex. They found that corticospinal excitability was increased during thumb movement (when an ERD of both alpha and beta bands is usually found), while it was decreased following movement offset, corresponding in time to the occurrence of the postmovement beta ERS.

3.3.3 ERD and attention.

Most of the research on ERD related to the performance of cognitive (in this case, attentional and memory) tasks has been performed by the group of Klimesch and coworkers, although other groups have addressed this issue as well (e.g. Sterman et al., 1996; Dujardin et al., 1999). On the basis of extensive research, Klimesch and coworkers have identified four distinct ERD patterns, respectively in the theta, lower-1 alpha, lower-2 alpha and upper alpha frequency bands (based on their definition of frequency bands as outlined in section 3.2.4; see Klimesch, 1999 for a review). For the present purpose, the results with respect to the relation between ERD in the alpha frequency band and attention are of considerable importance. Basically two studies (Klimesch et al., 1992; Klimesch et al., 1998b) have led these authors to conclude that the lower-1 alpha band reflects alertness, the lower-2 alpha band reflects expectancy, and the upper alpha band reflects sensory-semantic encoding. Below I will describe these studies in some detail.

In the first study (Klimesch et al., 1992), the effects of alertness and expectancy were studied in two fixed frequency bands, 8-10 Hz and 10-12 Hz. Two experiments were performed. In the first experiment, the effects of the alerting properties of a WS was investigated. Subjects were asked to read a series of target stimuli, consisting of words or numbers, presented in different experimental blocks. The words were to be classified in two semantic categories (tools or animals). The numbers were to be classified in two categories, odd or even. A WS preceded the onset of these stimuli at a randomly varying interval of 1, 2 or 3 s. The 8-10 Hz band displayed a shortlasting ERD in response to the WS, which was interpreted to reflect the alerting properties of the WS. The 10-12 Hz band did not react to the WS. Both frequency bands displayed an ERD following the target stimuli. Since the ERD following targets in the 10-12 Hz band was restricted to occipital and parietal areas, this was interpreted to reflect the encoding of the stimulus. With respect to the latter effect, it should be noted however that the target stimuli were preceded by a ERS, that disappeared when the targets were presented (cf. Klimesch et al., 1992 and Figure 3 therein). Since the authors strictly compared the pre- and post-stimulus intervals, they reported a post-stimulus ERD, whereas it can also be argued that the true effect was a prestimulus ERS.

The second experiment of the first study was aimed at separating the effects of alertness and expectancy. Alertness was again assessed by examining the post-WS ERD as a function of WS-target delay. Expectancy was manipulated by creating two experimental conditions. In one condition words and numbers were presented in a blocked design. Since in this condition the subjects knew exactly what the task was (semantic or numerical classification), it was argued that expectancy was high. In the other condition, words and numbers were presented randomly within each experimental block. Since the subjects did not know exactly which task was to be performed on each trial, it was argued that in this condition expectancy would be low. It should be noted that in the experiment, a response was required. (subjects were asked to indicate whether a stimulus belonged to a certain category by saying 'yes' or 'no').

Therefore, anticipatory attention for the target stimulus may be confounded with preparation for the verbal response. In the blocked (i.e., high expectancy) condition, the results were similar to those of experiment 1. In the random condition, the 8-10 Hz band displayed the same effects to the WS as described above; in the 10-12 Hz band however, there were no ERD or ERS effects preceding the targets, while following the targets a large ERD was present. The authors argued that this was due to the fact that the subjects were not able to predict (anticipate) the type of task, and as a result the post-target encoding process was more prominent. Together, these two experiments indicate a dissociation between the lower (8-10) and upper (10-12) alpha frequency bands, where the lower frequency band mainly reflects the alerting properties of the WS while the upper band reflects the encoding of task-specific stimuli. Importantly, the anticipation of the targets did not yield consistent ERD or ERS effects. However, in another report of the same experiment (Pfurtscheller and Klimesch, 1991), the authors were able to demonstrate an ERD in the 8-10 Hz band preceding the target stimuli, which was maximal over occipital leads. The fact that a verbal response was required however hampers a clear interpretation of this effect in terms of anticipatory attention for the target stimulus. In sum, the evidence from these experiments with respect to the existence of an ERD related to the anticipation of the stimuli are inconclusive.

In another study, a modified visual oddball task, Klimesch et al. (1998b) studied the ERD in the lower-1 and the lower-2 alpha bands (based on their definition of frequency bands, cf. section 3.2.4). They presented a Warning Signal (WS) to their subjects, which was followed by a second stimulus that could be either a (infrequent) target or a (frequent) non-target. Subjects were asked to ignore the non-target; the target served as an imperative stimulus, that was to be counted and to be followed by a response. Because of a regularity in the sequence of targets and non-targets, subjects were approximately able to predict the occurrence of targets. The WS elicited a short-lasting, phasic ERD in the lower-1 alpha band, that was larger for a WS that could be expected to be followed by a target. This effect was interpreted to reflect the alerting properties of the WS (since the alerting effects are considered to be larger if the WS is followed by a target). Most interestingly for our purposes however, prior to the presentation of the second stimulus a widespread ERD in the lower-2 alpha band was found that started as early as 1000 ms prestimulus, irrespective of whether the upcoming stimulus was a target or non-target. This effect was interpreted to reflect the expectancy for the upcoming stimulus. It should be noted however, that targets had to be followed by a response. Since preparing for a response also elicits ERD in the alpha frequency range (cf. section 3.3.2), it is unclear whether the alpha ERD was produced by motor preparatory processes or by anticipatory attention for the upcoming stimulus. Therefore the results of this study are considered to be equivocal with respect to whether anticipatory attention is accompanied by 10-Hz ERD.

Finally, one study should be mentioned in which evidence for the notion that anticipatory behavior may be reflected by an ERD response is more clear. Pfurtscheller (1992, his fig. 3) discusses an experiment in which subjects had to perform a reading task. Starting from 1 s pre-stimulus, ERD in the 10-11 Hz band was present at occipital electrode positions, while at central locations an ERS was measured. This is in line with the above-mentioned report of Pfurtscheller and Klimesch (1991).

In sum, two studies (i.e. Pfurtscheller and Klimesch, 1991, and Pfurtscheller, 1992) suggest that ERD may be present during anticipatory attention for an upcoming (visual) stimulus, although the results are far from being clear. Finally, two things should be noted with respect to these studies. First, and most importantly, in both experiments the anticipated stimuli were presented in the visual modality, and the ERD was maximal over the occipital areas. Second, the studies differ with respect to the frequency band used: 8-10 Hz in Pfurtscheller and Klimesch (1991), and 10-11 Hz in Pfurtscheller (1992).

Chapter 4: Anticipatory behavior: neurophysiological models and experimental data.

In the past decades basically two models have been proposed that provide an account of the neurophysiological basis of anticipatory behavior (and thus for anticipatory attention as well, since the latter is only a component of the former, as I outlined in chapter 1). Given that these models have played an important role in the generation of the central hypothesis of this thesis, I argued that a description of the different models is indispensable in the theoretical part of this thesis. Therefore, in the present chapter I will shortly describe these models (section 4.1). Next, I will consider three neurophysiological measures that appear to be suited to study anticipatory attention, and I will briefly review the literature that has addressed this issue (section 4.2).

4.1 Neurophysiological models of anticipatory behavior.

4.1.1 A thalamo-cortical gating model.

In the late seventies, Skinner and Yingling (1976, 1977; Yingling and Skinner, 1977) have presented a thalamo-cortical gating model describing the neurophysiological basis of intermodal selective attention. This represented an important attempt to explain how a between-modality choice might be brought about. The model concerns the role of attention in selecting one of the three main sensory modalities: auditory, visual and somatosensory. Skinner and Yingling formulated their model on the basis of a large number of experiments, in which rhythmic brain activity, slow potential shifts and evoked potentials were studied under different conditions in the cat. By stimulating, or applying functional lesions (through reversible cryogenic blockade) to the thalamus, reticular thalamic nucleus, frontal cortex or reticular formation, they were able to demonstrate a functional interplay between those structures. Goldberg (1985) and Brunia (1993, 1999) have extended the gating model proposed by Skinner and Yingling to the realm of anticipatory behavior, including both anticipatory attention for upcoming stimuli and motor preparation. In the following paragraphs I will briefly outline this extended model; for detailed descriptions, see Brunia (1993, 1999).

Stimuli of different modalities activate the appropriate sense organs and cause a stream of information ascending to the relevant brain areas. Although the sense organs differ in the way they process the information impinging upon their sensitive surface, there is a structural similarity between the different sensory systems as far as further processing is concerned. Each modality has its own primary projection area in the posterior cortex cerebri. To reach that area a final interruption of the sensory pathways takes place in the thalamus. Each of the sensory systems has a private first order thalamo-cortical relay (TCR) nucleus, from where the primary sensory projection area is reached (note that TCR nuclei do not serve as mere passive relay stations, but additionally serve the goal of the enhancement of the signal relative to the noise, as has been elegantly demonstrated by LaBerge et al., 1992). Just like the sensory areas, the different motor areas in the frontal cortex, the primary motor cortex, the pre-motor cortex and the supplementary motor area (SMA), have their own thalamic input (e.g. Guillery et al., 1998). This input stems from subcortical motor structures such as the cerebellum or basal ganglia, which just like the sensory afferents, transmit information to the cortex via specific motor TCR nuclei. Given that both sensory and motor cortical areas have a

comparable (i.e., thalamic) input, it is probable that there is a commonality in the control of this input as well.
For information to be transmitted to the primary projection cortex, TCR cells have to fire. As noted in chapter 2, the discharge of TCR cells takes place in two different modes: in a tonic mode, triggered by a depolarization of TCR cells, or in a burst mode, triggered by a hyperpolarization of TCR cells. In tonic mode information can pass to the cortex, in burst mode the information processing is blocked (cf. Steriade et al., 1990; Lopes da Silva, 1991; see chapter 2 for a discussion). The lateral aspect of the thalamus is covered by a thin sheet of GABA-ergic nuclei known as the reticular nucleus (RN). Neurons in the RN have a local inhibitory influence upon cells in the underlying TCR nuclei. That is, a given sector of the RN exclusively sends (inhibitory) projections to the underlying TCR nucleus. Therefore the RN plays a pivotal role in the switch between the two modes, burst or tonic. In terms of the model of Skinner and Yingling (1977), facilitation of the RN neurons leads to burst mode discharges, and closing of the gate. Disfacilitation or inhibition of RN neurons cells leads to tonic mode discharges and opening of the gate. In other words the transmission of information to the cortex, whether directed at sensory or motor areas, can be modulated by input to the RN.

Selectivity through the influence of the prefrontal cortex.

Skinner and Yingling (1977) suggested that the RN neurons have a dual input, both from the prefrontal cortex and from the brain stem. The former is thought to be selectively aimed at specific sectors of the RN, whereas the latter provides a more diffuse innervation. Skinner and Yingling (1977) suggested that this difference in innervation pattern is the basis for two different functions, realized via the RN neurons: arousal and selective attention (or, in the extension of the model by Brunia (1993, 1999), anticipatory behavior). Each TCR nucleus can be inhibited by a specific sector of the RN neurons (Guillery et al., 1998), if the latter receives excitatory input from the prefrontal cortex. On the other hand, given that the inhibitory RN neurons are aselectively inhibited by fibers from the brain stem reticular formation (RF), the resulting disinhibition will lead to an aspecific activation of the TCR nuclei. Thus, at the level of the TCR nuclei there is a balance between activation from the RF and inhibition from the prefrontal cortex. If there is an increase in activity from the RF, that balance will shift towards a predominance of activation in all TCR nuclei, leading to a generalized arousal. On the other hand, selection between one of the sensory modalities or the motor system can be realized by a selective lack of activation, from the prefrontal cortex, of a sector of the RN that overlies the TCR nucleus corresponding to the attended channel (Skinner and Yingling, 1977; Brunia, 1997). This lack of activation of that particular RN sector will lead to a less pronounced inhibition of the underlying TCR. This will result in a shift in the balance of activating and inhibiting inputs to that particular TCR nucleus towards a predominance of activating input. The TCR cells in that nucleus will be depolarized, and shift from burst mode to tonic mode, resulting in an open gate for the attended sensory modality (for anticipatory attention) or the motor system (for motor preparation). The result of this open gate would be that the corresponding cortical projection area becomes activated; more specifically, the apical dendrites of pyramidal neurons would be dominated by EPSPs causing a subthreshold depolarization of the cell membranes, and by consequence leading to an increased excitability of the cortical area corresponding to the attended channel. This mechanism would serve the role of preparing the relevant brain structures to do in advance what can be done, and/or reduce the threshold levels of the relevant brain structures in order to ensure a faster processing. This may form the neurophysiological basis for anticipatory behavior.

Selectivity through lateral inhibition in the reticular nucleus.

Some authors have suggested that selectivity may be brought about at the level of the RN nucleus itself rather than through the influence of the frontal cortex on this structure (Scherman and Koch, 1986; LaBerge and Brown, 1989; LaBerge et al., 1992; Suffczynski et al., 1999). In this view, the RN nucleus, by virtue of its lateral inhibitory properties, may introduce selectivity in anticipatory behavior. Evidence for this notion stems from two studies (LaBerge et al., 1992; Suffczynski et al., 1999) in which neural networks have been used to simulate a focal enhancement of target activity (in the case of anticipatory behavior this would be the anticipated stimulus or movement) relative to surrounding activity (e.g. other possibly occurring future stimuli or other possible future movements). Although the neural network models differed considerably, the model of Suffczynski et al. being physiologically plausible while that of LaBerge et al. used abstract units and abstract amounts of activation, the models yielded similar results with respect to the possibility of obtaining an enhancement of the target relative to surrounding distractors at the level of the RN nucleus. In the model of Suffczynski et al. (1999), this relative enhancement was be obtained by modeling the lateral inhibitory properties of the RN cells; in the model of LaBerge et al. (1992) it was produced by a combination of corticothalamic feedback, and by the mutually inhibitory influences of RN cells. In sum, although these simulation studies demonstrate that in principle, by virtue of the lateral inhibitory properties of the RN the RN-TCR circuitry has the potential for bringing selectivity into anticipatory behavior, there is as yet no direct neurophysiological or psychophysiological evidence for this claim.

Incidentally it should be added here that the neural network model of LaBerge et al. (1992) has been developed in the context of a neurophysiological model describing attentional processing mainly in the visual system. LaBerge (1995) describes a triangular model in which three components of attention are distinguished: the expression of attention, the control of attention, and a mechanism responsible for the enhancement of target activity (that is, the stimulus or action towards which attention is being directed) and/or suppression of non-target activity. Attention in the view of LaBerge is realized at the neurophysiological level by the simultaneous activation of three structures, which are connected by a triangular circuit. The three structures correspond to the three aspects of attention: the expression of attention is realized by clusters of neurons in the posterior and anterior cortex that serve cognitive functions, such as perceptions of objects and attributes, or the planning and organizing of actions; the control of attention is realized by clusters of neurons in the dorsolateral and ventrolateral frontal cortex; the enhancement of target input is realized by the thalamic and RN nuclei. The suppression of irrelevant information is thought to be realized through burst mode firing in the RN-TCR circuits not involved in the task, while the relevant information is enhanced through tonic mode firing and the lateral inhibitory properties of the RN. Thus, in the main the thalamic mechanism proposed by LaBerge is similar to that proposed in the previous paragraphs.

4.1.2 A threshold regulation model.

Elbert, Rockstroh and colleagues have proposed a model that describes a control system that regulates the amount of activity in the neocortex. This model has been termed the threshold regulation model (e.g. Elbert and Rockstroh, 1987; Rockstroh et al., 1989; Birbaumer et al., 1990; Elbert, 1993). It gives an account of a possible neurophysiological basis for anticipatory attention that is based on the occurrence of slow cortical potential (SCP) shifts. Although there are important similarities between the thalamo-cortical gating model described in the previous paragraphs and the threshold regulation model, the latter model diverges in some crucial aspects from the former. Below I will shortly describe the threshold

regulation model, and I will describe how this model may provide a neurophysiological basis of anticipatory behavior.

Surface negativity reflects cortical excitability.

Most of the scalp-recorded EEG is constituted of a summation of excitatory and inhibitory post-synaptic potentials (EPSPs and IPSPs, respectively) at the apical dendrites of pyramidal neurons (see for example Elbert, 1993 for a discussion). EPSPs lead to a depolarization of the dendrites, thereby increasing the excitability of the cell without directly causing it to fire. Whether or not a cell will actually fire is determined by the potential at the axon hillock, which typically must be depolarized beyond 50 mV in order to trigger an action potential. Such a depolarization is realized only when sufficient EPSPs arrive at the dendrites of the cell. Subthreshold depolarization of the apical dendrites of pyramidal cells causes an efflux of negative charges into extracellular space, which re-enter the neuron in deeper cortical layers (e.g. Birbaumer et al., 1990). This current flow results in a polarization of the cortex, with the negative poles near the surface. In other words, an increase in the excitability of pyramidal cells leads to a negative SCP shift, which can be recorded macroscopically with scalp electrodes. The opposite holds as well: if there is a predominance of IPSPs at the apical dendrites of pyramidal cells, the excitability of the latter will be reduced, and this will be accompanied by positive SCP shifts.

It has been proposed that negative SCPs reflect the availability and spatial allocation of resources for information processing in the cortical areas needed for performing the task at hand (e.g. Elbert and Rockstroh, 1987; Rockstroh et al., 1989; Birbaumer et al., 1990; Elbert, 1993) Evidence for this notion (reviewed e.g. by Elbert, 1993) stems, amongst others, from the relation between performance and SCP shifts. Stamm (1984) and Bauer (1984) have used a potential-related event (PRE) paradigm, in which subjects performed various tasks after they had learned to influence their SCPs systematically. It was found that task performance was better when a large negativity was present in cortical areas related to task processing, while subjects' performance was poorer if negativity was smaller or absent in those areas.

Feedback control of cortical excitability.

Pyramidal cells constitute 85% of all cortical neurons (Schüz and Palm, 1989). The connections between pyramidal cells are excitatory, and make up 70% of all cortical synapses (Schüz, 1990). This implies that there is a danger, intrinsic to such interconnected networks, that they become activated beyond control. If the number of activated cortical networks reaches a certain critical mass, the probability is high that the remaining ones become activated as well. This is exemplified for instance by SCP recordings in epileptic patients, which have shown the existence of extreme negative shifts preceding epileptic seizures (Rockstroh, 1993). Clearly, to prevent an ever-increasing activation of the cortex, a control mechanism must exist which regulates cortical excitability.

It has been hypothesized that such a threshold regulation mechanism is achieved by a feedback loop that runs from the cortex, through the basal ganglia, the thalamus and/or the reticular formation, back to the cortex, although clear evidence for this point of view is lacking (Elbert and Rockstroh, 1987; Rockstroh et al., 1989; Birbaumer et al., 1990; Elbert, 1993). The striatum, consisting of the caudate nucleus and the putamen, is a massive lateral inhibition system that receives input from virtually all cortical regions. The striatum sends its inhibitory efferents to the globus pallidus. From the pallidum inhibitory information is fed into the thalamus (see Alexander and Crutcher, 1990 for details). The non-specific (i.e. intralaminar and midline) thalamic nuclei project to the apical dendrites of pyramidal neurons in the entire neocortex, and thus are able to modulate cortical excitability on a large-scale basis. If cortical activation increases to excessive levels, the mechanism will work in the

opposite direction, raising the thresholds for pyramidal cells to fire, and as a consequence reducing cortical activity. It should be noted however that recently the non-specificity of the midline and intralaminar thalamic nuclei has been questioned (cf. Groenewegen and Berendse, 1994, for a review). Recent anatomical evidence suggests that different midline and intralaminar thalamic nuclei project preferentially to different parts of the cortex. Therefore these authors proposed that the major role of the midline-intralaminar nuclei lies in the regulation of the activity of individual, functionally segregated basal ganglia-thalamocortical systems. However, the authors also acknowledge that the midline-intralaminar thalamic complex may have a global function in the operation of the basal ganglia-thalamocortical system. In their view, concerted action, initiated by diffuse inputs from the brain stem reticular formation, might bring the entire basal ganglia-thalamocortical system to a higher level activation.

Threshold regulation and anticipatory behavior.

The feedback loop described above counteracts over-or underactivation of the cortex when it occurs. However, if we assume that the brain has the ability to adjust thresholds in advance, this threshold regulation mechanism could be considered to have the purpose of directing attention to future events. By increasing negativity over cortical areas that will be needed in the near future for the execution of a task, or the processing of a stimulus, the processing of the anticipated event will be improved once it occurs. In this way the threshold regulation model may be considered as a model for anticipatory behavior. Evidence for this notion stems from the negativities that can be recorded prior to the execution of movements and prior to the presentation of task-relevant stimuli (e.g. Brunia, 1988). These will be discussed in more detail in section 4.2.1.

4.1.3 Relationship between the models.

At first sight, the thalamocortical gating model and the threshold regulation model appear to make entirely different claims about the regulation of anticipatory behavior. However, upon further consideration there is no a priori reason to exclude the possibility that both mechanisms coexist. Elbert, Rockstroh and colleagues acknowledge that, next to the threshold regulation mechanism, the mechanisms involving the frontal cortex and reticular formation, which interact at the level of the thalamus and reticular thalamic nucleus as described by the thalamo-cortical gating model, probably play an important role in the regulation of anticipatory behavior as well. Inversely, Goldberg (1985, pp. 587) describes 'a process whereby cortical activation becomes focused on executive regions through dynamic operation of a widely distributed system'. In his view, this system includes a thalamocortical gating mechanism, as well as a basal ganglia dependent loop that gathers convergent input from wide regions of the cortex and then focuses its output back to the cortex via thalamic connections from the globus pallidus. Thus, the different authors seem to agree that both mechanisms may play a role in directing attention at a future event, and that both mechanisms lead to a subthreshold activation (or, in other words, an increased excitability) of cortical areas.

There is however one fundamental difference between these models. In the thalamic gating model the modulation of cortical excitability is realized through the influence of the RN nucleus on the *specific* thalamic nuclei; this should lead to *local* changes in cortical excitability. Exactly this specificity is lacking in the threshold regulation model. Here the modulation of cortical excitability is thought to be realized through *non-specific* thalamic nuclei (the midline intralaminar and paraventricular nuclei, cf. Birbaumer et al., 1990), which receive abundant cortical input and project to widespread areas of the cortex. Obviously this should then lead to *global* changes in cortical excitability. Note that recent neuroanatomical

evidence, as discussed in section 4.1.2, opens the possibility that to some extent selectivity is retained in the 'non-specific' midline-intralaminar thalamic nuclei (Groenewegen and Berendse, 1994). One possibility to integrate the two models, although somewhat speculative, would be to argue that threshold regulation serves the role of maintaining a balance in the overall level of cortical activity, which can aspecifically be increased or decreased depending upon (future) behavioral or environmental demands, while thalamocortical gating serves to introduce (anticipatory) selectivity in the cortical activation.

4.2 Indices of anticipatory behavior in the central nervous system.

In Chapter 1 I pointed out that the central question of this thesis is whether anticipatory attention for an upcoming stimulus in one of the main sensory modalities is realized at the neurophysiological level as a prestimulus activation of the relevant cortical area, that serves the goal of facilitating the processing of the upcoming stimulus. The majority of the experimental work that has been done in the study of anticipatory behavior is based on EEG and MEG measures, which mainly measure cerebral activity originating from the cortex. However, an important role in the regulation of anticipatory behavior is generally attributed to subcortical structures, as we have seen in section 4.1. Subcortical structures contribute only very weakly to the scalp-recorded EEG/MEG. Therefore most of the experimental data described in this section do not allow for any statements about the neural dynamics that bring about this cortical activity. However, as noted in Chapter 1, although EEG/MEG measures cannot provide any *direct* evidence in favor of either one of the neurophysiological models, data thus obtained can be considered in the light of these models, and may or may not be *in line with*, and thereby providing at least *indirect support* for, one model or another
Skinner and Yingling (1977) reasoned on the basis of their experiments that, if attention was directed at a particular sensory modality, this should lead to an opening of the thalamic gate corresponding to that modality. The result of this open gate would be that the corresponding cortical projection area becomes activated; more specifically, the apical dendrites of pyramidal neurons would be dominated by EPSPs causing a subthreshold depolarization, and by consequence leading to an increased excitability of the cortical area corresponding to the attended channel. In the scalp-recorded EEG this might be reflected in three ways: first, activation should be accompanied by a negative slow potential; second, amplitudes of evoked potentials elicited by sensory stimulation should be enhanced due to the larger excitability of the cortical projection area; third, the EEG over the relevant cortical area should be desynchronized. It is important to note that the former two hypotheses also follow from the threshold regulation model (e.g. Rockstroh et al., 1989). In the remainder of this chapter I will briefly review the existing evidence for the three hypotheses.

4.2.1 Slow potentials.

Readiness Potential.

Self-paced voluntary movements are preceded by a Readiness Potential (RP, Kornhuber and Deecke, 1965), a negative slow potential that develops as early as 1500 ms prior to movement execution. The early part of the RP starts as a bilaterally symmetrical slow wave with a maximum over the motor cortex, and becomes asymmetrical from 500 ms prior to movement onset, where it is larger over the hemisphere contralateral to the motor cortex. However, preceding foot movements the RP is larger over the ipsilateral motor cortex (Brunia, 1980; Brunia and Vingerhoets, 1981), which suggests that its maximum roughly corresponds to the cortical representation of the moving body part. Several components can be distinguished in the RP. The early, symmetrical part has been termed the BPsym; the contralaterally dominant part is usually termed Negative Shift, or NS'. In the last 100 ms

prior to movement onset, a short positive-going component can be identified, which is usually termed the pre-motion positivity. Finally, just prior to movement onset a sharp negative deflection can be identified which has been termed the Motor Potential, which is thought to reflect the activation of the pyramidal tract, i.e. the 'command to move'. It should be noted that different authors have been using different terminology to designate the separate components; a summary of the terminology used has been provided by Brunia (1987) and, more recently by Brunia and Van Boxtel (2000).

It is generally agreed that the RP reflects motor preparation. Evidence for this point of view stems, amongst others, from the following observations. (1) It precedes the movement. (2) Its scalp distribution of influenced by movement parameters, such as movement side, moving body part (e.g. Brunia and Vingerhoets, 1981), movement complexity (e.g. Lang et al., 1989) and number of fingers involved (Kitamura et al., 1993). (3) Source localization studies have consistently demonstrated that the most prominent neural generators of the RP are situated in the primary motor cortex (e.g. Bötzel et al., 1993; Toro et al., 1993; Böcker et al., 1994a, b). In sum, the existence of a negative slow potential that is maximal over the motor cortex prior to the execution of self-paced movements is in line with the hypotheses both of the thalamo-cortical gating model and of the threshold regulation model.

Contingent Negative Variation.

A negative slow potential shift has been recorded for the first time by Walter et al. (1964). They presented an auditory Warning Stimulus (WS) to their subjects, followed 1 second later by a Response Stimulus (RS), a series of flashes that were to be interrupted by a button press. During the foreperiod, that is, in the interval between WS and RS, they recorded a slow negative potential that was maximal at the vertex. This was termed the Contingent Negative Variation (CNV). Loveless and Sanford (1974) extended the foreperiod to 4 s, and showed that the CNV consists of two distinct waves, an early wave and a slow wave. The early wave, which immediately follows the WS, has a frontal maximum, and is generally interpreted to reflect the alerting properties of the WS. The interpretation of the CNV late wave, however, has been a matter of debate. Initially, the CNV late wave was interpreted in terms of expectancy (e.g. Loveless and Sanford, 1974), a concept that is closely related to anticipatory attention. Later it has been argued that the late wave exclusively reflects motor preparation, and can thus be equated to the RP (e.g. Rohrbaugh and Gaillard, 1983). Arguments in favor of such an interpretation are, amongst others, that the topography of both slow waves is highly comparable, and that the CNV late wave, just as the RP, is strongly influenced by movement parameters: shorter RTs are preceded by larger CNVs (e.g. Brunia, 1980, Böcker et al., 1989), and the paradoxical lateralization of the RP preceding foot movements reported by Brunia and Vingerhoets (1981) is also present in the CNV late wave (e.g. Böcker et al., 1994c).

However, others have proposed that the CNV late wave reflects both motor preparation and anticipatory attention for the RS (see Brunia, 1988; Brunia and Van Boxtel, 2000, for reviews). Arguments for this point of view are, amongst others, the fact that the CNV late wave is usually larger than the RP (e.g. Brunia and Vingerhoets, 1981; Van Boxtel and Brunia, 1994), suggesting the presence of additional negativity that is not caused by the anticipation of the response. This is supported by a study of Ikeda et al. (1994), who did not record any RP in a patient with a cerebellar lesion, while a frontal negativity could be recorded in a CNV paradigm. In addition, slow negative potentials can be recorded prior to certain types of stimulus, even when no motor response is required (see next section). In sum, although it is clear that the CNV late wave largely reflects motor preparation, there are indications that it includes a negative slow potential that might be related to the anticipation of the RS stimulus.

Stimulus-Preceding Negativity.

A disadvantage of the CNV paradigm is that two processes are simultaneously active during the foreperiod: the preparation for the movement and the anticipation of the RS. In order to solve this problem, Damen and Brunia (1987a, b) used an experimental paradigm that allows for a temporal separation of both processes. In this paradigm, which is essentially a time estimation task, subjects are asked to perform voluntary movements at intervals of 20 to 22 seconds. After each movement a stimulus was presented providing Knowledge of Results (KR) about the correctness of their timing. A similar task had been used previously by Lacey and Lacey (1973), who found a heart rate deceleration not only preceding the movement, but also preceding the KR stimulus. The latter was interpreted to reflect attention. Damen and Brunia (1987b) recorded both slow potentials and heart rate in the time estimation paradigm, and replicated the results of Lacey and Lacey with respect to cardiac deceleration. In the EEG, they found the expected RP with a contralateral maximum preceding the voluntary movement. In addition however, preceding the KR stimulus they found a negative slow potential with a right-hemispheric dominance and a scalp distribution that was different from that of the RP. This slow potential was labeled Stimulus-Preceding Negativity (SPN). Brunia and Damen (1988) further examined the morphology and scalp distribution of the SPN. Damen and Brunia (1994) found that the SPN had a frontal plateau and a parietal ramp-like potential. After subtraction of the post-movement potentials recorded in a separate voluntary movement condition, they found that the right-hemisphere dominance was preserved irrespective of response side. This demonstrated that the SPN is not movement-related. Subsequent research was aimed at clarifying the functional significance and neuroanatomical substrates of the SPN. Since detailed reviews have been presented elsewhere (e.g. Van Boxtel, 1994; Böcker and Van Boxtel, 1997), I will discuss only the main results of these studies here. It should be noted beforehand that if the SPN is a purely perceptual anticipatory process such as described by the neurophysiological models presented earlier in this chapter, one would expect the SPN (1) to be independent of the type of information conveyed by the anticipated stimulus, and (2) to be maximal over the sensory cortex corresponding to the modality of the stimulus.

Ad (1). The SPN has been found prior to three types of stimuli. (1) KR stimuli (e.g. Grünewald et al., 1984; Damen and Brunia, 1987a, 1987b; Brunia and Damen, 1988; Chwilla and Brunia, 1991a; Damen and Brunia, 1994; Böcker et al., 1994c). In this case, the SPN usually has a parietal maximum and a right-hemispheric preponderance. (2) Instruction stimuli, transmitting information about a future task (e.g. Gaillard and Van Beijsterveld, 1991; Rösler, 1991; Damen and Brunia, 1994; Van Boxtel, 1994; Van Boxtel and Brunia, 1994). In this case the SPN has a parietal maximum, is bilaterally symmetrical, and is much smaller than the pre-KR SPN. (3) Probe stimuli, with which the outcome of a previous task has to be matched (e.g. Ruchkin et al., 1988; Chwilla and Brunia, 1991b, 1992). In this case the SPN again has a parietal maximum, but a left-hemispheric dominance is found. In sum, the amplitude and lateralization of the SPN vary with the type of stimulus that is anticipated.

Ad (2). The SPN has been recorded prior to auditory and visual stimuli. However, only two studies have directly compared its scalp distribution as a function of stimulus modality in a within-subjects design. The first study, by Grünewald et al. (1984), reported no differences in SPN scalp topography between auditory and visual stimuli; however, in this study, which mainly addressed the right-hemispheric dominance of the SPN, only two precentral and two parietal electrodes have been used. Since modality-specific differences would be expected to occur mainly over temporal and occipital areas, this severely limits the value of the results as far as scalp topography is concerned. The second study, by Böcker et al. (1994c) used a larger set of electrodes (that is, 23) approximately equally distributed over the entire scalp. Although the SPN was larger preceding auditory stimuli, there was a striking similarity in

scalp topography of the SPN for the two modalities: both had a frontotemporal maximum. However, recent results from our laboratory show small but significant differences in SPN scalp topography preceding auditory and visual KR stimuli (Brunia, personal communication). In sum, although a small part of the SPN might be related to perceptual processes, the results do not support the hypothesis that the SPN is maximal over the sensory cortex corresponding to the modality of the anticipated stimulus.

The available experimental evidence does not support the notion that the SPN primarily reflects perceptual anticipatory attention for an upcoming stimulus. This leaves the question of what kind of process is reflected by the SPN. Since the SPN differs with the type of stimulus anticipated, it appears reasonable to hypothesize that the SPN at least partially reflects the presetting of cortical areas specifically related to the execution of the task at hand rather than the presetting of the sensory cortex. Therefore, the notion of the SPN as a unitary phenomenon should be abandoned. If we consider the types of stimuli that evoke an SPN, two of the three stimulus types (KR stimuli and probe stimuli) evaluate the past performance of the subject. Therefore, it could be argued that these two instances of 'the' SPN reflect the anticipation of affective-motivational stimuli. Support for this interpretation comes from three studies. First, Kotani et al. (in preparation) performed an EEG study using the time estimation + KR paradigm, in which they manipulated the motivational and the affective value of the KR stimulus independently. Motivation was manipulated by introducing monetary awards for each correctly timed movement in one condition, while affect was manipulated by presenting the KR as pure tones vs. aversive noise. Higher motivation led to larger SPN amplitudes, while the affective manipulation did not influence the SPN amplitude. Second, Böcker et al. (1994c) have constructed a spatiotemporal dipole model of the pre-KR SPN. In this model, a large part of the pre-KR SPN could be explained by a bilateral pair of frontotemporal dipoles that probably represent activity of the Insulae Reili. This is a bilateral cortical structure buried within the Sylvian fissure, which is assumed to be involved in the affective-motivational coloring of stimuli (Mesulam and Mufson, 1985). Third, Brunia et al. (2000) performed a PET study, using the time estimation + KR paradigm. They compared conditions with false KR to conditions with true KR (note that the subjects were informed about the status of the KR stimuli beforehand). Next to a prefrontal and posterior parietal activation, these authors also found activation of the posterior part of the Insulae Reili, therewith confirming the results of the dipole modeling study of Böcker et al. (1994c). Together, these three studies suggest that the SPN preceding stimuli that evaluate past performance (such as KR stimuli, or probe stimuli with which the outcome of a previous task has to be matched) reflects the anticipation of the affective-motivational aspects of the stimulus rather than perceptual anticipatory attention.

The third type of stimulus that evokes an SPN is an instruction stimulus. Van Boxtel (1994) has performed a series of experiments in which instruction stimuli were used that differed in the amount of information conveyed by the stimulus and/or the time at which information was delivered with respect to the subsequent motor task. Depending on the exact type of instruction stimulus, he found two different instances of an SPN. The first, which preceded stimuli containing an instruction about the subsequent response, was interpreted to reflect the anticipation of task-relevant sensory input, and displayed a parietal maximum. A second, which preceded a similar stimulus that was closer in time to the subsequent response, was interpreted to reflect control of task performance, and displayed a frontal maximum. Together, these experiments suggest that the scalp distribution and functional significance of the SPN are strongly task-specific.

In conclusion, it appears that as far as anticipatory behavior in the motor domain (that is, motor preparation) is concerned, the available evidence supports the existence of slow negative potential shifts with a maximum over the motor areas preceding the execution of

movements, which was predicted both from the thalamocortical gating model and the threshold regulation model. However, research into anticipatory behavior in the sensory domain (that is, anticipatory attention) has not yielded evidence for the hypothesis that anticipating an upcoming stimulus is accompanied by a negative slow potential shift that is restricted to, or maximal over, the sensory cortex corresponding to the modality of that stimulus.

4.2.2 Probes.

Presenting a standard stimulus in a certain sensory modality to a subject while he is not especially expecting it will produce an evoked potential (EP) of a certain amplitude. If however the subject is anticipating the stimulus, an open thalamic gate, or lower firing thresholds will lead to an increased cortical excitability. As a result, one would expect the same standard stimulus to produce an EP with higher amplitudes over the sensory cortex corresponding to the modality of the stimulus when this stimulus is anticipated.

Three studies have addressed the modulation of probe-evoked EPs during the foreperiod of a CNV paradigm. In the study of Rockstroh et al. (1993), WS was the onset of a visual stimulus, RS the offset of the same stimulus. Probes were presented in the auditory modality, at different times in the foreperiod, during the baseline period prior to WS, or following the RS, and required a response. RTs to probes presented in the foreperiod were shorter than RTs to probes presented outside the foreperiod. EPs to probes in the foreperiod were larger than those to probes presented during baseline, and gradually increased as the probe was presented later in the foreperiod (thus, EPs increased with increasing scalp negativity). Böcker et al. (1993) applied somatosensory probes in a CNV paradigm in which the WS was auditory and the RS visual. EPs elicited by probes presented at the end of the foreperiod were compared to EPs elicited by probes presented in the intertrial interval (ITI). These authors found that, although SEP amplitudes were modulated during the foreperiod, some components (P45/N70 and N70/P100) showed the expected decrease, while another component (P100/N140) showed an increase. Bastiaansen (1995), in collaboration with Indra, has applied auditory and visual probes in a CNV paradigm in which the RS was either visual or auditory. The crucial comparisons in this study were between EPs elicited by probes of the same or different modality of that of the RS (the experimental conditions), vs. EPs elicited by probes in the ITI (the control condition). The N1 of auditory probes was larger than control when they were followed by an auditory RS, while the P2 was smaller than control when probe and RS were of a different modality. In contrast, The P1 elicited by visual probes was larger than control regardless of RS modality, while the P2 was smaller than control when probe and RS modality differed.

In sum, although most EP components are modulated in the foreperiod of a warned RT task, the direction of the effects, both within and between studies, is rather inconsistent. The notion of an increase of EP components as a result of an open thalamic gate (in which case the increase should be restricted to the cortical area corresponding to the modality of the anticipated stimulus) or of lower firing thresholds (in which case the increase should be present over the entire cortex, regardless of stimulus modality) is not supported by the experimental findings.

4.2.3 Event-related desynchronization.

In chapter 3 I have argued that event-related desynchronization (ERD) most probably reflects cortical activity. If cortical activity preceding the presentation of an (anticipated) stimulus reflects anticipatory attention, one would expect a prestimulus ERD that is restricted to the cortical area corresponding to the modality of the stimulus. In section 3.3.3, I have discussed the results of three studies that have more or less incidentally addressed this question. These

studies addressed only the anticipation of visual stimuli, and their results are inconsistent with respect to time course and topographical distribution of the ERD. Systematic research into the relationship between ERD and anticipatory attention, in which stimulus modality is carefully manipulated has not been performed. The experimental part of the present thesis aims at filling this gap; therefore a discussion of the anticipatory ERD is postponed to the concluding chapter of this thesis.

Chapter 5: General methodology and research questions.

In the previous chapters a theoretical framework has been outlined that describes the neural basis and functional significance of rhythmic EEG/MEG activity. In Chapter 2 I have reviewed the evidence for a thalamic genesis of 10-Hz rhythmic EEG/MEG activity, in Chapter 3 it was described that modulations in 10-Hz rhythmic activity have functional significance. The available evidence strongly suggests that suppression of 10-Hz activity reflects increased cortical activity, and may be used in the study of a broad range of psychophysiological phenomena. Next, I have described basically two models that provide an account of the neurophysiological basis of anticipatory behavior. Thus, in chapters 2-4 I have tried to set the stage for an experimental investigation into the processes which are active at the neurophysiological level when one engages in anticipatory attention for an upcoming stimulus. The present chapter first aims at integrating the foregoing (section 5.1). In section 5.2 I will account for the general research methods that I will use to investigate the aforementioned processes. Finally, in section 5.3 specific hypotheses are formulated that allow for an experimental evaluation.

5.1 Using ERD to study anticipatory behavior.

For several reasons it can be argued that analyzing the reactivity of 10-Hz rhythms may possibly be a useful approach in the psychophysiological study of anticipatory behavior. First, if we consider the processes underlying the genesis of 10-Hz rhythms on the one hand (cf. sections 2.2 and 2.3), and the thalamocortical gating mechanism that has been proposed to underlie anticipatory behavior on the other hand (cf. section 4.1.1), one can note that there is a striking similarity between the two mechanisms in the neuroanatomical structures involved, and their dynamical interactions. Therefore, from a neurophysiological point of view it seems plausible that the ERD technique is well suited for the task at hand, that is, studying anticipatory behavior.

Second, as far as anticipatory behavior in the motor domain (i.e., motor preparation) is concerned, there is ample evidence that it is accompanied by an ERD that is restricted to that part of the motor cortex where the body part to be moved is represented (cf. section 3.3.2). This clearly supports the idea that anticipatory behavior is realized by an activation of that part of the cortex that will be involved in processing the anticipated event (in this case, performing a movement). For anticipatory behavior in the sensory domain (i.e., anticipatory attention), the picture is less clear, since only very little attention has been devoted to studying the anticipatory ERD in the sensory domain. The existing evidence suggests that anticipating a visual stimulus is accompanied by an ERD, but the results of the few studies that addressed this issue are equivocal and therefore inconclusive (cf. section 3.3.3). In this respect however, the apparent existence of modality-specific 10-Hz rhythms, alpha, mu and tau (cf. section 3.3.1) that react differentially to stimulation in one of the three main sensory modalities (visual, somatosensory and auditory, respectively) is promising, since their very existence opens the possibility that they independently may show a local desynchronization when a stimulus in the corresponding sensory modality is anticipated.

Third, ERD analyses contain information (non-phase-locked, or induced EEG or MEG activity) that is lost when one computes a signal average as is done in the computation of ERPs, which leaves only the phase-locked (or evoked) part of the signal in the resulting

average (cf. section 3.2.2). ERPs (negative slow potentials and probe-elicited EPs) have as yet not provided a clear support for a modality-specificity of anticipatory attention (cf. sections 4.2.1 and 4.2.2). From a signal-analytic point of view however it is very well possible that the relevant information in this respect may be hidden in the non-phase-locked part of the EEG/MEG. This would mean that the modality-specificity has been overlooked because the analyses have focused only on the phase-locked part of the EEG signal. ERD, with its focus on non-phase-locked activity, can be used to investigate this possibility.
In sum, there are neurophysiological, experimental and signal-analytical reasons to hypothesize that ERD might be a useful tool to investigate whether anticipatory attention for an upcoming stimulus in one of the three main sensory modalities is accompanied by an activation of the cortical areas corresponding to the modality of the anticipated stimulus. The experimental work described in this thesis constitutes an attempt to give an answer to this question. In the next section I will outline the general methodological approach that has been followed to this end.

5.2 Methodological considerations.

5.2.1 Experimental paradigm.

In section 4.2.1 I noted that anticipatory attention for an upcoming stimulus has been studied basically in relation to three types of stimuli: stimuli providing Knowledge of Results (KR) about the execution of a motor task (usually a time estimation task), stimuli that provide an instruction about a subsequent task, and stimuli with which the outcome of a previous mental operation (usually an arithmetic task) has to be matched. These paradigms have the advantage that the anticipatory attention preceding the stimuli of interest is not confounded in time with the preparation for a movement, as is the case in the forewarned reaction time task usually employed to elicit a CNV (cf. section 4.2.1). In order to induce anticipatory attention in my subjects I have chosen to use the time estimation + KR paradigm throughout the experiments described in the experimental part of this thesis for several reasons.
(1) This paradigm has been extensively used, and has generally yielded a relatively large-amplitude anticipatory slow potential (i.e., the pre-KR SPN, cf. section 4.2.1). The neuroanatomical substrates of the pre-KR SPN are better understood than those of the other types of SPN, since the processes underlying the generation of the pre-KR SPN have been studied with source localization and PET imaging techniques, in contrast to the other types of SPN. This makes a comparison between this slow potential and the hypothesized anticipatory ERD both easier and sounder. (2) The main interest of the present study is to compare the differences in the scalp distribution of the anticipatory ERD preceding stimuli of different modalities. Using different paradigms would lead to a confounding of task-specific effects and modality-specific effects, both within and between experiments. Moreover, the use of one and the same paradigm allows for replications of the results in different groups of subjects and in different experimental settings (e.g. an EEG laboratory vs. a MEG laboratory). Thus, the results obtained by using this approach will be more reliable than if paradigms differed between, or even within, the different experiments.
Alternatively, it might be argued that a weakness of this approach is that the results of the present thesis cannot be straightforwardly extrapolated to other experimental paradigms, let alone the real world outside the laboratory. The implication is that the generalizability of the results obtained with the one-paradigm approach is reduced compared to an approach in which multiple paradigms are used. Admittedly, this is true. However, using multiple paradigms in a rather limited number of experiments would not provide a very strong basis for the results, since this approach does not allow the results to be replicated across experiments, and as a result they may be much influenced by factors such as the group of

subjects and the exact experimental setting. In sum, the choice is between a slow, but empirically sound approach on the one hand, and an approach that may lead to more generalizable results that are however less firmly established on the other hand. I chose the former.

5.2.2 ERD methodology.

In section 3.2 I summarized the different approaches that are available for studying the synchronization and desynchronization of the EEG or MEG. Throughout this thesis I have used the classical ERD method for the analysis of the data. Below I will point out why the classical ERD is well suited for the task at hand.

The ERPs that can be expected to be evoked in the experimental paradigm that has been used are the Readiness Potential (RP) and the Stimulus-Preceding Negativity (SPN, cf. section 4.2.1 for a description of these ERPs). Both ERPs are negative slow potentials that exclusively contain frequencies below 1 Hz. Since the lowest frequency component that will be studied with the ERD technique is the 8-10 Hz band, the ERPs will not interfere with the ERD. Therefore there is no need to use the method of ERD based on intertrial variance described in section 3.2.2.

Recall from section 3.2.3 that the problem of the relatively poor time resolution of the ERD can be solved by using the Hilbert transform. However, the processes under study in this thesis are rather slow: the RP and SPN develop over more than 1 second; the anticipatory ERD preceding movements lasts for 2 seconds or more; the anticipatory ERD preceding visual stimuli that has been reported both by Klimesch and by Pfurtscheller (cf. section 3.3.3) starts as early as 1 second prestimulus. Thus, there is no need for improving the temporal resolution of the ERD for investigating the phenomenon of anticipatory behavior.

One last point concerns the selection of frequency bands. In section 3.2.4 I noted that when carrying out purely explorative research, i.e. when there are no hypotheses about which frequency bands will react on the experimental manipulations, it is warranted to use fixed, predefined frequency bands. Since ERD analyses have as yet not been used in the time estimation + KR paradigm, it was decided to use fixed frequency bands. Since there are good reasons to hypothesize that the frequency range around 10 Hz will be reactive to anticipatory processes (cf. Chapters 2,3 and 4), I will focus on this frequency range. Furthermore, I want to verify whether our data support the differentiation between the lower alpha band and the upper alpha band, as has been proposed by Klimesch (cf. section 3.3.3). Therefore I will systematically compare the lower (8-10 Hz) and upper (10-12 Hz) alpha frequency ranges in all the experiments.

5.3 Research questions.

In the present thesis I will experimentally address the question whether anticipatory attention for an upcoming stimulus in one of the main sensory modalities, that is, auditory, visual or somatosensory, is realized trough a local cortical activation of the sensory cortex corresponding to the modality of the anticipated stimulus. Anticipatory attention will be induced in subjects by having them perform the following task. After the presentation of an auditory Warning Stimulus (WS), they must indicate the end of a 4-second interval by a motor response (pressing a button or squeezing a force transducer). Two seconds after the response they will be informed about the quality of their time estimation by a stimulus providing Knowledge of Results (KR), that can be either auditory, visual or somatosensory. Note that the subjects are informed beforehand about the modality of the KR stimulus, which is constant within experimental blocks. Therefore, the subjects are assumed to be engaged in anticipatory attention preceding the KR stimulus. Event-related desynchronization of the EEG and MEG will be used as a dependent measure in order to quantify cortical activation.

Thus, in the main the following hypotheses will be tested in the experimental part of this thesis:

1. Anticipatory attention for a visual stimulus will be accompanied by an ERD that is localized over the occipital cortex.
2. Anticipatory attention for an auditory stimulus will be accompanied by an ERD that is localized bilaterally over the temporal cortex.
3. Anticipatory attention for a somatosensory stimulus will be accompanied by an ERD that is localized over the postcentral cortex.

Part II:
Experimental part

Chapter 6. Event-related desynchronization related to the anticipation of a stimulus providing Knowledge of Results[1].

6.1 Abstract.

In the present paper event-related desynchronization (ERD) in the alpha and beta frequency bands is quantified in order to investigate the processes related to the anticipation of a Knowledge of Results (KR) stimulus. In a time estimation task 10 subjects were instructed to press a button four seconds after the presentation of an auditory stimulus. Two seconds after the response they received auditory or visual feedback on the timing of their response. Preceding the button press a centrally maximal ERD is found. Preceding the visual KR stimulus an ERD is present that has an occipital maximum. Contrary to expectation, preceding the auditory KR stimulus there are no signs of a modality-specific ERD. Results are related to a thalamo-cortical gating model (Skinner and Yingling, 1977; Brunia, 1993, 1997) which predicts a correspondence between negative slow potentials and ERD during motor preparation and stimulus anticipation.

6.2 Introduction.

Anticipatory behavior serves the goal of a faster and/or more efficient information processing. It can occur both at the input and at the output stages of information processing (Gottsdanker, 1980). The processes involved can be referred to as anticipatory attention and motor preparation, respectively. Two EEG measures seem particularly adequate to study these anticipatory processes: negative slow potentials and event-related desynchronization (ERD). Negative slow potentials are interpreted to reflect a depolarization of cortical cells, indicating an increase in the readiness of cells to fire. ERD reflects the interruption of synchronized activity in functionally related groups of cortical neurons, which again can be seen as a correlate of increased cellular excitability (cf. Pfurtscheller, 1994).

Motor preparation has been extensively studied with slow potentials. It manifests itself as the Readiness Potential (RP, Kornhuber and Deecke, 1965), which can be recorded prior to simple self-paced movements (for reviews, see Brunia et al., 1986; McCallum, 1988). The RP starts as early as 1500-1000 ms before movement onset, as a bilaterally symmetric negativity that is largest over the pre- and postcentral scalp areas. At about 500 ms prior to movement onset RP amplitudes become larger contralateral to the movement side, at least with finger movements. This has been termed the negative slope (Shibasaki et al., 1980). At about movement onset the negativity reaches its peak amplitude over the contralateral scalp. This so-called motor potential is thought to be a reflection of the activation of the pyramidal tract (see Arezzo et al., 1977). The most prominent neural generators of the RP are situated in the primary motor cortex (e.g. Bötzel et al., 1993; Toro et al., 1993; Böcker et al., 1994a, b).

A number of studies have investigated patterns of event-related synchronization (ERS) and desynchronization (ERD) in the alpha and beta frequency bands in a voluntary movement

[1] This chapter is a slightly modified version of a paper with identical title by M.C.M. Bastiaansen, K.B.E. Böcker, P.J.M. Cluitmans and C.H.M. Brunia which has been published in Clinical Neurophysiology, 1999, 110: 250-260.

paradigm (e.g. Pfurtscheller and Aranibar, 1977; Pfurtscheller and Berghold, 1989; Pfurtscheller, 1992; Derambure et al., 1993; Toro et al., 1994; Stancák and Pfurtscheller, 1995; Pfurtscheller et al., 1996; Defebvre et al., 1996). These studies show consistent results, that can be summarized as follows: the first sign of ERD can generally be found at around 1500 ms pre-movement, and is strictly localized to the contralateral pre- and postcentral scalp. At approximately 750 - 500 ms before movement onset desynchronization of a comparable magnitude can be measured over the ipsilateral scalp as well. Simultaneously, starting at about 1000 ms prior to the movement an ERS can be measured over the occipital cortex. After movement onset, there is a slow recovery of the power both in the alpha and the beta frequency bands at pre- and postcentral leads, with the higher frequencies (20-30 Hz) recovering fastest. The higher frequencies eventually show an ERS at about 1000 ms post-movement, that has not yet been reported for the lower frequencies (8-12 Hz).
In conclusion, although the time courses and spatial distributions of the RP and the pre-movement ERD show a relatively good correspondence, there is an obvious difference in the lateralization of both measures: the RP starts symmetrically and becomes contralaterally dominant at about 500 ms pre-movement, whereas the pre-movement ERD starts contralaterally and becomes symmetric at about 500 ms pre-movement. Although both measures are interpreted as a reflection of preparatory processes related to movement execution, the underlying mechanisms are different. It is unclear at present what might cause these differences between slow potentials and ERD.
Anticipatory attention for an upcoming stimulus has been studied in a series of experiments employing a time estimation paradigm. In this paradigm subjects are instructed to press a button some seconds after a warning stimulus, and are subsequently confronted with a Knowledge of Results (KR) stimulus providing feedback about the accuracy of the estimated time interval. A negative slow potential can be recorded prior to the KR stimulus, which has been called the Stimulus-Preceding Negativity (SPN; for reviews, see Brunia, 1988, 1993, 1997; van Boxtel, 1994, pp. 15-18). Its onset has been reported to be at least as early as 2000 ms pre-stimulus (Damen and Brunia, 1994; Böcker et al., 1994c). The SPN has a widespread scalp distribution, with a frontal plateau and a parietal ramp-like potential, usually with a right-hemisphere preponderance (Brunia and Damen, 1988). It has been recorded prior to auditory and visual stimuli. The SPN has been recorded in different experimental paradigms: preceding instruction stimuli (e.g. Rösler, 1991; Van Boxtel and Brunia, 1994), probe stimuli (Chwilla and Brunia, 1991a, 1992) and KR stimuli (Grünewald and Grünewald-Zuberbier, 1983; Damen and Brunia, 1985, 1987a; Brunia and Damen, 1988), and preceding stimuli evoking emotional arousal (Simons et al., 1979; Klorman and Ryan, 1980; Rockstroh et al., 1989). However, the SPN has been recorded unequivocally in two experimental conditions only: prior to KR stimuli and prior to stimuli evoking emotional arousal. Both situations have two things in common: there is no immediate relation to motor activity, and the stimuli have an affective-motivational valence. Thus, the anticipatory attention is confounded with the anticipation of an affective stimulus, but not with motor preparation. The scalp distribution of the SPN varies with the type of stimulus that is anticipated. Prior to KR stimuli a right-hemispheric dominance is usually found. Instruction and probe stimuli, however, have a more direct relation to subsequent motor activity. This has consequences for hemisphere differences: preceding instruction stimuli the results are contradictory: sometimes a left- and sometimes a right hemispheric dominance is found (e.g. Rösler, 1991; Van Boxtel and Brunia, 1994; Damen and Brunia, 1994). Prior to probe stimuli, Chwilla and Brunia (1991a, 1992) found an SPN with a left hemispheric preponderance.

So far, with the exception of one study (Lang et al., 1984), no evidence has been found for a contribution of modality-specific processes to the SPN, contrary to what would be expected if the SPN were to reflect anticipatory attention. Thus, anticipatory attention *per se*

does not seem to be a sufficient condition for an SPN to develop (see Damen and Brunia, 1994). It has been suggested that the occurrence of an SPN depends on whether the anticipated stimulus has an affective-motivational value (Damen and Brunia, 1994). This interpretation is further supported by a spatiotemporal dipole modeling study (Böcker et al., 1994c), where a large part of the pre-KR SPN could be explained by a pair of dipoles which probably represents activity in the *Insulae Reili*, a bilateral cortical structure buried within the Sylvian fissure. This structure has connections which suggest that the insular cortex is involved in the processing of affective-motivational stimuli (Mesulam and Mufson, 1985). In conclusion, slow potential research has as yet not been very successful in identifying physiological correlates of perceptual anticipatory attention.

In the present study, it will be investigated whether ERD might constitute a better candidate for identifying physiological correlates of preparation for perception, since there is a remarkable lack of experimental data on this topic. To our knowledge, there are no studies that have explicitly investigated ERD phenomena during the anticipation of a stimulus. Two studies should be mentioned, however, which provide some indirect support for the hypothesis that there is an ERD component reflecting anticipatory attention. Pfurtscheller (1992, his fig. 3) discusses an experiment in which subjects had to perform a reading task. Starting from 1 s pre-stimulus, ERD was localized on occipital electrode positions, while at central locations an ERS was measured. In another experiment, Pfurtscheller and Klimesch(1991) asked subjects to perform a visual-verbal reading and classification task. Preceding the presentation of the visual stimuli that were to be classified, he found a widespread, long lasting (± 1 s) ERD with a left-hemisphere dominance in the 8-10 Hz band. The author interpreted this ERD as being related to the anticipation of the stimulus. These two instances of an occipitally localized ERD prior to visual stimuli suggest a modality specificity of ERD during anticipatory attention. In the present study we will more explicitly investigate ERD related to anticipatory attention. More specifically, we will investigate the patterns of synchronization and desynchronization prior to the presentation of auditory and visual KR stimuli, paying specific attention to possible modality specific effects on ERD. Subjects performed a time estimation task, and received feedback about the timing of their response by means of an auditory or a visual KR stimulus. We expect five components to become manifest: (1) an ERD which is localized at the primary motor cortex prior to response execution; (2) a centrally maximal ERS following response execution; (3) an ERD which is localized at primary auditory cortex prior to auditory KR stimuli, reflecting a modality-specific anticipation of the auditory KR; (4) an ERD which is localized at the primary visual cortex prior to visual KR stimuli, reflecting a modality-specific anticipation of the visual KR; and (5) a frontotemporal ERD prior to KR stimuli in both modalities, reflecting anticipatory activity in the *Insulae Reili*, which is related to the affective-motivational value of the KR stimulus.

6.3 Methods.

Subjects.

Ten right-handed subjects (4 men and 6 women) aged 21 - 36 (M = 24.7) participated in the experiment. They were volunteers, and received Dfl. 7.50 per hour for participating in the experiment.

Design and procedure.

The experiment consisted of three conditions: voluntary movement, time estimation with auditory KR, and time estimation with visual KR. In the voluntary movement task, subjects were instructed to produce rapid self-paced flexions of index-finger and thumb at a slow pace

(4-6 movements per minute, with a minimum inter-response interval of 6 s), with either the left or the right hand. A total of 100 trials were recorded for each hand.
The other two conditions consisted of a time estimation task, in which the subjects were instructed to produce a rapid unilateral flexion of index-finger and thumb, starting at 4000 ms after the onset of an auditory warning stimulus (1000 Hz, 70 dB(A), 60 ms). Two seconds after the response they were informed about the correctness of the estimated time interval by either an auditory or a visual Knowledge of Results (KR) stimulus. The auditory KR stimulus was a 500 Hz tone at 70 dB(A), the visual KR stimulus consisted of the illumination of two red LEDs mounted inside a box with a circular translucent front, placed about 1.5 m in front of the subject. In both modalities the information conveyed by the KR stimulus was encoded in its duration, which was either 50, 250 or 750 ms, corresponding to the estimation of an interval that was too short, correct or too long, respectively. The width of the time interval considered correct was individually adjusted during a training block, in order to obtain about 40 percent correct trials. A total of 100 trials was recorded for each hand in each KR-modality. The voluntary movement condition always preceded both time estimation tasks, in order to prevent carry-over effects from the time estimation to the voluntary movement task.

Electrophysiological recordings.

For the EEG-recordings 23 non-polarizing Beckman 8 mm Ag-AgCl electrodes were affixed to the scalp, most of them placed according to the international 10-20 system. Standard positions were Fp1, Fp2, F7, F3, F4, F8, T3, Cz, T4, P3, Pz, P4, O1, and O2. Non-standard positions were C3' and C4', which are 1 cm anterior to C3 and C4, respectively; T5an, T5po, T6an and T6po, which are at one third and two third of the distances between T3 and O1 and between T4 and O2, respectively; TP3 and TP4, which are in the centre of T3, P3, T5 and C3 and in that of T4, P4, T6 and C4, respectively. Electrode impedance was kept below 5 kΩ. Software-linked mastoids served as a reference. The EEG was amplified by home-made amplifiers, with a 30 s time constant, and a 30 Hz (-42 dB / octave) lowpass filter. Epochs of 3000 ms pre-movement to 3500 ms post-movement were AD-converted with a sampling frequency of 128 Hz.
The horizontal EOG from the outer canthi, and the vertical EOGs of both eyes were recorded, and an off-line EOG correction was performed (van den Berg-Lenssen et al., 1989). Next, an automatic artifact detection was performed, discarding trials containing spikes that exceeded 100 μV and trials containing large drift. Two criteria were used to define drift: after applying a 2 Hz lowpass filter to the data, (1) individual sample values in an epoch may not differ from each other by more than 80 μV, and (2) the mean amplitude in 4 subsequently sampled intervals of equal length may not differ from baseline by more than 35 μV.

ERD computation.

In order to obtain reference-free data and to remove ERD/ERS effects at the reference electrodes, the recorded potentials were transformed to Scalp Current Density (SCD) fields by estimating a spherical spline function, which is the recommended procedure by Perrin et al. (1987, 1989; see Böcker et al., 1994c for the resulting SCD maps). This method has the advantage of yielding reliable estimates of the SCD at electrode positions that are at the border of the electrode montage, so it is preferable to computing a local average reference (Hjorth, 1975), as is mostly done in ERD computation (e.g. Pfurtscheller, 1991). Next, data were bandpass filtered in the frequency domain according to the following procedure: First an FFT was performed on the entire sampling epoch, after which the data were smoothed twice using a moving Hamming window with a 3-sample length. Next the weights for frequencies outside the desired band were set to zero, and finally the data were transformed

back to the time domain. Five different frequency bands were thus obtained: 8-10 Hz, 10-12 Hz, 12-16 Hz, 16-20 Hz, and 20-25 Hz.
The data then were transformed into power values by squaring the amplitudes. Intervals of 32 consecutive samples were averaged, giving rise to 26 time intervals of 250 ms each (since the lowest frequency band considered was 8-10 Hz, this 250 ms interval still covers 2 periods of the slowest frequency component in this band). Since the data were recorded on a trial-by-trial basis, the first and the last 250 ms intervals of the 6500 ms sampling epoch were invalid because of an inherent discontinuity in the data. For each subject data were averaged over trials, and ERD was computed as the percentage power increase (ERS) or decrease (ERD) for a particular time interval in a particular frequency band, relative to the reference interval from 2750 to 2000 ms pre-movement. The end of this reference interval corresponds to the point in time when movement-related ERD starts (Pfurtscheller and Berghold, 1989). Finally percentages ERD were averaged over all subjects for display purposes.

Statistical analyses.

t-tests.

In order to assess whether the power during the performance of the task differs significantly from the power in the reference interval, i.e. whether ERD or ERS is significant, we performed single-sample t-tests. These tests are essential since differences in ERD or ERS - between conditions, which are assessed by an ANOVA for repeated measures (see below), can only validly be tested if there *is* a significant ERD or ERS.
In order to limit the number of t-tests, tests were performed only on a selection of time intervals and channels: an early pre-movement interval (from 1000 - 750 ms pre-response), which is probably dominated by a contralateral ERD at central (C3' and C4') channels; a late pre-movement interval (250 - 0 ms pre-response), where we expect a bilaterally symmetric ERD at central (C3' and C4') channels, and a pre-KR interval (250 - 0 ms pre-KR), which is the main interest of this study: here we do not only expect post-movement ERS at central (C3' and C4') channels, but also ERD related to the anticipation of the KR stimulus at occipital (O1, O2), temporal (T3, T4) and frontotemporal (F7, F8) channels. These tests were performed in all five frequency bands for all three conditions
We subtracted the grand averages of the percentages ERD in the voluntary movement condition from the percentages ERD in both time estimation conditions. On these subtracted data, the similar t-tests were performed as on the non-subtracted data. The t-tests concerning the movement-related ERD after subtraction can be used to assess whether the subtraction effectively eliminated the movement-related ERD. If this is the case, the power changes related to the anticipation of the KR stimulus can be assessed without running the risk of confounding pre-KR activity with post-movement activity.
A 5% significance level was adopted for the t-tests. However, since using a large number of t-tests could result in an overall increase of type I errors, only those results will be considered significant that show a consistent pattern of significances (for example, movement-related effects should be consistent over conditions, while pre-KR effects should be consistent over response sides).

ANOVA's.

Next, differences in power changes between conditions were tested by an ANOVA for repeated measures. Similar time intervals and electrode positions were selected as for the t-tests. Factors were Task Condition (voluntary movement, auditory KR, visual KR), Response Side (left, right), Frequency Band (8-10, 10-12, 12-16, 16-20 and 20-25 Hz), Time Interval (early pre-movement: late pre-movement, pre-KR), Electrode Position (F, C, T, O) and Hemisphere (left, right). The subtracted data were subjected to a second ANOVA, which now

included only two task conditions (auditory and visual KR). Where necessary, Greenhouse-Geisser corrected degrees of freedom were used (Vasey and Thayer, 1987). A 5% significance level was adopted for the ANOVA's. Significant interactions were clarified either by breaking them down into simple effects or by computing post-hoc contrasts.
A statistical analysis of the behavioral data and the potential data, as well as a spatiotemporal dipole model of the potential data have been presented elsewhere (Böcker et al., 1994c).

6.4 Results.

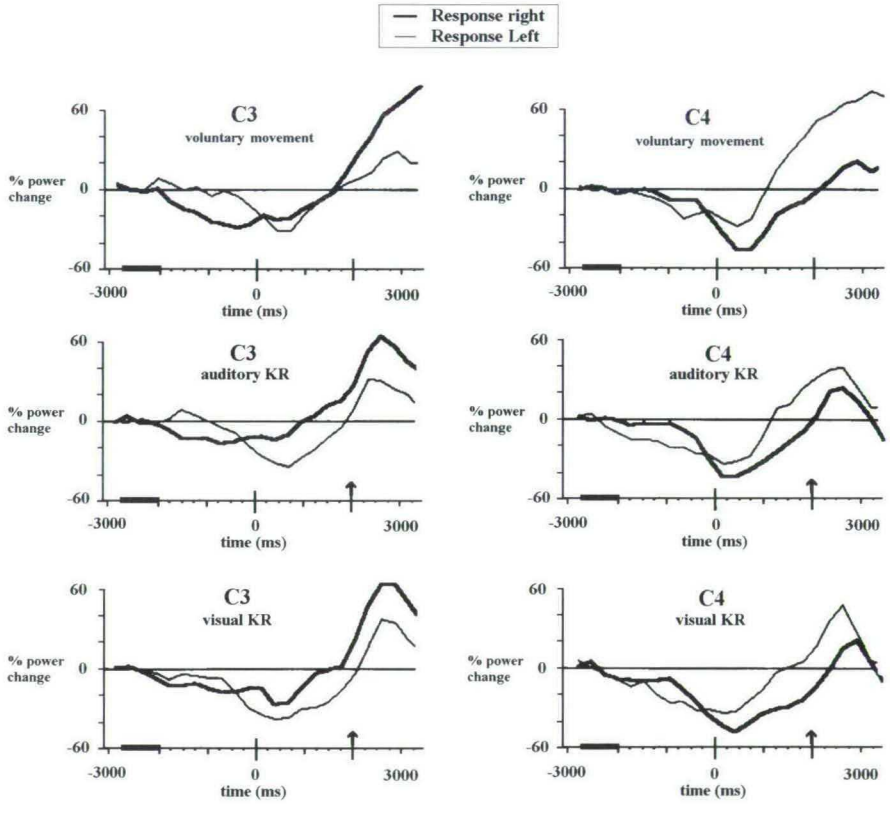

Figure 6.1. ERD/ERS time courses on non-subtracted data, for left- and right-hand responses at central channels in the 10-12 Hz frequency band. Y axis indicates magnitude of power change. Marked area on the x-axis indicates reference interval. Arrows indicate presentation of KR stimulus. The initially contralateral pre-movement ERD gradually develops into a post-movement ERS in all three conditions. Note the similarity of movement-related ERD in the three conditions.

Figure 6.1 shows the time courses of the movement-related ERD at central electrode positions. At the early pre-movement time interval a centrally maximal, contralateral ERD is present in all three task conditions, as indicated both by the t-tests and the ANOVA (see Table 6.1: T*R*H and E*T*R*H; simple effect of response side * hemisphere in the early

pre-response interval at central positions: $F_{1,\ 9} = 5.68$; $p = 0.0410$). Note that although the ANOVA indicates no differences between frequency bands, the t-tests[2] show that the contralateral ERD is consistently significant in the 8-10 and 10-12 Hz bands only.
At the late pre-movement interval the t-tests indicate that in all three task conditions, the contralateral ERD has shifted to a bilateral ERD that is consistently present in the 8-10, 10-12 and 20-25 Hz bands. This is further supported by the ANOVA, which shows simple effects of response side * hemisphere in this time interval.
At the pre-KR interval a centrally maximal, contralaterally dominant ERS is present in all three task conditions, including the voluntary movement condition. The t-tests show that this effect is present in all frequency bands, but that in the 20-25 Hz band the ERS is also present over the ipsilateral hemisphere. The contralateral ERS is supported by the ANOVA (simple effect of response side * hemisphere in the pre-KR time interval at central channels: $F_{1,\ 9} = 10.21$; $p = 0.0109$), but again the ANOVA does not indicate differences between frequency bands.

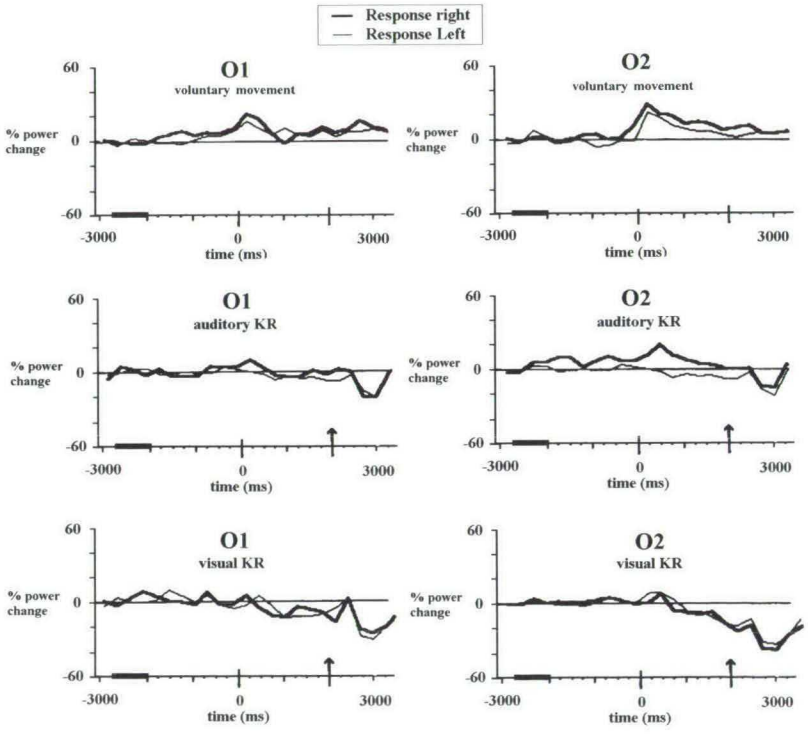

Figure 6.2. ERD/ERS time courses on non-subtracted data, for left- and right-hand responses, at occipital channels. The 12-16 Hz frequency band is displayed because in this band the t-tests indicate a significant ERD (see Table 6.2). Legends as indicated in Figure 6.1. Note the relatively large ERD preceding visual KR stimuli only.

Together, the pre-movement ERD and the pre-KR ERS produce a cluster of interactions in the ANOVA on the non-subtracted data (Table 1: T*R*H; E*R*H; T*E*R*H). Over fre-

[2] For the sake of brevity, the full t-test results will be presented only if their interpretation could be considered equivocal. Full significance tables can be obtained from the author.

quency bands however, the magnitude of the pre-KR ERS is such that in addition to the above-mentioned interactions it produces both the main effect of time interval (over electrode positions, response side and hemisphere an ERS is present at the pre-KR interval)and the interaction T*E (this effect is strongest at central electrode positions). Note that since the pre-KR ERS is also present in the voluntary movement conditions, it should be attributed to post-movement processes rather than to the anticipation of the KR stimulus. The initially contralateral pre-movement ERD and the post-movement ERS are displayed in Figure 6.1.
Over time intervals the power changes at central electrode positions are different in the different frequency bands: the alpha bands (8 -10 Hz and 10 - 12 Hz) are dominated by ERD, while the higher frequency bands are dominated by ERS (Table 6.1: B * E; contrast of alpha vs. beta at central channels: $F_{1, 9} = 6.76$; $p = 0.0287$).

Table 6.1. Significant ($p < 0.05$) effects of the ANOVA on non-subtracted data (B: frequency band; E: electrode position; T: time interval; R: response side; H: hemisphere; ε: Greenhouse-Geisser epsilon).

Effect	F	df	p	ε
Time interval	6.41	2, 18	0.0139	0.80
B * E	2.82	12, 108	0.0334	0.37
T * E	12.20	6, 54	0.0038	0.20
T * R * H	12.08	2, 18	0.0050	0.56
E * R * H	6.64	3, 27	0.0066	0.68
E * T * R * H	7.99	6, 54	0.0110	0.22

Figure 6.2 shows the ERD time courses in the 12-16 Hz frequency band at occipital electrode positions. Preceding visual KR stimuli there is an ERD that is not present preceding auditory KR or following the voluntary movement. Although the ANOVA revealed no condition effects, the t-tests indicate that the above-mentioned effect is significant (see Table 6.2): irrespective of response side, a significant ERD is consistently present preceding visual KR stimuli, not preceding auditory KR. Because these effects are never present in the voluntary movement condition, they can truly be attributed to the presentation of the visual KR stimulus.
In the 10-12 Hz band a significant ERD appears as a result of the subtraction, indicating that movement-related ERD was masking this effect before subtraction. In the 12-16 Hz band the ERD is consistently significant before as well as after subtraction.
At temporal electrode positions, the t-tests indicate a significant ERD preceding both auditory and visual KR stimuli following left-hand movements only (see Table 6.3). Figure 6.3 shows that the ERD at temporal electrode positions is small and rather inconsistent. Moreover, Figure 6.3 shows that it is also present in the voluntary movement condition, although in the latter condition it is not significant according to the t-tests.
After subtraction of the voluntary movement condition from the KR conditions, the t-tests reveal that both the pre-movement ERD and the post-movement ERS are almost entirely eliminated. This is supported by the ANOVA on the subtracted data, where the only movement-related effect is an intricate condition * response side * frequency band * electrode position * hemisphere interaction ($F_{12, 108} = 2.56$; $p = 0.0368$; $\varepsilon = 0.44$). This interaction is considered to be uninterpretable, since none of the possible simple effects reach significance. Because this interaction includes the factors response side and hemisphere its significance is probably caused by some small and inconsistent residual movement-related ERD.

Table 6.2: significance levels of t-tests on pre-KR ERD at occipital electrode positions before (+= p<0.05; ++=p<0.01) and after (= p<0.05; **=p<0.01) subtraction of RP conditions from KR conditions. In the 10-12 Hz band a significant ERD appears as a result of the subtraction, indicating that postmovement ERS was masking this effect before subtraction. In the 12-16 Hz band the ERD is consistently significant before as well as after subtraction. S denotes significant synchronization.*

	Auditory KR Response left		Auditory KR Response right		Visual KR Response left		Visual KR Response right	
	O1	O2	O1	O2	O1	O2	O1	O2
8-10 Hz					*			
10-12 Hz						*	*	*
12-16 Hz					+ *	+ *	+ **	++
16-20 Hz				+ S			+	
20-25 Hz	+ S	++ S				*		

Table 6.3. Significance levels of t-tests on pre-KR ERD (250-0 ms pre-KR) at temporal electrode positions before (+= p<0.05; ++=p<0.01) and after (= p<0.05; **=p<0.01) subtraction of RP conditions from KR conditions. Note that the inconsistent effects before subtraction become even more inconsistent as a result of the subtraction. S denotes significant synchronization.*

	Auditory KR Response left		Auditory KR Response right		Visual KR Response left		Visual KR Response right	
	T3	T4	T3	T4	T3	T4	T3	T4
8-10 Hz	++ **	*			+ *	+		
10-12 Hz	+					+		
12-16 Hz					++ *			
16-20 Hz								
20-25 Hz	++ S							

With respect to the pre-KR ERD, the results are more clear-cut than before the subtraction. At occipital channels a consistent ERD is found preceding a visual KR both in the 10-12 and the 12-16 Hz bands, while no ERD is present preceding auditory KR stimuli (see Table 6.2). At temporal electrode positions however, the t-tests reveal no consistent ERD (see Table 6.3). This difference between KR modalities is supported by the ANOVA, that indicates that the ERD is larger prior to visual than prior to auditory KR stimuli (condition * time interval interaction: $F_{2, 18} = 8.63$; $p = 0.0074$; $\varepsilon = 0.70$; simple effect of condition at the pre-KR interval: $F_{1, 9} = 6.31$, $p=0.0332$; see Figure 6.4). It should be noted that the factor Electrode Position is not included in this interaction, although the t-tests clearly indicate that the ERD is significant at occipital channels only. The difference in ERD between KR conditions, as well as the posterior maximum of the ERD preceding a visual KR is illustrated in Figure 6.4.

Finally it should be noted that at electrode positions F7 and F8 no consistent ERD or ERS was found, neither before nor after subtraction.

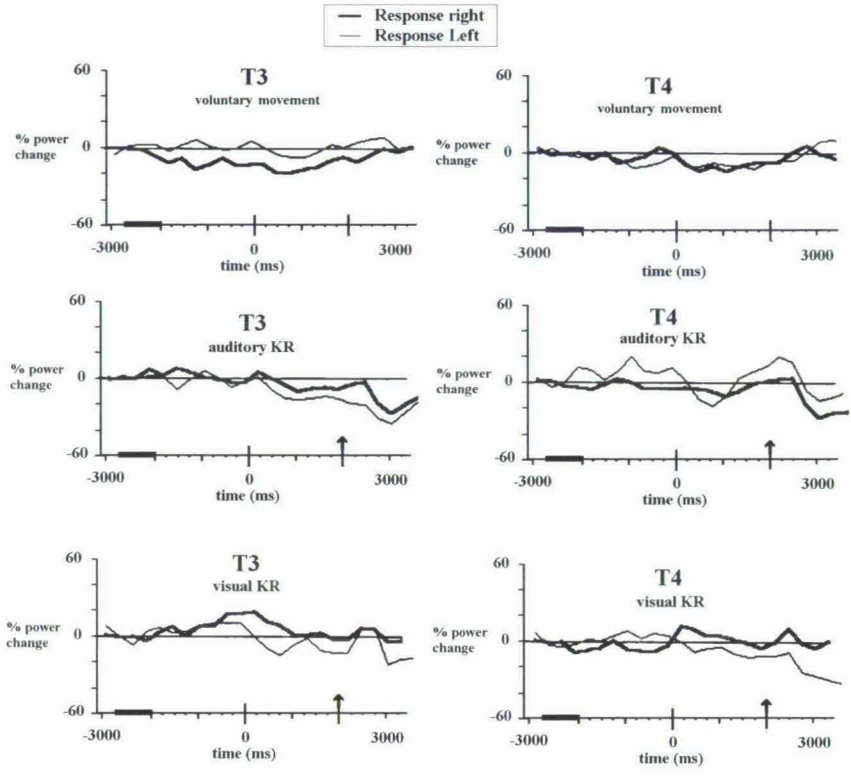

Figure 6.3. ERD/ERS time courses on non-subtracted data, for left- and right-hand responses at temporal channels. The 8-10 Hz frequency band is displayed because this is the band in which ERD is most consistently significant according to the t-tests (see Table 6.3). Legends as indicated in Figure 6.1.

6.5 Discussion.

We investigated the event-related power changes (ERD and ERS) in the EEG related to the anticipation of a stimulus, using a paradigm in which subjects were instructed to perform a time estimation task, and were informed about the quality of their time estimation by a KR stimulus. These event-related power changes are characterized by three components: (1) an initially contralateral, centrally maximal ERD preceding the response, (2) a contralaterally dominant, centrally maximal ERS following the response, and (3) an ERD with a posterior maximum preceding the visual KR stimulus.

The statistical analyses indicated that there were no differences, neither in time course nor in spatial distribution, between the three conditions in the premovement central ERD and the post-movement central ERS. The pattern of effects replicates the findings usually described

in the literature (e.g. Pfurtscheller and Berghold, 1989), which formed the basis for hypotheses (1) and (2) formulated in the introduction.

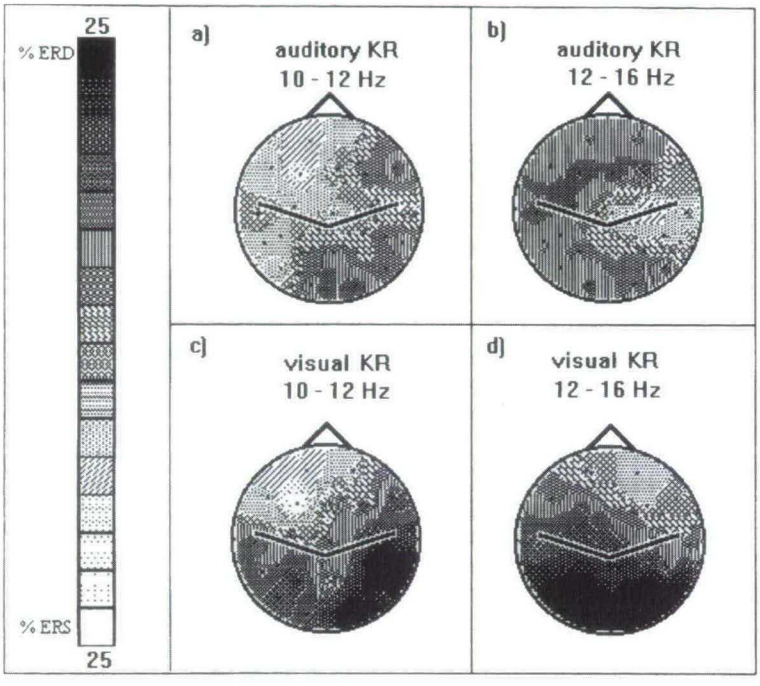

Figure 6.4. ERD maps after subtraction of the voluntary movement condition from the auditory and visual KR conditions in two different frequency bands, in the time interval from 250 - 0 ms preceding the KR. Note that (1) the ERD preceding a visual KR is localized to posterior electrode positions and (2) the post-movement central ERS has disappeared as a result of the subtraction. Data are from right-hand responses.

The absence of statistically significant differences in movement-related ERD/ERS between conditions justifies the subtraction of the voluntary movement condition from the KR conditions: since the movement-related ERD/ERS pattern was similar in all three conditions, the subtraction effectively eliminated the movement-related effects from the KR conditions. This is indicated by the t-tests, which show only a sporadic significant result after subtraction, and by the fact that the ANOVA on the subtracted data shows neither a clear response side * hemisphere interaction (only an intricate 5^{th} order interaction), nor any significant effects at central electrode positions. Thus, any condition effects in the subtracted data can only be attributed to the anticipation of the KR stimulus.
However, when we consider differences between conditions in the time interval preceding the KR stimulus, the t-tests and the ANOVA on the non-subtracted data show differential power. The ANOVA does not reveal any condition effects, whereas the t-tests indicate two differences between conditions.

First, the t-tests reveal a significant ERD on occipital electrode positions preceding a visual KR stimulus that is not present in the voluntary movement and auditory KR conditions. This condition effect is consistently present only in the 12-16 Hz band before subtraction, whereas the t-tests on the subtracted data reveal that the effect is present in the 10-12 Hz band as well. The condition effect is also present in the ANOVA on the subtracted data, which supports the notion that the ERD preceding a visual KR is partially masked by post-movement ERS before subtraction. It should be noted that on the basis of the ANOVA on the subtracted data, we should conclude that the scalp distribution of the ERD preceding a visual KR stimulus is flat, since there are no interactions with the factor Electrode Position. However, if we consider the t-test results on the subtracted data (see Tables 6.2 and 6.3), and Figure 6.4 (c and d), it is clear that the ERD preceding a visual KR stimulus was indeed restricted to posterior electrode positions. This is in accordance with the corresponding hypothesis formulated in the introduction. The observed ERD preceding a visual KR is modality-specific in the sense that it is only present in the visual KR condition.

Second, the t-tests before subtraction reveal a significant ERD on T3 from 8-10 Hz preceding an auditory KR, but only when the subjects responded with the left hand. In order for this effect to be modality-specific, we would expect it to be absent preceding a visual KR. In the latter condition however, both T3 and T4 show similar effects. Moreover, the effect is rather inconsistent, and together with the fact that after subtraction the t-tests indicate that this condition effect has largely disappeared, we conclude that the effect is too inconsistent to be reliable. Thus, no indications of modality-specific desynchronization were found at all in the auditory modality, contrary to the corresponding hypothesis formulated in the introduction.

We did not find any ERD components that could be related to activity in the *Insulae Reili*, contrary to hypothesis (5) formulated in the introduction. This is in contrast with a dipole model of the SPN that was based on the same data set as has been used in the present experiment (Böcker et al., 1994c). Together with the fact that we found no right hemisphere dominance in the ERD as opposed to what is usually reported for the SPN, this could suggest that ERD is less sensitive to the anticipation of an affective-motivational event than its slow potential analogue. This would make ERD an excellent candidate for identifying perceptual anticipatory attention.

In conclusion, the present study provides evidence of the primary motor cortex being in a preparatory state prior to movement execution, and of the primary visual cortex being in a preparatory state preceding the presentation of a visual KR stimulus. However, preceding an auditory KR we do not find any indications of preparatory activity in primary auditory cortex.

The present data are also relevant with respect to a model of intermodal selective attention that has been proposed by Skinner and Yingling (1976, 1977; Yingling and Skinner, 1977). This so-called gating model describes a thalamo-cortical gating mechanism, in which the thalamus, which itself is in turn controlled by the frontal cortex, serves as a gate in the regulation of the transmission of information from subcortical sensory and motor structures to the primary sensory and motor cortices (for a detailed description of the model, see Brunia, 1993, 1997). As proposed by Brunia (1993, 1997), the gating model, which was initially developed to describe intermodal selective attention, could provide an explanation, in functional and structural terms, of motor preparation and anticipatory attention as well. It would predict a correspondence between slow potentials and ERD during motor preparation and anticipatory attention. According to the model, these preparatory processes should be reflected both by negative slow waves and ERD that are maximal over the respective primary sensory cortex when a stimulus is anticipated, and over the pre- and postcentral cortex when a movement is prepared for.

The predictions based on the gating model are confirmed both by slow potential data and by ERD data as far as motor preparation is concerned: there is a close correspondence between

the two measures in a voluntary movement paradigm. However, it is unclear why both measures display a different lateralization. This suggests that the thalamo-cortical gating circuit might not be the only, and maybe not even the principle circuit through which motor preparation is realized.

As we pointed out in the introduction, slow potential research has consistently failed to find correlates of modality-specific anticipatory attention (with the exception of Lang et al., 1984). The present experiment, that has been directed at identifying patterns of ERD related to anticipatory attention, has been at least partially successful in this respect (i.e., in the visual modality, not in the auditory). However, there is a lack of a correspondence between ERD and slow potentials in the present study. A possible explanation hereof may lie in the fact that the time estimation paradigm is not adequate for isolating the relevant preparatory process: the affective-emotional value of presenting a KR stimulus might be masking the slow potential correlate of the pure anticipatory attention, whereas ERD might be less sensitive to the anticipation of an affective-motivational event, as has been suggested above.

In future research other paradigms, like those employing probe and instruction stimuli, should also be studied with the ERD technique. Furthermore, event-related power changes in the higher frequency bands must be considered as well (for example the 40 Hz band, see Pfurtscheller et al., 1993; Pfurtscheller et al., 1994), in order to have a complete picture of synchronization and desynchronization patterns in the entire frequency spectrum of the EEG.

Chapter 7. Event-Related Desynchronization during anticipatory attention for an upcoming stimulus: A comparative EEG/MEG study[1].

7.1 Abstract.

Our neurophysiological model of anticipatory behavior (e.g. Brunia, 1999, Bastiaansen et al., 1999b) predicts an activation of (primary) sensory cortex during anticipatory attention for an upcoming stimulus. In this paper we attempt to demonstrate this by means of Event-Related Desynchronization (ERD). Five subjects performed a time estimation task, and were informed about the quality of their time estimation by either visual or auditory stimuli providing Knowledge of Results (KR). EEG and MEG were recorded in separate sessions, and ERD was computed in the 8-10 Hz and 10-12 Hz frequency bands for both datasets. Both in the EEG and the MEG we found an occipitally maximal ERD preceding the visual KR for all subjects. Preceding the auditory KR, no ERD was present in the EEG, whereas in the MEG we found an ERD over the temporal cortex in two of the five subjects. These subjects were also found to have higher levels of absolute power over temporal recording sites in the MEG than the other subjects, which we consider to be an indication of the presence of a 'tau' rhythm (e.g. Lehtelä et al., 1997). It is concluded that the results are in line with the predictions of our neurophysiological model.

7.2 Introduction.

Most of the events that we experience everyday do not happen unexpectedly. This enables us to anticipate events that (probably) will happen in the near future. From a functional point of view, this anticipatory behavior is aimed at a faster and better perception, and a faster and more accurate response than would have been possible under unwarned conditions. In other words, it becomes manifest both in the sensory domain and in the motor domain. In the present paper we will address only the anticipatory behavior in the sensory domain; more specifically, we will investigate anticipatory attention to sensory stimulation in the visual and auditory modalities. Clearly, the anticipation of an upcoming stimulus in an ever-changing environment is based upon continuous processing of the information from that environment. Attention in general implies that a *selection* has to be made in order to process what is relevant, and to ignore what is irrelevant. This applies to anticipatory attention as well. Anticipating an image that will soon be flashed onto a screen implies preparing the visual system to process the upcoming information, while not paying attention to the auditory or somatosensory modalities; anticipating an electric stimulus that will be applied on, say, the forearm implies paying attention to the somatosensory modality while ignoring auditory and visual stimuli.

From a neurophysiological point of view, anticipatory attention is directed either at preparing the relevant brain structures to do in advance what can be done (e.g. Requin et al., 1991), and/or to reduce the threshold levels of the relevant brain structures (e.g., Birbaumer et al., 1990) in order to ensure a faster/more efficient processing. This should manifest itself

[1] This chapter is a slightly modified version of a paper with identical title by M.C.M. Bastiaansen, K.B.E. Böcker, C.H.M. Brunia, J.C. de Munck and H. Spekreijse, which is currently under review at Clinical Neurophysiology.

as an anticipatory activation of the primary sensory cortex corresponding to the modality of the anticipated stimulus, which *precedes* the presentation of the stimulus. In other words, we think that the mechanism underlying anticipatory attention is similar for stimuli in different modalities. This results in topographic differences in cortical activation during the anticipation of these stimuli. Elsewhere, we have presented a neurophysiological model (Brunia, 1993; Brunia, 1999; Bastiaansen et al.,1999b), in which we propose that anticipatory behavior is based on a thalamo-cortical gating mechanism. This gating mechanism has previously been put forward by Skinner and Yingling to account for intermodal selective attention (Skinner and Yingling, 1977; Yingling and Skinner, 1977).

Anticipatory attention for an upcoming stimulus has been studied in a series of experiments employing a time estimation paradigm. In this paradigm subjects are instructed to press a button some seconds after a warning stimulus, and are subsequently confronted with a Knowledge of Results (KR) stimulus providing feedback about the accuracy of the estimated time interval. A negative slow potential can be recorded prior to the KR stimulus, which has been called the Stimulus-Preceding Negativity (SPN, Damen and Brunia, 1994; for reviews, see Brunia, 1993, 1999; Böcker and Van Boxtel, 1997). The SPN has been observed preceding auditory and visual KR stimuli. On the basis of our model for anticipatory behavior we would in principle expect visual stimuli to be preceded by an occipitally maximal SPN, and auditory stimuli by a temporally maximal SPN; at the very least, we would expect the SPN to display differences in scalp distribution preceding stimuli of different modalities. This has not been found to be the case (Böcker et al., 1994c), although in a recent experiment in our laboratory we found small but significant differences in SPN amplitude over the auditory and visual cortices preceding auditory and visual KR stimuli, which go in the expected direction (Brunia, personal communication). Furthermore, a spatiotemporal dipole analysis of the SPN prior to auditory and visual KR stimuli did not detect dipoles in the primary auditory or visual cortices (Böcker et al., 1994c). In sum, the conclusion seems warranted that slow potential research has as yet not been very successful in identifying physiological correlates of anticipatory attention as described in the thalamo-cortical gating model.

Skinner and Yingling (1977) predicted that during selective attention for a specific sensory modality one should find a coincidence of negative slow potentials, enhanced evoked potential amplitudes and desynchronization of 10 Hz rhythmic activity over the corresponding sensory cortex. Support for the notion of desynchronization can be found in two comprehensive review papers by Steriade et al. (1990) and Lopes da Silva (1991). These authors point out that under influence of the reticular nucleus, thalamic relay nuclei can operate in two modes. In burst mode the transmission of information from sensory afferents through the thalamus to the cortex is blocked. In the scalp-recorded EEG this is reflected in synchronized, rhythmic activity with a frequency of approximately 10 Hz above the corresponding cortical area. In the tonic mode afferent information is transmitted to the cortex. At the scalp this is reflected in a desynchronization of 10 Hz rhythmic activity. In terms of Skinner and Yingling, this would imply that synchronization of EEG activity over a sensory cortex indicates that the gate of the corresponding sensory modality to the cortex is closed, whereas desynchronization indicates an open gate.

These findings suggest that analyzing the spatiotemporal patterns of synchronization and desynchronization of the EEG might be another means of studying thalamo-cortical gating, that can be used in addition to slow potential analyses. An analysis method known as Event-Related Desynchronization (ERD; Pfurtscheller and Aranibar, 1977) can be used to quantify such event-related changes in rhythmic EEG activity. At a signal-analytic level, the major difference between slow potentials and ERD is that, due to the averaging procedure used in their computation, slow potentials only contain activity that is both time- and phase-locked to

the occurrence of an event. For ERD it holds that the relevant phenomena need only be time-locked to the event, i.e. phase-locking is not required. Therefore ERD and ERP's may contain complementary information.

In a previous study, we investigated the spatiotemporal patterns of ERD based on EEG data of 10 subjects, during the anticipation of auditory and visual KR stimuli in a time estimation task (Bastiaansen et al., 1999a). On the basis of the thalamo-cortical gating model we expected an occipital ERD preceding the visual KR, and an ERD over the left and right temporal cortices preceding the auditory KR. Preceding visual KR stimuli we indeed found an ERD with an occipital maximum; however, preceding auditory KR stimuli no appreciable ERD was present. In sum, although we clearly found a topographic dissociation between the two modalities, we did not find evidence for anticipatory attention in the auditory modality.

Niedermeyer (1990, 1991, see also Niedermeyer, 1997 for a review) reported the existence of rhythmic activity originating in the temporal lobe. This 10 Hz rhythm could be measured by means of epidural and intracortical EEG recordings, but could not be picked up by simultaneously recorded scalp EEG. This indicates that normal, scalp-recorded EEG is blind to this kind of rhythmic activity. Niedermeyer termed it the "third rhythm", and showed that it could be functionally differentiated from alpha and mu activity on the basis of the observation that it did neither display any reactivity to opening or closing of the eyes, nor to activity of the somato-motor system. On the other hand, Tiihonen et al. (1991) and Lehtelä et al. (1997) reported the existence of a magnetoencephalographic (MEG) rhythm originating from the temporal lobe, which was termed the tau rhythm (Hari, 1993; see also Hari et al., 1997 for a review). They demonstrated that the tau rhythm was, in most of the subjects, clearly attenuated following auditory stimulation. The suppression of the tau rhythm was found to be much stronger over the right than over the left temporal cortex. This, together with the fact that source analyses demonstrated that the sources of the tau rhythm were located very close to the sources of the auditory evoked responses, namely in the supratemporal plane, suggests strongly that the tau rhythm is an intrinsic rhythm of the auditory cortex.

Together, these studies demonstrate that the auditory cortex generates a 10 Hz rhythm that can be measured with MEG, but not with scalp-recorded EEG. This might be explained by the fact that MEG is particularly sensitive to sources that are oriented tangentially with respect to the cortical surface, which is mostly the case for cell columns in the supratemporal plane. The fact that EEG is blind for rhythmic activity from the auditory cortex might explain why we didn't find an ERD over the temporal cortex preceding auditory KR stimuli in our previous EEG study (Bastiaansen et al., 1999a): if we cannot pick up rhythmic activity from the auditory cortex with scalp EEG, then we surely cannot demonstrate a desynchronization of this rhythmic activity. The experiment described in the present paper is aimed at testing this possibility. Five subjects performed a time estimation task, and the ERD preceding the presentation of the - auditory or visual - KR stimulus was computed on both EEG and MEG. With the EEG data we expect to replicate the results of our previous study (Bastiaansen et al., 1999a), that is, an occipital ERD preceding visual KR stimuli and no ERD preceding auditory KR stimuli. With MEG we expect to find similar results preceding the visual KR, but we expect to find an additional ERD bilaterally over the temporal cortex preceding auditory KR stimuli.

7. 3 Methods.

Subjects.

Five normal, healthy subjects (4 men, 1 woman, age range 25-35) participated in the experiment. They received Dfl.10,- (approximately 5 USD) per hour plus travel expenses for their participation.

Design and procedure.

Our recording devices did not allow for simultaneous recording of EEG and MEG. Therefore each subject performed the experiment twice, first for the EEG recordings and then for the MEG recordings. The experimental conditions were highly similar for the two recording sessions, although there were small, and for the present purposes irrelevant, differences in the presentation of the KR stimuli (see later in this section).

Subjects were seated in a dimly illuminated, sound-attenuating chamber. The experiment consisted of two conditions: time estimation followed by auditory KR and time estimation followed by visual KR. For the time estimation task, subjects were instructed to shortly press a button either with their left or their right hand 4000 ms after the onset of an auditory warning stimulus (WS; 1000 Hz, 70 dB(A), 100 ms). Two seconds after response onset they were informed about the correctness of the estimated time interval by either an auditory or a visual KR stimulus. The auditory KR stimulus could be a 2000 Hz, 1000 Hz or a 500 Hz tone (80 dB(A), 200 ms), corresponding to the estimation of an interval that was too short, correct or too long, respectively. For the EEG recordings the stimuli were presented through a loudspeaker situated 1.5 m in front of the subject, for the MEG recordings the stimuli were presented binaurally through earphones. The visual KR stimulus was presented on a computer screen (a VGA monitor for the EEG recordings, and an LCD screen for the MEG recordings) placed about 1.5 m in front of the subject, and could be a minus sign (for a premature response), a vertical bar (for a correctly timed response) or a plus sign (for a response that was too late). A response between 3700 and 4300 ms after WS onset was considered correct. The time-out was set at 4750 ms after WS onset (this led to an average of 1.04 % timeouts), and was followed by a KR corresponding to a response too late; these trials were discarded from further analysis.

Subjects received a 20 min training on the task prior to data collection. Subsequently, both for the EEG and the MEG recordings a total of 180 trials was recorded for each condition, divided in two experimental blocks of 90 trials. The order of the resulting 8 experimental blocks (2 response sides * 2 KR modalities * 2 blocks per condition) within each recording session was randomized over subjects.

Data recording.

Behavioral data.

Reaction times were measured from WS onset to response onset for each trial, and were stored for off-line analysis.

Physiological data.

The EEG was measured from 27 non-polarising Beckman 8 mm Ag-AgCl electrodes, most of which were placed according to the international 10-20 system. Standard positions were Fp1, Fp2, F7, F3, Fz, F4, F8, T3, Cz, T4, P3, Pz and P4. Non-standard positions were C3' and C4', which are 1 cm anterior to C3 and C4, respectively; TC3 and TC4, which are located at

one third of the distance between T3 and C3, and between T4 and C4, respectively; TP3 and TP4, which are in the centre of T3, P3, T5 and C3 and in that of T4, P4, T6 and C4, respectively; O1', Oz' and O2', which are located 2 cm anterior to O1, Oz and O2 respectively; O1", Oz" and O2", which are located 1 cm posterior to O1, Oz and O2 respectively. The electrode montage was chosen as to provide a good coverage of the auditory and visual cortices. Electrode impedance was kept below 3 kΩ. Software-linked mastoids served as a reference. The EEG was amplified by home-made amplifiers, with a 30 s time constant, and a 70 Hz (-42 dB / octave) lowpass filter. Epochs of 3000 ms pre-movement to 3000 ms post-movement were digitized with a sampling frequency of 256 Hz, and stored for off-line analysis. The horizontal EOG from the outer canthi, and the vertical EOGs of both eyes were recorded, and an off-line EOG correction was performed (van den Berg-Lenssen et al., 1989).

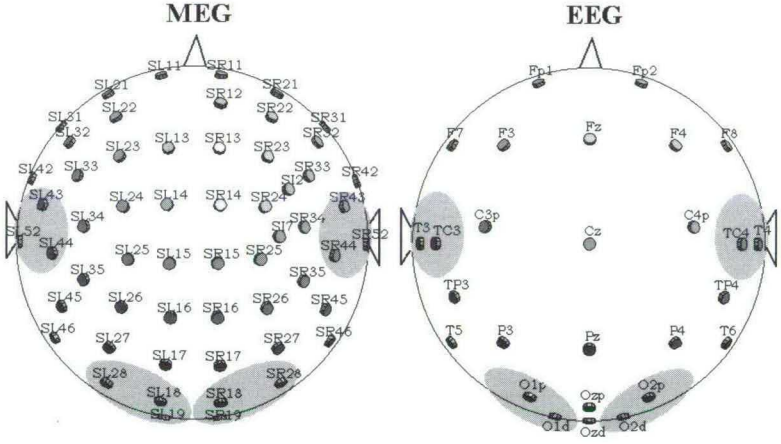

Figure 7.1 Orthogonal projection of the electrode and gradiometer positions used for the EEG and MEG measurements. Shaded areas indicate regions of interest (ROIs) used for the statistical analyses. Note that the labels p and d correspond to primes (') and doubles (") respectively.

For the MEG recordings , we used a 64-channel whole-cortex MEG system (CTF Systems Inc., Vancouver, Canada). The 64 axial gradiometers are uniformly distributed on the helmet surface with mean spacing of 4.5 cm. Figure 7.1 presents the sensor configurations for the EEG and MEG measurements. MEG epochs from 3000 ms pre-movement to 3000 ms post-movement were digitized at 250 Hz, and stored for off-line analysis. Filter settings were from DC to 45 Hz, with additional notch filters at 50 and 60 Hz. The MEG data were later resampled to 256 Hz for practical purposes. Preceding and following each experimental block the position of the sensors relative to the subject's head was determined on the basis of three head localization coils attached to the nasion and both pre-auricular points, and the average of the pre- and post-run was used as the sensor position for that particular block. Subsequently, in order to allow for a comparison between experimental conditions and subjects, extrapolated the data on a grid of averaged sensor positions using the algorithm developed by Hämäläinen and Ilmoniemi (1994).

Data reduction and statistical analyses.

Behavioral data.

Two behavioral measures were derived from the reaction time (RT) data. First, the quality of time estimation was monitored by computing the percentages of too fast, correctly timed or too slow responses. These data were analyzed by an ANOVA with Response category (too early, correct, too late), KR Modality (auditory, visual), Response side (left, right) and Recording Session (EEG, MEG) as repeated measures. Second, the effectiveness of the KR stimulus was assessed as follows: for trials with too early or too late responses, we computed the percentage of subsequent trials for which the RT changed in the desired direction (that is, an RT decrease following a trial with a too late response, and an RT increase following a trial with a too early response). These data were analyzed by an ANOVA with KR Modality (auditory, visual), Response side (left, right) and Recording Session (EEG, MEG) as repeated measures. Where necessary, degrees of freedom were corrected using the Greenhouse-Geisser Epsilon (GGE, Vasey and Thayer, 1987).

Physiological data.

On the EEG data, after the EOG correction a semi-automatic artifact detection was performed, discarding trials containing spikes that exceeded 100 μV and trials containing large drift. Two criteria were used to define drift: after applying a 2 Hz lowpass filter to the data (for artifact detection only), (1) individual sample values in an epoch may not differ from each other by more than 80 μV, and (2) the mean amplitude in 4 subsequently sampled intervals of equal length may not differ from baseline by more than 35 μV. The MEG data were visually inspected, and trials that contained eye-movement or other artifacts were discarded from further analysis.

The ERD was computed as follows. In order to obtain reference-free data, the EEG data were transformed to Scalp Current Density (SCD) fields by estimating a spherical spline function (Perrin et al., 1987, 1989). This step was omitted for the MEG data, since MEG data are inherently of a reference-free nature. The next steps were performed both on the EEG and the MEG data. The data were bandpass filtered using an FFT filter. Two different frequency bands were thus obtained: 8-10 Hz and 10-12 Hz. These frequency bands were chosen because it has previously been suggested that ERD in the upper and lower alpha bands reflect different cognitive processes (Pfurtscheller and Klimesch, 1990). These authors proposed that ERD in the lower alpha band reflects attention and expectancy, whereas ERD in the upper alpha band reflects task-specific cortical activation.. The data then were transformed into power values by squaring the amplitudes. Intervals of 64 consecutive samples were averaged, giving rise to 24 time intervals of 250 ms each. Since the data were recorded on a trial-by-trial basis, the first and the last 250 ms intervals of the 6000 ms sampling epoch were invalid because of an inherent discontinuity in the data. For each subject data were averaged over trials, and ERD was computed as the percentage power increase (or Event-Related Synchronization, ERS) or decrease (or Event-Related Desynchronization, ERD) for a particular time interval in a particular frequency band, relative to the reference interval from 2750 to 2000 ms pre-movement. The end of this reference interval corresponds to the point in time when movement-related ERD starts (e.g. Pfurtscheller and Berghold, 1989).

For the statistical analyses we restricted ourselves to the ERD in the last 250 ms interval immediately preceding the presentation of the KR stimulus, which is the primary interest of the study. The pre-movement ERD will be presented only at a descriptive level. Since there was a large inter-individual variability in the pre-stimulus ERD (see results section), and because of the small sample size, we decided to perform the statistical analyses at the level of individual subjects.

In order to obtain reliable spatial estimates of the event-related power changes, for each subject sensors overlying the auditory and visual cortices were pooled into four topographic regions of interest (ROIs): Left Temporal (LT), which included electrodes T3 and TC3 for the EEG, and gradiometers SL43, SL44 and SL52 for the MEG; Right Temporal (RT), which included the same sensors at homologous positions over the right hemisphere; Left Occipital (LO), which included electrodes O'1 and O"1 for the EEG, and gradiometers SL18, SL19 and SL28 for the MEG, and Right Occipital (RO), which included electrodes O'2 and O"2 for the EEG, and gradiometers SR18, SR19 and SR28 for the MEG. See Fig 7.1 for the resulting ROIs. The distinction between left and right hemisphere was made for two reasons. First, we want to be able to compare our results to those of Lehtelä et al. (1997), who found a clear right-hemisphere dominance in the reactivity of the tau rhythm to auditory stimuli. Second, we want to relate the pre-stimulus ERD to the results obtained by slow potential studies, and the latter have consistently demonstrated a right-hemisphere preponderance of the SPN, at least in the time estimation paradigm that is used in the present study (Damen and Brunia, 1994).
For each ROI, the power in the 750 ms baseline interval and the power in the 250 ms pre-KR interval were averaged over sensors (electrodes or gradiometers) for each single trial. Then, for each subject and each condition, non-parametric sign tests were used to assess the significance of the power decrease (ERD) or increase (ERS) in the pre-KR interval relative to the baseline interval, for all four ROIs separately , using single trials as observations. This was done for both frequency bands (8-10 and 10-12 Hz) separately.

7.4 Results.

Behavioral data.

With respect to the quality of the time estimation, the ANOVA on the percentages too early, correct and too late responses reveals only one significant effect: subjects produced more correct responses (64%) than too early or too late responses (16 and 20 %, respectively; main effect of Response Category: $F_{2, 8} = 29.29$, $p = 0.0016$, GGE = 0.689). There were no statistically significant differences in these figures between recording session, response side and KR modality.

KR stimuli indicating that a response was too early or too late resulted, on the subsequent trial, in an average of 79 % of the cases in an adjustment of the RT in the desired direction. The ANOVA on these figures revealed no statistically significant differences in the percentage correctly adjusted RT's between recording session, response side or KR modality. In sum, the lack of effects of Recording Session in the behavioral data indicates that subjects performed equally well on the task during the EEG and the MEG measurements and suggests that the experimental conditions were indeed very similar over recording sessions.

Physiological data.

Pre-movement ERD.

Visual inspection of the grand average pre-movement ERD on EEG and MEG data in the 8-12 Hz frequency band (see Figure 7.2) reveals the usual pattern of an ERD with a central maximum and a contralateral preponderance, both in the EEG and in the MEG. Figure 7.2 also suggests that the pre-movement ERD is of a larger magnitude in the EEG than in the MEG.

Pre-stimulus ERD.

In Figure 7.3 subject averages of the ERD in the 8-10 Hz band are presented, for the conditions in which a right-hand response was required. A quick view on Figure 7.3 reveals

that for the MEG there is a considerable amount of individual variation in the pre-stimulus ERD, while for the EEG the effects are much more consistent over subjects. Table 7.1 summarizes the results of the statistical analyses of the pre-stimulus ERD, for both frequency bands and both response sides. A general inspection of Table 7.1 indicates that the effects shown in Figure 7.3 are highly consistent over response sides and, although similar for the two frequency bands, more pronounced in the 8-10 than in the 10-12 Hz frequency band.

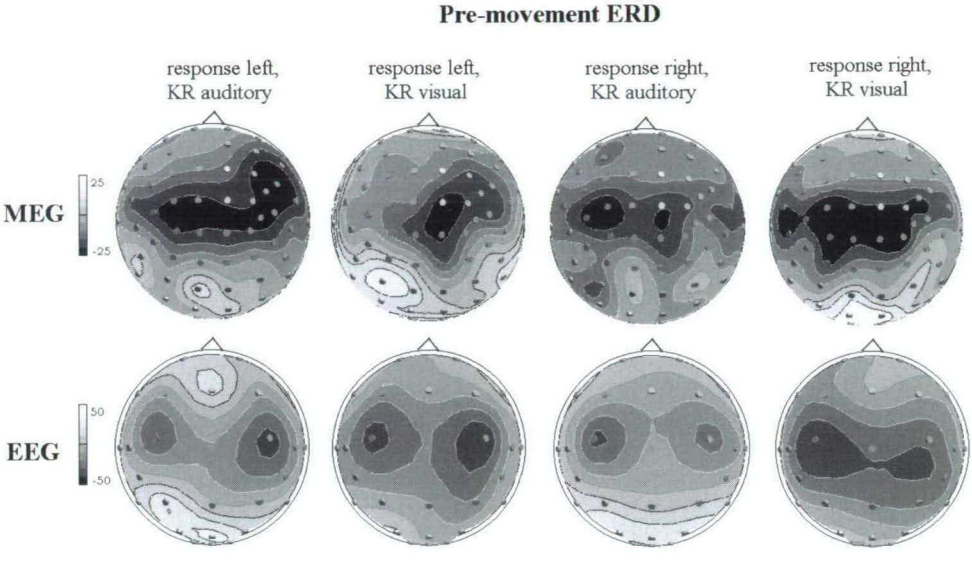

Figure 7.2 Grand average (n=5) premovement ERD maps in the 8-12 Hz frequency band, for all 4 conditions. The top row presents the ERD on MEG data, the bottom row the ERD on EEG data. ERD, or power decrease, is depicted in dark gray surrounded by white contour lines, while ERS, or power increase, is depicted in light gray, surrounded by black contour lines. The gray contour lines correspond to zero power change. Spacing of contour lines is 5 % power change for the MEG, and 10 % power change for the EEG. Scaling as indicated in the figure. Note the contralateral dominance of the pre-movement ERD, both in the EEG and MEG data.

The ERD computed on EEG data (see Figure 7.3, right-hand panel) reveals that all the subjects studied display an ERD with an occipital maximum preceding the visual KR stimulus. For all subjects, this effect is significant at both left and right occipital ROIs, irrespective of response side and frequency band (see Table 7.1). It should be noted that for subjects MF and RP the ERD preceding the visual KR stimulus is rather widespread, and is occasionally significant at left and right temporal ROIs as well. There are no clear differences in ERD between left-and right occipital ROIs. Preceding auditory KR stimuli, none of the subjects display an appreciable ERD, irrespective of response side and frequency band (see Figure 7.3 and Table 7.1). In essence the ERD results on the present EEG data are a confirmation of the results of our previous study (Bastiaansen et al., 1999).

For the MEG data the picture is more complex. Therefore we will discuss the results separately for each subject (see Table 7.1 and Figure 7.3, left-hand panel). Two of the five subjects (subjects EM and RK) show a clear modality-dependent ERD scalp distribution in

the MEG. Preceding auditory KR stimuli these subjects display a clear, focal ERD over the left and right temporal ROIs, that is highly significant for both response sides in the 8-10 Hz frequency band, and to a lesser extent in the 10-12 Hz frequency band.

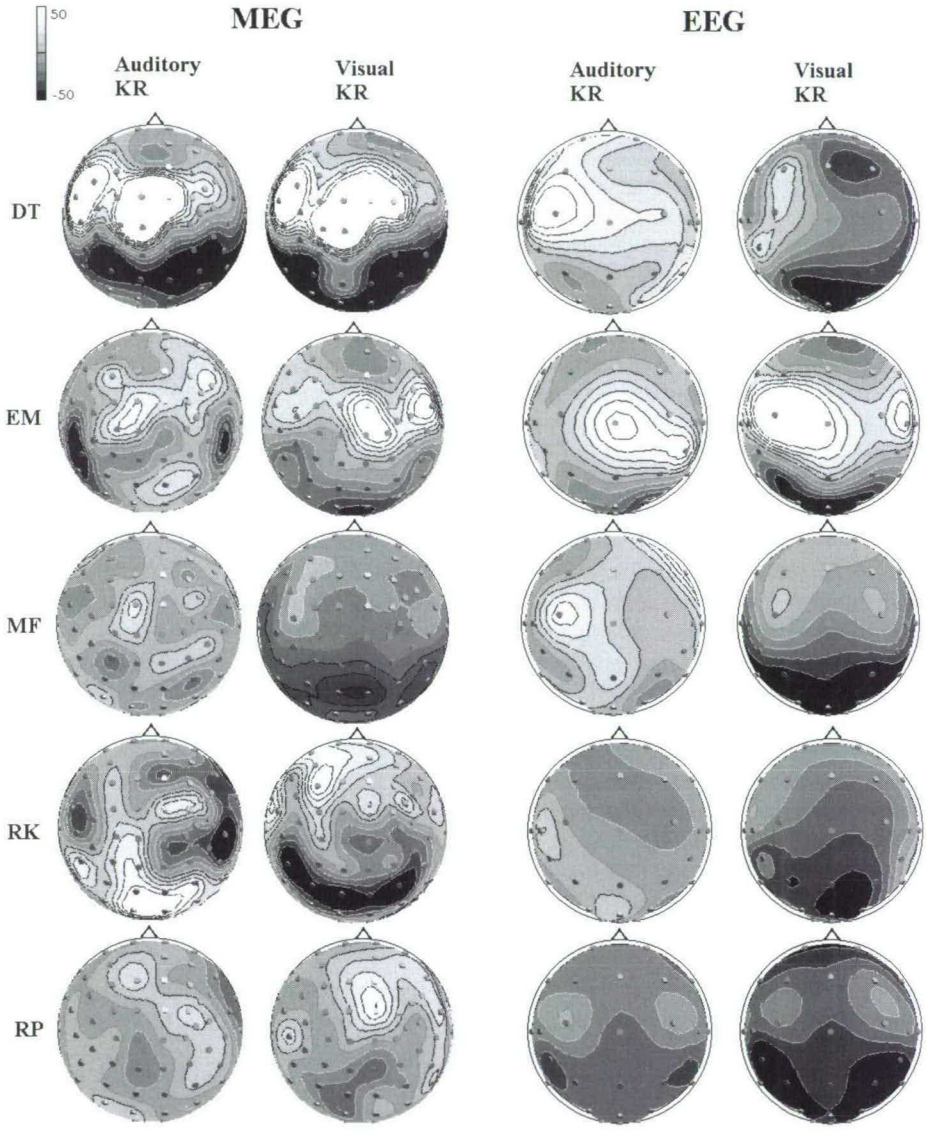

Figure 7.3 Subject averages of the ERD in the 8-10 Hz frequency band, in the last 250 ms interval preceding the presentation of the KR stimulus. Left-hand panel: ERD on MEG data. Right-hand panel: ERD on EEG data. ERD, or power decrease, is depicted in dark gray surrounded by white contour lines, while ERS, or power increase, is depicted in light gray, surrounded by black contour lines. The gray contour lines correspond to zero power change. Scaling as indicated in the figure. Spacing of contour lines is 5 % power change.

Table 7.1 Significance levels of the sign tests on the change in power from baseline interval to pre-KR interval. For each subject, results are presented separately for each response side, each frequency band and each Region Of Interest (ROI) LT: left temporal; RT: right temporal; LO: left occipital; RO: right occipital. Power decrease (ERD) : - = $p < 0.05$; -- = $p < 0.01$; --- = $p < 0.001$ Power increase (ERS) : + = $p < 0.05$; ++ = $p < 0.01$

ERD 8-10 Hz, Left- hand responses											ERD 8-10 Hz, Right- hand responses									
		MEG					EEG				MEG					EEG				
Subject	ROI → KR ↓	LT	RT	LO	RO		LT	RT	LO	RO	LT	RT	LO	RO		LT	RT	LO	RO	
DT	Aud	+		---	--						+		--	---						
	Vis			---	--			-	--	--	++		---	---				-	-	
EM	Aud	--	--								--	-							-	
	Vis			---	---			+	-	--		+	---	---			+	-	---	
MF	Aud																			
	Vis			-	-		-	-	---	---			-	-		-	-	---	---	
RK	Aud	--	--	++	++						-	---	++	++						
	Vis			-	--				--	-			-	---				--	--	
RP	Aud									-		-							-	
	Vis				-			-	---	---			-			-	-	---	---	

ERD 10-12 Hz, Left- hand responses											ERD 10-12 Hz, Right- hand responses									
		MEG					EEG				MEG					EEG				
Subject	ROI → KR ↓	LT	RT	LO	RO		LT	RT	LO	RO	LT	RT	LO	RO		LT	RT	LO	RO	
DT	Aud			-	-								-	--						
	Vis			-	--				---	---			-	---			++	--	---	
EM	Aud		-	+							-	-								
	Vis			---	---				--	--			---	---				-	--	
MF	Aud													+						
	Vis				-			-	--	--			-	-				---	-	
RK	Aud	-	-								-	--		+						
	Vis			--	-				-	-			---	--				-	-	
RP	Aud											-		++				-		
	Vis			-	-		-		-	---			--	-				-	---	

At the same time an ERS is present over both occipital ROIs that reaches significance only for subject RK. It should be noted that these effects are not present in the ERD computed on the EEG data for these two subjects. Preceding visual KR stimuli, subjects EM and RK display an ERD over both occipital ROIs, while no ERD is present over temporal sites. One subject (subject DT) shows an occipitally maximal ERD, irrespective of KR modality, response side and frequency band. Finally, subjects MF and RP show a significant ERD preceding the visual KR stimulus (although for subject RP this effect only borders on significance in the 8-10 Hz frequency band). Preceding the auditory KR stimulus subjects RP and MF do not show any ERD. For none of the subjects there are clear differences in pre-stimulus ERD between left and right hemispheres.

In order to investigate the possibility that individual differences in the ERD over the left and right temporal ROIs preceding auditory KR stimuli were caused by between-subject differences in the level of power during baseline intervals, we computed for each frequency band the absolute power (averaged over trials, conditions and response sides, and over left

and right ROIs) during all the baseline intervals, for each subject separately. Means and 95% confidence intervals (M ± 2SD) are depicted in Figure 7.4, and clearly indicate that the two subjects that display a temporal ERD preceding auditory KR stimuli (subjects EM and RK) have significantly higher levels of absolute baseline power than the subjects in which this effect is not present.

7.5 Discussion.

We investigated the event-related power changes (ERD and ERS) related to the anticipatory attention for an upcoming stimulus in the EEG and MEG of five subjects, using a paradigm in which the subjects were instructed to perform a time estimation task, and were informed about the quality of their time estimation by either an auditory or a visual KR stimulus.
The results of the ERD computed on the EEG data are a confirmation of the results from our previous study (Bastiaansen et al., 1999a). For all five subjects we investigated, an ERD with an occipital maximum was present preceding the visual KR stimuli, whereas preceding the auditory KR stimuli no ERD was found at all. It should be noted however, that in the present study the occipital ERD was strongest in the 8-10 Hz frequency band, whereas in the earlier study we found the strongest effects in the 10-12 Hz and even in the 12-16 Hz frequency bands. These differences between studies in maximally reactive frequencies may well be accounted for by the fact that we did not select frequency bands based on individual alpha peak frequencies, as is sometimes done in ERD research (e.g. Klimesch et al., 1997). Klimesch (1996, 1997) points out that individual alpha peak frequency is negatively correlated with age, and that even within a group of subjects of the same age an inter-individual difference in alpha peak of 2 Hz is quite common. We admit that our results might have been more consistent with respect to the maximally reactive frequency band, but this does not affect our finding that anticipating a visual stimulus is consistently reflected by a desynchronization of rhythmical EEG activity with a frequency of *approximately* 10 Hz over the occipital cortex, as we hypothesized on the basis of our thalamo-cortical gating model.
For the MEG, we found an occipital ERD preceding visual stimuli in all of the subjects studied. There was however a large inter-individual variability in the ERD preceding auditory stimuli: we found a clear ERD over temporal recording sites during anticipatory attention for an auditory stimulus only in two out of the five subjects. This means that in these two subjects we found the differences between EEG and MEG we expected on the basis of previous research (Niedermeyer, 1990, 1991; Tiihonen et al., 1991; Lehtelä et al., 1997; see Niedermeyer, 1997 and Hari et al., 1997 for reviews). In addition, we found significantly higher levels of absolute power in the MEG over temporal recording sites for these two subjects than for the other three subjects. Of the other three subjects, two displayed no ERD preceding auditory stimuli, while the third displayed an occipitally maximal ERD preceding auditory stimuli.
The main question is then, why did we find evidence for anticipatory attention for the auditory stimuli only in two out of five subjects? To (at least partially) answer this question we have to take into consideration that in these two subjects we found a larger level of absolute power over the temporal cortex. An explanation then might be that only these two subjects had a well-developed tau rhythm, or that only in these two subjects the generators of the tau rhythm were oriented in such a way (namely tangentially to the cortical surface) that their activity could be measured with the MEG sensors. The -relative- absence of a tau rhythm in the other three subjects might then explain the lack of desychronization in these subjects over the temporal cortex preceding auditory KR stimuli. Such a tentative explanation finds support in the results of Lehtelä et al (1997), where (the reactivity of) the tau rhythm could not be demonstrated for all subjects, although the ratio of 8 out of 9 was much higher in the latter study. An important difference between the results of the present study and those of

Lehtelä et al. (1997) is that we did not find evidence for a right-hemisphere dominance in the reactivity of the tau rhythm. It is unclear at present what might have caused these differences. In any case the data provide supportive evidence for the existence of a 'tau' rhythm that is suppressed when the auditory cortex engages in active processing (cf. Tiihonen et al., 1991; Hari, 1993, 1997; Lehtelä et al., 1997) or, as in the present study, in anticipatory attention. The results are also in line with the idea that scalp-recorded EEG is not suited to measure rhythmic activity originating from the temporal cortex, as has been demonstrated by Niedermeyer (1990, 1991).

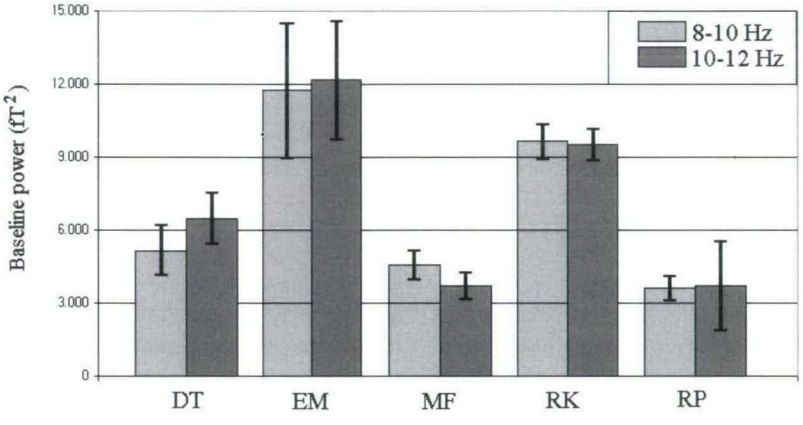

Figure 7.4 Means and 95 % confidence intervals (mean ± 2 times the standard deviation) of absolute power of the MEG averaged over both temporal ROI's during the baseline interval, for the 8-10 Hz and 10-12 Hz frequency bands separately. For each subject, means and confidence intervals are computed over conditions, response sides, and averaged over left and right temporal ROIs. Note that the baseline power for subjects EM and RK is significantly larger than for the other subjects.

However, for the present purpose the most important conclusion is that the data support the notion that anticipatory attention in the auditory modality can be detected by studying the patterns of synchronization and desynchronization of 10 Hz rhythmical activity of the MEG, at least in some subjects. Anticipatory attention in the visual modality on the other hand can be demonstrated both with EEG and with MEG. The combined results of this and the previous study are for a large part in accordance with the predictions of the neurophysiological model of anticipatory attention that we have described elsewhere (e.g. Brunia, 1999; Bastiaansen et al., 1999b).

In order to establish a firmer experimental basis for our neurophysiological model for anticipatory behavior, a number of issues have yet to be clarified. First, just as differences in movement parameters have been shown to influence reactivity of EEG and MEG (e.g. Salmelin et al., 1995; Pfurtscheller et al., 1998), it has to be established whether differences

in stimulus parameters will have an effect on the pre-stimulus ERD. For example, we would expect that pre-stimulus ERD is larger preceding degraded stimuli than preceding normal stimuli, because degraded stimuli are more difficult to perceive and thus will require more anticipation. This would be convincing evidence for the notion that the pre-stimulus ERD we have reported here truly reflects anticipatory attention. Furthermore, demonstrating anticipatory attention in the somatosensory modality would be the obvious complement to the experiments we carried out up until now, that addressed only the auditory and visual modalities. The spatial proximity of the motor and somatosensory cortices have made it difficult in the past to separate post-movement activity from pre-stimulus activity in this modality in our time estimation paradigm, especially with slow potential research. Results of recent experiments comparing 10 Hz and 20 Hz rhythms generated in the motor and somatosensory cortices suggest that there may be a qualitative difference between these two frequency components (e.g. Salmelin and Hari, 1994; Salmelin et al., 1995). With the frequency-based functional segregation of motor and somatosensory rhythms proposed by these authors the way may now be open to study anticipatory attention to somatosensory stimuli without running the risk of confounding post-movement processes with pre-stimulus processes in the time estimation paradigm employed in the present study.

Chapter 8. Tangential derivative mapping of axial MEG applied to event-related desynchronization (ERD) research[1].

8.1 Abstract.

A problem with the topographic mapping of MEG data recorded with axial gradiometers is that field extrema are measured at sensors located at either side of a neuronal generator instead of at sensors directly above the source. This is problematic for the computation of event-related desynchronization (ERD) on MEG data, since ERD relies on a correspondence between the signal maximum and the location of the neuronal generator.

We present a new method based on computing spatial derivatives of the MEG data. The limitations of this method were investigated by means of forward simulations, and the method was applied to a 150-channel MEG dataset.

The simulations showed that the method has some limitations. (1) Fewer channels reduce accuracy and amplitude. (2) It is less suitable for deep or very extended sources. (3) Multiple sources can only be distinguished if they are not too close to each other. Applying the method in the calculation of ERD on experimental data led to a considerable improvement of the ERD maps.

The proposed method offers a significant advantage over raw MEG signals, both for the topographic mapping of MEG and for the analysis of rhythmic MEG activity by means of ERD.

8.2 Introduction.

Event-Related Desynchronization (ERD, Pfurtscheller and Aranibar, 1977) is a technique used to quantify the spatiotemporal evolution of event-related changes in oscillatory EEG activity. ERD has proved to be a sensitive indicator of cortical activity in movement-related brain research as well as in cognitive brain research (cf. Pfurtscheller and Lopes da Silva, 1999, for a comprehensive review of the state of the art of ERD research). Because of the inherently better spatial resolution of MEG signals as compared to EEG, and because of the differential sensitivity of EEG and MEG for radial and tangential dipoles, it would be desirable to apply the ERD technique to MEG measurements as well. There is, however, a problem with the straightforward computation of ERD on certain types of MEG data. Many modern MEG systems use pickup coils that are sensitive to the component of the magnetic field which is approximately normal to the head surface. Such pickup coils may be axial gradiometers, or magnetometers that have an axial orientation with respect to the scalp. As a consequence, a dipole at a given location will produce maximum signal at either side of the dipole, while just above the source the signal will be zero. This is depicted in Figure 8.1. ERD mapping relies on a reasonable correspondence between the maximum signal and the location of the activated brain area. Since the extrema of the normal components of the magnetic field can be quite distant from the location of the activation, the interpretation can be difficult.

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[1] This chapter is an extended version of a paper with identical title by M.C.M. Bastiaansen and T.R Knösche, which has been accepted for publication in Clinical Neurophysiology on February 2nd, 2000.

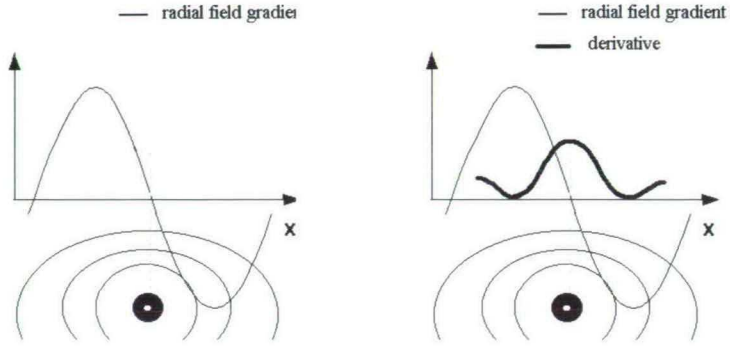

Figure 8.1 Schematic, two-dimensional representation of the magnetic field as measured by axial gradiometers. The x-axis represents the plane connecting all sensors. The y-axis represents magnetic flux: positive values represent influx, negative values represent outflux, zero corresponds to no magnetic flux. Below the x-axis a dipole is depicted that points out of the page (solid black circle), surrounding ovals represent isoflux lines. Left hand panel: The radial field gradient (i.e., the signal measured by axial gradiometers) is maximal at either side of the source, and zero above the source. Right-hand panel: the spatial derivative of the radial field gradient is a signal whose maximum corresponds to the position of the dipole.

With MEG systems that use so-called planar gradiometers (where the pick-up coil and the compensation coil are in the same plane, which is tangential to the scalp surface) this problem does not arise. Here, a dipole at a given location produces maximal signal at the sensors overlying it. Therefore MEG measured with planar gradiometers is well suited for topographic analyses such as ERD. It has been shown that ERD (or, more precisely, Temporal-Spectral Evolution, (TSE, Salmelin and Hari, 1994), a method that uses a slightly different way of quantifying changes in oscillatory activity) can be successfully applied to 'planar' MEG data (see Hari and Salmelin, 1997, for a review). This has, amongst others, led to new insights about the nature and the generators of the mu and beta rhythms (e.g. Salmelin et al., 1995), and has revealed the existence of 10 Hz rhythmic activity originating from the auditory cortex. (Tiihonen et al., 1991; Lethelä et al., 1997). These findings demonstrate that ERD analyses on MEG data do have an added value compared to ERD analyses on EEG data.

In the present paper we propose a solution to the problem of computing ERD on MEG data recorded with an axial gradiometer system. We have developed a method that is based on computing spatial derivatives of the recorded MEG. ERD can then be computed on the spatial derivatives instead of on the untreated MEG. We will present results from forward simulations that will give us an indication of the limitations and possibilities of the proposed method, and we will apply it in the calculation of ERD on a 150-channel MEG dataset in order to evaluate its usefulness in ERD research.

8.3 Methods.

Computation of MEG derivatives.

The normal component of the magnetic field, which is measured by axial gradiometers or magnetometers is considered a scalar field on a surface defined by the sensor array: $B(u,v)$.

The local coordinates u and v are locally tangential and mutually orthogonal. The gradient of *B* denotes the direction and the steepness of the slope of *B* within the sensor surface:

$$\nabla B(u,v) = (\partial B/\partial u, \partial B/\partial v)^T \qquad \text{(Eq. 8.1)}$$

The steepness of the slope of *B(u,v)*, i.e. the density of contour lines in a contour plot, is the measure we want to express (see Figure 8.1). The reason for this is that the field gradient is largest just above the generator (cf. Figure 8.2a). Therefore, the new measure is defined as the Euclidian norm of the abovementioned gradient:

$$\| \nabla B(u,v) \| = \text{sqrt}((\partial B/\partial u)^2 + (\partial B/\partial v)^2) \qquad \text{(Eq. 8.2)}$$

The derivatives are computed using a 3D spline interpolation of *B(u,v)*.
Spatial derivatives, no matter whether computed or directly measured using planar gradiometer arrangements, work as spatial high-pass filters. This has several consequences. First of all, the signal-to-noise ratio (SNR) is decreased. Hence, if a spatial derivative is applied, we have to make sure that the SNR is not too poor initially. Furthermore, suitable regularization should be applied to the derivation procedure. A second consequence of using a derivative is that sharp, distinct features in the signal are favored over smoother structures. That means, the method is expected to be particularly sensitive to focal and superficial sources.

Simulations.
For the simulations we used a spherical head model. Test source configurations were used to simulate MEG measurements. Then the spatial derivatives of the MEG were computed with the software package ASA (A.N.T. Software B.V., the Netherlands).
Seven simulation parameters were systematically varied: [1] relative source depth as distance between sensors and source divided by the distance between sensors and the middle of the head (0.36, 0.52, 0.68), [2] number of sources (1 and 4), [3] distance between two sources (4 cm and 10 cm), [4] the mutual orientation of multiple sources (see figure 8.2c), [5] focality of the sources (focal sources and current sheets of extent 1 cm^2, 2 cm^2, 3cm^2, and 6cm^2), [6] Signal-to-noise ratio (SNR)[2] defined as signal maximum divided by the standard deviation of the noise (20, 10, 5, 2, 1), and [7] number of sensors (64 and 150). Simulations with noise were repeated 20 times with different noise realizations. A result was considered stable if the maxima of the derivative map could be correctly identified for all noise realizations.

MEG recordings and experimental set-up.
For the MEG recordings a 150-channel whole-cortex MEG system (CTF Systems Inc., Vancouver, Canada) was used. The axial gradiometers (2 cm coil diameter and 5 cm baseline) are uniformly distributed on the helmet surface with mean spacing of 3.1 cm.
Six healthy, paid volunteers participated in the experiment. They were seated in a dimly illuminated, sound-attenuating and magnetically shielded chamber, and were asked to perform simple self-paced flexions of the index finger, with a rate of approximately 4-6 movements per minute. For each subject, approximately 100 MEG epochs from 3000 ms pre-movement to 3000 ms post-movement were digitized at 250 Hz, and stored for off-line analysis. Filter settings were from DC to 45 Hz, with additional notch filters at 50 and 60 Hz.

[2] Along the rules of elementary mathematics, the average of a set of derivatives is equal to the derivative of the average. Therefore in the simulations we used SNR values that are typical for MEG data averaged over epochs: although for ERD computation the derivatives are computed at the single epoch level, the ERD is subsequently averaged over epochs.

For each subject, we determined the position of the sensors relative to the subject's head on the basis of three head localization coils attached to the nasion and both pre-auricular points. Subsequently, we computed the average of the sensor positions for all subjects, and interpolated all the MEG data to these average sensor positions using the algorithm developed by Hämäläinen and Ilmoniemi (1994). The data were visually inspected for eye-movement and other artifacts, and contaminated epochs were discarded from further analysis. From the remaining epochs two datasets were created: one time-locked to movement onset for the computation of the pre-movement ERD, and the other time-locked to movement offset for the computation of the post-movement ERS.

ERD computation.

The movement onset data were filtered in the 8-12 Hz band, and the movement offset data were filtered in the 17-23 Hz band. Next, MEG derivatives were computed using the method described above. This step was performed after the filtering, because using the absolute values of the derivatives (which is necessary in order to avoid cancellation of gradients with opposite signs) changes the frequency content of the MEG signal. The subsequent steps were performed both on the untreated, filtered MEG and on the derivatives of the filtered MEG. The data were squared, and averaged over intervals of 250 ms. For each subject data were averaged over trials, and ERD was computed as the percentage power increase (Event-Related Synchronization, ERS) or decrease (Event-Related Desynchronization, ERD) for a particular time interval in a particular frequency band, relative to a pre-movement reference interval.

8.4 Results.

Simulations.

A first set of simulations, investigating the influence of the spatial sampling (number of sensors), noise, and source depth on the detectability of focal sources revealed that both tested sensor configurations were capable of detecting a single dipole. However, lower sampling resolutions decrease the accuracy of the exact peak location. Due to the undersampling with only 64 sensors, the rather sharp peak above the source location cannot be properly reconstructed by the spline interpolation, reducing its amplitude. Since we define the SNR as the ratio of the peak of the signal amplitude and the standard deviation of the noise, this effectively diminishes the SNR, which explains the poorer correspondence between the location of the source and the maximum of the MEG derivative (see Fig. 8.2a). Moreover, we noticed that for very deep dipoles, side maxima occur. This is readily explainable, since the source is now evenly near to more than one region of the sensor array. Due to the low amplitude of signals from the depth (for 150 channels, the signal amplitude produced by a source at a relative depth of 0.68 is less than 10 % of that produced by a source at a relative depth of 0.36), these artifacts will be masked by noise and more prominent superficial activity in most practical cases. Additionally, the SNR necessary for the detection of a single source increases with depth (see Fig. 8.2b), adding to the relative invisibility of deeper sources. These effects also underline the necessity of a small distance between head surface and sensors, especially near the brain regions of interest. Note that for the performance of the derivative method, the relative depth, i.e. the distance between sensors and source divided by the distance between the sensors and the middle of the head, is relevant. This value is influenced not only by the anatomical location of the source, but also by the sizes of the head and the sensor array. In a small head, all sources appear deeper.

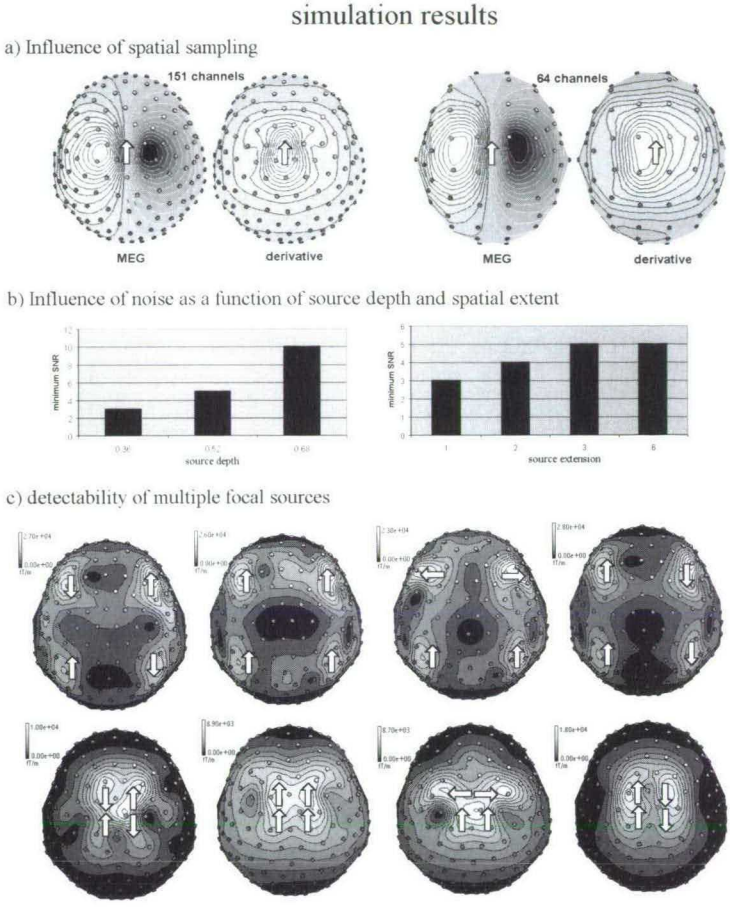

Figure 8.2 Results of the forward simulations. a). Maps of untreated MEG and of spatial derivatives for 64 and 150 sensors. White arrows indicate the position of the generating source. b). Critical values of SNR at which sources can still be reliably identified, presented separately for different source depths (left) and different source extensions (right). c). Maps of MEG derivatives showing the detectability of muliple focal sources for different source configurations. Arrows represent source locations and orientations.

In a second set of simulations, the influence of noise on the localisability of extended sources is explored using a 151- channel sensor set. The tangential extent of a (superficial) source had a smaller effect than expected. The SNR necessary to localize the centre of mass of the source reliably was similar to the value found with a focal source, except for the 6 cm^2 generator. In this case, e.g. if the cortex of an entire lobe is active, an SNR of 8 was necessary (see Figure 8.2b).

The third set of simulations dealt with the detection of multiple focal sources. In Figure 8.2c, the used source configurations are depicted. They involve different mutual orientations and distances. The simulations revealed that mutual distances of a few centimetres (here 4 cm) do not allow for a reliable resolution. However, multiple sources in different brain regions can be distinguished.

Experimental data.

As a first step, in order to determine whether quality of the experimental data is sufficient for the use of the proposed method, we determined the SNR separately for the movement-onset data and for the movement-offset data. For both datasets, the SNR was 4.5, which according to the simulation results (cf. Figure 8.2b) should be sufficient for a successful application of the derivatives method. In Figure 8.3 the ERD and ERS on untreated MEG and on MEG derivatives is presented. When comparing both methods, three things should be noted. First, the location of the maximal ERD on untreated MEG data shows quite some variability over time, whereas the ERD on MEG derivatives has a high degree of spatial stability. This was verified by computing a measure of topological change between successive ERD time intervals, defined as 1 – absolute(correlation (map1, map 2)). A comparison of this measure between the ERD maps computed on the untreated MEG and on MEG derivatives, both for the pre-movement ERD and for the post-movement ERS (see Figure 8.4a) confirmed the higher spatial stability of the ERD on MEG derivatives . Second, visual inspection of Figure 8.3 indicates that both the pre-movement ERD and the post-movement ERS on MEG derivatives are more focal than the ERD/ERS on the untreated MEG. Moreover, the early (1000 to 500 ms pre-movement) ERD on the untreated MEG shows two maxima, roughly located at either side of the hand motor area, while the ERD on MEG derivatives shows only one focus which lies in between these maxima, and which nicely corresponds to the motor hand area. This is even more clearly seen in the post-movement ERS. Note that this phenomenon occurs also at the level of single-subject averages. In order to quantify the gain in focality resulting from the use of the MEG derivative, we computed the Global Field Power (GFP; Lehmann, 1971; see also Skrandies, 1995) for each ERD time interval, both for the pre-movement ERD and the post-movement ERS. As Figure 8.4b illustrates, the GFP was indeed larger for the ERD on MEG derivatives for all ERD time intervals but one. Finally, just prior to as well as during the movement, the ERD on MEG derivatives reveals the bilateral ERD over both motor cortices that was expected on the basis of the results usually described in the literature (see e.g. Pfurtscheller and Berghold, 1989, and Salmelin et al., 1995 for a description of this effect on EEG and MEG data, respectively). In contrast, with untreated MEG, the two peaks are mislocated at much more medial sites over the frontocentral midline.

8.5 Discussion.

The simulations showed that the method has some limitations, the most important being the requirement that simultaneously active sources should be at more than 4 cm apart in order to be detected. Furthermore, the method is less suited for deep sources. Finally a dense sensor array increases the localization accuracy and the signal-to-noise ratio. Applying the method as a first step in the calculation of ERD on experimental MEG data led to a higher spatial stability, and a more focal ERD and ERS that corresponded better to the hand motor areas for the MEG derivatives than for the untreated MEG.

These results indicate that it is possible to produce virtual planar MEG gradiometers from axial MEG data, which is particularly valuable for studying ERD/ERS effects. This method may also be useful for mapping axial MEG data in general. ERD of axial MEG signals has recently been the focus of interest of other research groups as well, and other methods for the calculation of ERD on MEG data are currently being developed (Edlinger et al., 1999, Babiloni et al., 1999). These methods aim at an integration of EEG and MEG by means of inverse linear estimation (LE) procedures (Edlinger et al. 1999), that can further be extended with fMRI-based constraints (Babiloni et al., 1999).

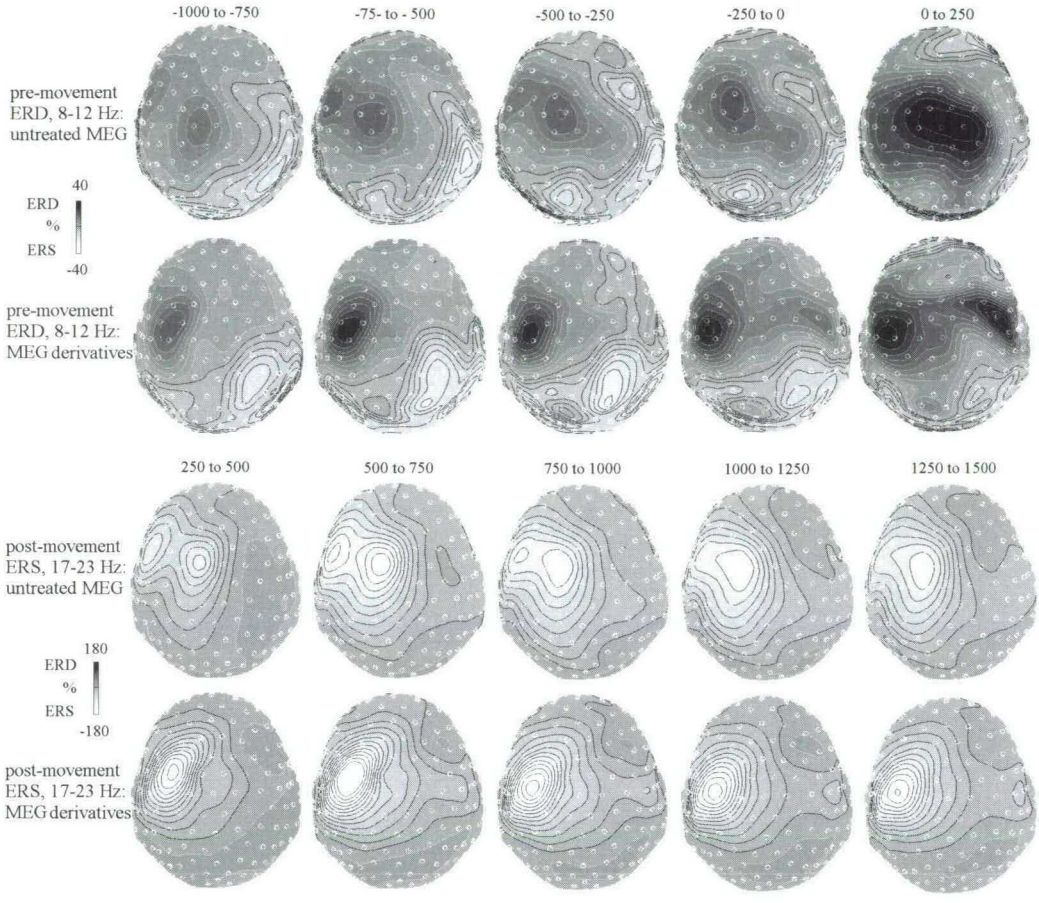

Figure 8.3. Grand averages (N=6) of pre-movement ERD in the 8-12 Hz frequency band (top rows) and post-movement ERS in the 17-23 Hz frequency band (bottom rows), on untreated MEG and on MEG derivatives. ERD, or power decrease, is depicted in dark gray surrounded by white contour lines, while ERS, or power increase, is depicted in light gray, surrounded by black contour lines. The gray contour lines correspond to zero power change.

The main advantage of using LE on a combination of EEG and MEG over the method proposed in the present paper is that LE makes optimal use of the complementary information that is present in EEG and MEG. Future research should point out whether this results in a significant enhancement of the spatial resolution of ERD. A practical problem of these methods is that they require the availability of simultaneously recorded EEG and MEG, and of structural MRI scans for the generation of realistic volume conduction models, while the method proposed by Babiloni et al. (1999) additionally requires availability of fMRI facilities. If such facilities are not available, the presently proposed method may be a valuable tool for investigating ERD on MEG data recorded with axially oriented magnetometers or axial gradiometers.

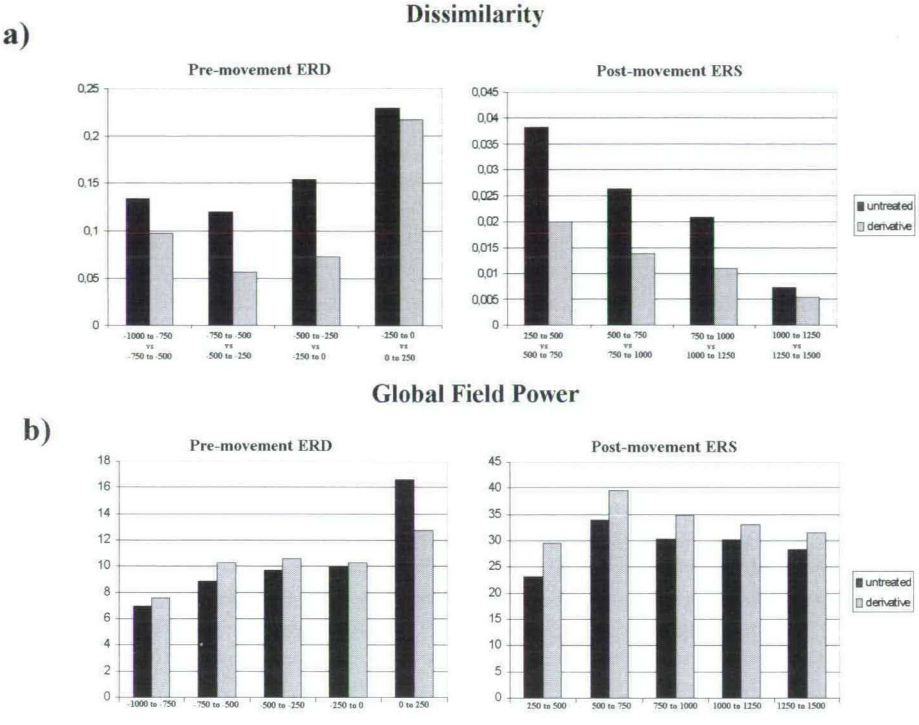

Figure 8.4 a) Dissimilarity between successive ERD time intervals, for the untreated MEG and for the MEG derivatives, both for the pre-movement ERD (left-hand diagram) and for the post-movement ERS (right-hand diagram). The dissimilarity, which is defined as 1 – absolute(correlation(map1, map2)), is larger for the ERD on untreated MEG in all comparisons. This confirms that the ERD on MEG derivatives has a higher spatial stability, as a visual inspection of Figure 8.3 suggested. b) Global Field Power for all ERD time intervals for the untreated MEG and for the MEG derivatives, both for the pre-movement ERD (left-hand diagram) and for the post-movement ERS (right-hand diagram). The Global Field Power is larger in the ERD on MEG derivatives in all time intervals but one, which supports the notion that the ERD on MEG derivatives is more focal than the ERD on untreated MEG.

The ERD analyses on the MEG data presented in Chapter 7 have been performed on the untreated MEG data. It is therefore important to address the question of whether the presently developed method has implications for the validity of the results of the analyses presented in Chapter 7. The spatial derivatives method presented in the present chapter has been tentatively applied to the MEG data of Chapter 7. Unfortunately this led to uninterpretable results. Most probably this is due to a combination of the lower spatial sampling (only 64 MEG sensors) and the lower signal-to noise ratio (between 2.2 and 2.8, depending on the specific subject) of the MEG data presented in Chapter 7. Although independently a lower number of sensors and a lower SNR should be just acceptable (See Figure 8.2a, and 8.2b,

respectively), the combination of the low SNR and the small number of sensors is fatal for the spatial derivatives method. However, the fact that the presently developed method could not be applied to the MEG data of Chapter 7 does not invalidate the results presented there. Although using the new method leads to a spatial enhancement of the ERD, inspection of Figure 8.3 shows that the maxima of the ERD on untreated MEG data still roughly correspond to the location of the source (for the data of Figure 8.3 this is the hand representation area in the motor cortex). Since the crucial comparisons in Chapter 7 were between the - spatially distant - temporal and occipital areas, the interpretation of the results remains unchanged. It may be expected however that, had it been possible to compute the ERD on the MEG derivatives, the exact location of the ERD and ERS maxima of the MEG data of Chapter 7 would have corresponded better to the 'true' ERD and ERS generator sites. Finally, it seems unlikely that either less or more subjects would have showed the bilateral temporal ERD if the spatial derivatives method could have been used. The reason for this is that the application of the new method in the computation of ERD, as compared to the computation of ERD without spatial derivatives, does not introduce additional ERD phenomena, nor does it lead to the disappearance of existing phenomena, as can be seen in Figure 8.3. In sum, although the ERD on the MEG data of Chapter 7 might have showed more focal, and more spatially stable effects if it had been possible to use the spatial derivatives method, it can be assumed that the general pattern of results would have remained the same, since the crucial comparisons in Chapter 7 involved spatially distant areas (temporal vs. occipital).

Chapter 9. ERD as an index of anticipatory attention? Effects of stimulus degradation[1].

9.1 Abstract.

Previous research has suggested that the Stimulus-Preceding Negativity (SPN) is independent of stimulus modality. In contrast, the scalp topography of the Event-Related Desynchronization (ERD) related to the anticipation of stimuli providing Knowledge of Results is modality-dependent. These findings, combined with functional SPN research, lead to the hypothesis that anticipatory ERD reflects anticipatory attention, while the SPN depends on the affective-motivational properties of the anticipated stimulus. In order to verify this, 12 subjects performed a time estimation task, and were informed about the quality of their time estimation by an auditory or a visual stimulus providing Knowledge of Results (KR). The KR stimuli could be either intact or degraded.

Auditory degraded KR stimuli were less effective than other KR stimuli in guiding subsequent behavior, and were preceded by a larger SPN. As expected, preceding auditory KR stimuli no ERD was present, while preceding visual stimuli an occipital ERD was found. The latter was larger preceding intact than preceding degraded stimuli. It is concluded that the data largely support the interpretation of the pre-KR SPN as a reflection of the anticipation of the affective-motivational value of KR stimuli, and of the pre-stimulus ERD as a perceptually based anticipatory attention process.

9.2 Introduction.

Anticipatory behavior is directed at a predictable, upcoming event. It serves the goal of a faster or more efficient information processing as would have been possible without anticipation. If the event in question is an action, or sequence of actions, the process would be termed motor preparation. If the event is a stimulus, the process would be termed anticipatory attention. In our view, the neurophysiological basis of anticipatory behavior lies in a modulation, at the thalamic level, of the transmission of information from sensory afferents (for anticipatory attention) or subcortical motor structures (for motor preparation) through the thalamus to the relevant cortical areas. In other words, we propose that anticipatory attention is realized through a thalamo-cortical gating mechanism (see e.g. Brunia, 1993, 1999; Bastiaansen et al., 1999b) for detailed descriptions of the proposed neurophysiological model).

The present paper focuses on the sensory aspect of anticipatory behavior, that is, the anticipatory attention for an upcoming stimulus. Our neurophysiological model for anticipatory behavior predicts that anticipatory attention manifests itself as a cortical activation *preceding* the presentation of stimuli, which is restricted to the cortical area corresponding to the modality of the stimulus. This cortical activation serves the function of presetting the necessary physiological processes in the sensory cortex, in order to achieve a faster and/or more efficient processing of the upcoming sensory input. Two EEG measures might be appropriate for revealing cortical activation. (1) Negative slow potentials, which stem from a predominance of excitatory post-synaptic potentials at the dendrites of cortical pyramidal neurons, leading to a subthreshold depolarization of these cells and a concurrent

[1] This chapter is the final version of a paper with identical title by M.C.M. Bastiaansen, K.B.E. Böcker and C.H.M. Brunia, which has been submitted to Psychophysiology on April 17th, 2000.

increase in the readiness of these cells to fire (Birbaumer et al., 1990). (2) Desynchronization of the EEG over the activated cortex, reflecting a disruption of synchronized activity in functionally related groups of cortical neurons (Steriade et al., 1990; Lopes da Silva, 1991). This can be seen as a transition of cortical idling to cortical activity .

In the last two decades, much attention has been devoted in our laboratory at identifying slow negative potential shifts related to the anticipation of sensory input. To this end, a paradigm has been developed in which subjects are asked to perform a time estimation task, and are subsequently informed about the quality of their time estimation by a stimulus providing Knowledge of Results (KR; Damen and Brunia, 1987). Preceding the KR stimulus, a negative slow potential can be recorded that has been termed the Stimulus-Preceding Negativity (SPN). Subsequent research has been aimed at clarifying the functional significance and neuroanatomical substrates of the SPN. Since detailed reviews have been presented elsewhere (e.g. Van Boxtel, 1994; Böcker and Van Boxtel, 1997), we will discuss only the main results of these studies here. If the SPN is a purely perceptual anticipatory process, one would expect the SPN (1) to be independent of the type of information conveyed by the anticipated stimulus, and (2) to be maximal, or at least clearly distinguishable over the sensory cortex corresponding to the modality of the stimulus.

Ad (1). The SPN has been found prior to three types of stimuli. (1) KR stimuli (e.g. Grünewald et al., 1984; Damen and Brunia, 1987; Brunia and Damen, 1988; Chwilla and Brunia, 1991a; Damen and Brunia, 1994; Böcker et al., 1994c). In this case, the SPN usually has a parietal maximum and a right-hemispheric preponderance. (2) Instruction stimuli, transmitting information about a future task (e.g. Gaillard and Van Beijsterveld, 1991; Rösler, 1991; Damen and Brunia, 1994; Van Boxtel, 1994; Van Boxtel and Brunia, 1994). In this case the SPN has a parietal maximum, is bilaterally symmetrical, and is much smaller than the pre-KR SPN. (3) Probe stimuli, with which the outcome of a previous task has to be matched (e.g. Ruchkin et al., 1988; Chwilla and Brunia, 1991b, 1992). In this case the SPN again has a parietal maximum, but a left-hemispheric dominance is found. In sum, the amplitude and lateralization of the SPN vary with the type of stimulus that is anticipated.

Ad (2). The SPN has been recorded prior to auditory and visual stimuli. However, only two studies have directly compared its scalp distribution as a function of stimulus modality in a within-subjects design. The first study, by Grünewald et al. (1984, experiment B), reported no differences in SPN scalp topography between auditory and visual stimuli. However, in this study, which mainly addressed the right-hemispheric dominance of the SPN, only two precentral and two parietal electrodes have been used. Since modality-specific differences would be expected to occur mainly over temporal and occipital areas, this severely limits the value of the results as far as scalp topography is concerned. The second study, by Böcker et al. (1994c) used a larger set of electrodes (that is, 23) approximately equally distributed over the entire scalp. Although the SPN was larger preceding auditory stimuli, there was a striking similarity in scalp topography of the SPN for the two modalities: both had a frontotemporal maximum. In sum, although in a recent experiment carried out in our laboratory we found a small but significant difference in SPN scalp topography preceding auditory and visual KR stimuli in the expected direction (Brunia, personal communication), the results do not support the hypothesis that the SPN is maximal over the sensory cortex corresponding to the modality of the anticipated stimulus.

The available experimental evidence does not support the notion that the SPN primarily reflects (perceptual) anticipatory attention for an upcoming stimulus. This leaves the question of what kind of processes are reflected by the SPN. Since the SPN differs with the type of stimulus anticipated, it appears reasonable to hypothesize that the SPN mainly reflects the presetting of cortical areas specifically related to the execution of the task at hand rather than the presetting of the sensory cortex. This suggests that the SPN is not a unitary phenomenon.

If we consider the types of stimuli that evoke an SPN, two of the three stimulus types (KR stimuli and probe stimuli) evaluate the past performance of the subject. Therefore, it could be argued that these two instances of 'the' SPN reflect the anticipation of affective-motivational stimuli. Support for this interpretation comes from three studies. First, Kotani et al. (1999) performed an EEG study using the time estimation + KR paradigm, in which they manipulated the motivational and the affective value of the KR stimulus independently. Motivation was manipulated by introducing monetary rewards for each correctly timed movement in one condition, while affect was manipulated by presenting the KR indicating a wrong time estimation as pure tones vs. aversive noise. Higher motivation led to larger SPN amplitudes, while the affective manipulation did not influence SPN amplitude. Second, Böcker et al. (1994c) have constructed a spatiotemporal dipole model of the pre-KR SPN. In this model, a large part of the pre-KR SPN, regardless of stimulus modality, could be explained by a bilateral pair of frontotemporal dipoles that probably represent activity of the Insulae Reili. This is a bilateral cortical structure buried within the Sylvian fissure, which is assumed to be involved in the affective-motivational coloring of stimuli (Mesulam and Mufson, 1985). Third, Brunia et al. (2000) performed a PET study, using the time estimation + KR paradigm. They compared conditions with false KR to conditions with true KR (note that the subjects were informed about the status of the KR stimuli beforehand). Next to a prefrontal and posterior parietal activation, these authors also found activation of the posterior part of the Insulae Reili, therewith supporting the results of the dipole modeling study of Böcker et al. (1994c). Together, these three studies suggest that the SPN preceding stimuli that evaluate past performance (such as KR stimuli, or probe stimuli with which the outcome of a previous task has to be matched) reflects the anticipation of the affective-motivational aspects of the stimulus rather than perceptual anticipatory attention. This is in agreement with more general suggestions by Simons (1984) and by Rockstroh et al. (1989) that affective-motivational factors are of critical importance for the emergence of negative slow potentials in the absence of a motor response.

Another candidate for identifying an activation of the sensory cortex during anticipatory attention for an upcoming stimulus is EEG desynchronization, as we mentioned above. EEG desynchronization can be quantified by a technique known as Event-Related Desynchronization (ERD, Pfurtscheller and Aranibar, 1977). This technique may be more appropriate to study anticipatory attention, since the same interactions between the thalamic reticular nucleus, the thalamo-cortical relay nuclei and the cortex that are thought to underlie the mechanism of anticipatory attention (Brunia, 1999) also form the neural basis of ERD measures (e.g. Steriade et al., 1990; Lopes da Silva and Pfurtscheller, 1999). To investigate this, the SPN data of the Böcker et al. (1994c) study were re-analyzed with the ERD technique (Bastiaansen et al., 1999a). The results showed an ERD preceding visual KR stimuli that was maximal over occipital electrode positions, whereas preceding auditory KR stimuli no appreciable ERD was found. In addition, there was no ERD at frontal sites preceding the KR stimulus. Based on these results a number of conclusions could be drawn. First, the ERD preceding visual KR stimuli indicates a pre-stimulus activation of the visual cortex, just as our gating model predicts. Second, there were clear differences in the scalp topography of the pre-stimulus ERD as a function of stimulus modality, which again was predicted by our model. Third, however, we did not find any sign of anticipatory attention in the auditory modality. Finally, the absence of a frontal component in the pre-KR ERD suggests that the ERD is independent of the affective-motivational value of the stimulus.

A possible explanation of the absence of the expected bilateral temporal ERD preceding auditory stimuli might be that rhythmic activity from the auditory cortex cannot be measured with scalp-recorded EEG, as has been demonstrated by Niedermeyer (1990, 1991, see also Niedermeyer, 1997 for a review). Instead, with MEG it is possible to record such a rhythm,

which has been termed the tau rhythm (Tiihonen et al., 1991; Lehtelä et al., 1997; see Hari et al., 1997, for a review). If this was the reason for the absence of an ERD over the auditory cortex preceding the auditory KR, then this effect should be present in MEG data. In a subsequent study we therefore investigated the ERD both on EEG and on MEG data during the anticipation of auditory and visual KR stimuli (for a preliminary report on the MEG data, see Bastiaansen et al., 1999b; detailed analyses of both EEG and MEG are presented in Bastiaansen et al., 2000). In two out of the five subjects studied, we found a bilateral temporal ERD preceding auditory KR stimuli in the MEG that was not present in the EEG. These two subjects also had a larger level of absolute power at the MEG sensors overlying the auditory cortex than the other three subjects, suggesting a well-developed tau rhythm only for the two subjects displaying the temporal ERD. We concluded that this study provided at least partial evidence for anticipatory attention in the auditory modality.

The main purpose of the present paper is to further elucidate the functional significance of the pre-stimulus ERD. ERD has proved to be a very sensitive measure of cortical activation in the study of movement-related brain activity, in the sense that the magnitude and scalp topography of the movement-related ERD consistently vary with movement parameters (see e.g. Pfurtscheller and Lopes da Silva, 1999 for a review). Along the same lines, we feel that if we can influence the magnitude and/or scalp topography of the pre-stimulus ERD by varying stimulus parameters, the interpretation of this phenomenon in terms of anticipatory attention would gain strength. To this end, we conducted an experiment in which subjects were asked to perform a time estimation task, and were subsequently informed about the quality of their time estimation by a KR stimulus. The KR stimulus could be either auditory or visual, and either intact or perceptually degraded.

We argued that stimulus degradation might have two effects. First, it asks for a more efficient stimulus processing in order to extract the relevant information from the KR stimulus. This implies that perceptual anticipatory attention should be more prominent preceding degraded than preceding intact KR stimuli. If the prestimulus ERD we have previously reported is a true index of perceptual anticipatory attention, one would expect the (compensatory) increase in perceptual anticipatory attention called for by stimulus degradation to be reflected in an increase in this index. Second, stimulus degradation may lead to an increase in task difficulty if the degree of degradation is such that the stimuli are not always recognized. At the behavioral level, this should be reflected in a decrease in task performance, and/or a decrease in the effectiveness of the KR stimulus in guiding the subsequent behavior (i.e., the time estimation on the next trial). Furthermore, an increase in task difficulty should affect the subject's motivation. If the SPN reflects the anticipation of the processing of the affective-motivational value of a stimulus, one would expect this to be reflected in an increase in the amplitude of the SPN (e.g. Chwilla and Brunia, 1991a; Kotani et al., 1999). This effect on the SPN amplitude should be independent of stimulus modality.

To our knowledge, the effect of stimulus discriminability upon the pre-stimulus ERD has not been investigated yet. Furthermore, the effect of stimulus discriminability on the amplitude of the SPN has been addressed only by two studies (Chwilla and Brunia, 1991b; Kotani and Aihara, 1999) that yielded contradictory results: while Chwilla and Brunia (1991b) found an increase in SPN amplitude in the degraded KR condition, Kotani and Aihara reported an decrease. On the basis of our interpretation of the SPN as a manifestation of affective-motivational anticipation, and of the pre-stimulus ERD as a manifestation of a perceptually based anticipatory attention process, we expected the following effects to occur. (1) A larger prestimulus ERD preceding degraded KR stimuli than preceding intact KR stimuli. Based on the results of previous experiments however, we expect the prestimulus ERD to occur only in the visual modality. (2) No differences in scalp topography in the SPN preceding auditory

and visual KR stimuli and (3) an increase in amplitude of the SPN preceding degraded KR stimuli compared to intact stimuli, provided that notion of increased task difficulty as a result of stimulus degradation is supported by the behavioral data.

9.3 Methods.

Subjects.

Twelve right-handed subjects, 1 man and 11 women, aged 18 - 29 (M= 21, SD = 3) participated in the experiment. All were undergraduate students. They either received course creditpoints or were paid a small fee (Dfl. 10.00, about US$ 5.00 per hour).

Design and procedure.

Subjects were seated in a dimly illuminated, sound-attenuating chamber. The experiment consisted of two tasks: a voluntary movement task and a time estimation task. In the voluntary movement task, subjects were instructed to produce rapid self-paced unilateral flexions of index finger and thumb at a slow pace (4-6 movements per minute), with either the left or the right hand. Trials were discarded from further analysis if the inter-response interval was shorter than 8.5 s. A total of 80 behaviorally correct trials were recorded for each response side.

In the time estimation task, subjects were instructed to produce a rapid unilateral flexion of index finger and thumb, 4000 ms after the onset of an auditory warning stimulus (WS; 1000 Hz, 70 dB(A), 100 ms). Two seconds after response onset subjects were informed about the correctness of the estimated time interval by either an auditory or a visual KR stimulus, that could be either intact or degraded (see below). The KR stimulus indicated whether the response was too early, correct or too late. During two initial training blocks (one with auditory KR and one with visual KR), the window defining a correct response was individually adjusted according to the algorithm described by Wetherill and Levitt (1965), so as to obtain about 60 % correct responses. This window was used in the remainder of the experiment. The time-out was set at 4750 ms after WS onset, and was followed by a KR corresponding to a response too late. Trials in which the estimated time interval was shorter than 3500 ms or longer than 4500 ms were discarded from further analysis.

A total of 80 behaviorally correct trials was recorded for each condition. The order of the 8 time estimation conditions (2 response sides * 2 KR modalities * 2 stimulus types) was randomized over subjects. The 2 voluntary movement conditions (one for each response side) always preceded the time estimation conditions, in order to prevent carry-over effects from the time estimation task to the voluntary movement task.

Responses were recorded by force transducers, mounted on both arms of the chair. The criterion force was defined as 20 % of the subject's maximum voluntary force, which was determined prior to the experiment during a unilateral tonic contraction of 3 s duration, separately for the left and right hand. Response onset was defined as the moment the criterion force was reached.

KR Stimuli.

Visual KR stimuli (duration 150 ms) were presented on a 15" computer monitor located 1.2 m in front of the subject. The KR stimulus could be a horizontal bar (in case the estimated interval was too short), a vertical bar (for a correctly timed response) or a plus sign (indicating that the estimated time interval was too long). In the intact KR condition, the KR appeared as a white figure on a black background. In the degraded KR condition, random patterns of small squares were overlaid on the stimulus. Within each square the colors of fore- and background were inverted. A total of 20 different random square patterns was used.

Figure 9.1 presents examples of intact and degraded visual KR stimuli in all three response categories.

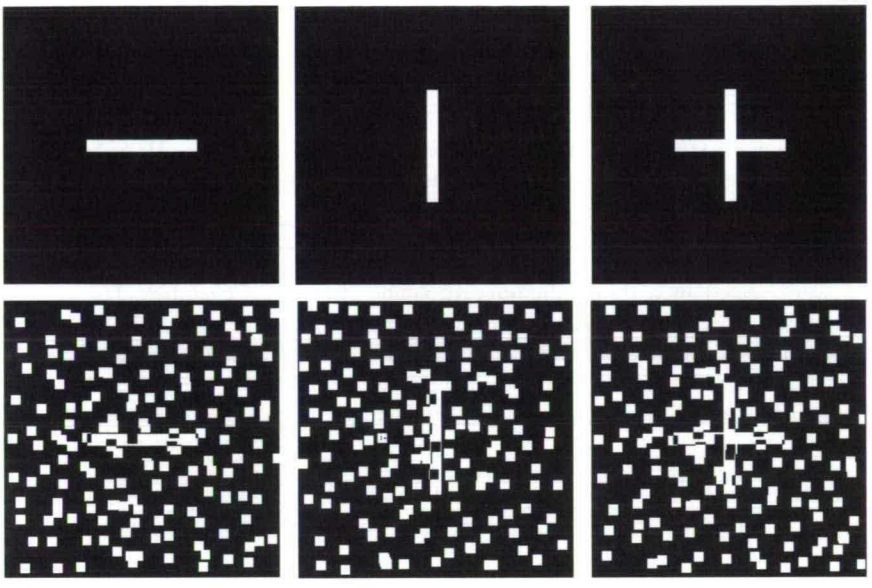

Figure 9.1. Examples of intact and degraded visual stimuli in all three response categories.

Auditory KR stimuli (70 dB(A), 150 ms)were presented through a loudspeaker located 1.2 m in front of the subject, just underneath the computer monitor. In the intact KR condition, the KR stimuli were pure tones with a frequency of 2000, 1000 or 500 Hz, corresponding to estimated intervals that were too short, correct or too long, respectively. In the degraded KR condition, white noise was added to the tones, but the overall output amplitude was kept constant at 70 dB(A).

In a behavioral pilot experiment, a 3-choice reaction time task with 9 subjects (who were not included in the actual experiment), we determined the level of stimulus degradation, that is, the amount of squares for visual stimuli and the ratio of the white noise to the tone for auditory stimuli. For each modality, we presented 1 block of 60 intact stimuli, and 5 blocks of 60 degraded stimuli differing in the level of degradation. The subjects were asked to classify both the intact and the degraded stimuli by pressing that response button, out of the three response buttons mounted on the right arm of the chair, that corresponded to the KR stimulus. Based on a visual inspection of the classification results, for each modality one level of stimulus degradation was selected in which the percentage of correct classifications was identical to that of the intact stimuli (that is, between 99.6 and 99.8 % correct classifications). The reason for this is that we wanted to manipulate only perceptual difficulty, not task difficulty, in order to prevent a confounding of both processes. On these stimuli, the RT effects were tested by an ANOVA for repeated measures with factors Modality (Auditory, Visual) and Stimulus Type (Intact, Degraded). This analysis yielded a main effect of modality ($F_{1, 8} = 6.51$; $p = 0.0340$) indicating that RT was longer following visual (738 ms) than following auditory (605 ms) stimuli, and a main effect of degradation ($F_{1, 8} = 5.96$; $p = 0.0405$), indicating that RT was longer in the degraded (751 ms) than in the intact (592 ms)

condition. The absence of an interaction effect indicated that the RT effect of stimulus degradation was similar for both modalities.

Electrophysiological recordings.

For the EEG-recordings 27 non-polarizing Beckman 8 mm Ag-AgCl electrodes were affixed to the scalp, most of them placed according to the international 10-20 system. Standard positions were Fp1, Fp2, F7, F3, F4, F8, T3, Cz, T4, P3, Pz, and P4. Non-standard positions were C3' and C4', which are 1 cm anterior to C3 and C4, respectively; TC3 and TC4, which are at one third of the distance from T3 to C3 and from T4 to C4, respectively; TP3 and TP4, which are in the center of T3, P3, T5 and C3 and in that of T4, P4, T6 and C4, respectively; O1', Oz' and O2', which are 1 cm anterior to O1, Oz and O2, respectively; and O1", Oz" and O2", which are 2 cm posterior to O1, Oz and O2, respectively. Electrode impedance was kept below 5 kΩ. Software-linked mastoids served as a reference. The EEG was amplified with a 30 s time constant, and a 70 Hz (-42 dB / octave) lowpass filter. Epochs of 3000 ms pre-movement to 3000 ms post-movement were digitized with a sampling frequency of 256 Hz.
The horizontal EOG from the outer canthi, and the vertical EOGs of both eyes were recorded, and an off-line EOG correction was performed (Van den Berg-Lenssen et al., 1989). Subsequently, a semi-automatic artifact detection was performed, discarding trials containing spikes and large drift.

Data reduction and analysis.

Behavioral data.

Two behavioral measures were derived from the reaction time (RT) data. First, the quality of time estimation was monitored by computing the percentages of too fast, correctly timed or too slow responses. These data were analyzed by an ANOVA with KR Modality (auditory, visual), KR Type (Intact, Degraded), Response side (left, right) and Response category (too early, correct, too late) as repeated measures. Second, the effectiveness of the KR stimulus was assessed as follows: for trials with too early or too late responses, we computed the percentage of subsequent trials for which the RT changed in the desired direction (that is, an RT decrease following a trial with a too late response, and an RT increase following a trial with a too early response). These data were analyzed by an ANOVA with KR Modality (auditory, visual), KR Type (intact, degraded) and Response side (left, right) as repeated measures.

Slow potentials.

For the computation of the slow potentials, artifact-free trials, from 3000 ms pre-movement to 3000 ms post-movement were averaged, and the data were baseline-corrected from 2750 to 2000 ms prior to movement onset. The Readiness Potential (RP; Kornhuber and Deecke, 1965) was quantified as the average amplitude in a 100 ms window preceding response onset. These data were subjected to an ANOVA with factors Condition (Voluntary Movement, KR Auditory Intact, KR Auditory Degraded, KR Visual Intact, KR Visual Degraded), Response Side (Left hand, Right Hand), Electrode Pair (Frontal (F3 + F4), Central (C3' + C4'), Temporal (TC3 + TC4), Occipital (O1' + O2')) and Hemisphere (Left, Right).
The Stimulus-Preceding Negativity (SPN, Damen and Brunia, 1987) was quantified as the average amplitude in a 100 ms window preceding the presentation of the KR stimulus. These data were subjected to an ANOVA with factors KR Modality (Auditory, Visual), KR Type (Intact, Degraded), Response Side (Left hand, Right Hand), Electrode Pair (Frontal (F3 + F4), Central (C3' + C4'), Temporal (TC3 + TC4), Occipital (O1' + O2')) and Hemisphere (Left, Right).

ERD.

The ERD was computed as follows. First a weighted local average reference (Hjorth, 1975) was computed, as is mostly done in ERD computation (e.g. Pfurtscheller, 1991). Next, the EEG was bandpass filtered using an FFT filter in two frequency bands: 8-10 Hz and 10-12 Hz. The data then were transformed into power values by squaring the amplitudes. Intervals of 64 consecutive samples were averaged, giving rise to 24 time intervals of 250 ms each. For each subject data were averaged over trials, and ERD was computed as the percentage power increase (ERS) or decrease (ERD) for a particular time interval in a particular frequency band, relative to the reference interval from 2750 to 2000 ms pre-movement. The end of this reference interval corresponds to the point in time when movement-related ERD starts (e.g. Pfurtscheller and Berghold, 1989).

For the statistical analysis of the ERD, we were mainly interested in condition differences in the ERD immediately preceding the presentation of the KR stimulus. First however, we wanted to determine if differences between conditions in ERD can be attributed to differences in the level of alpha power in the reference interval. Therefore two ANOVA's were performed on the absolute power in the reference interval, one for the 8-10 Hz band and one for the 10-12 Hz band. For both ANOVA's, factors were Condition (Voluntary Movement, KR Auditory Intact, KR Auditory Degraded, KR Visual Intact, KR Visual Degraded), Response Side (Left hand, Right hand), Electrode Pair (Frontal (F3 + F4), Central (C3 + C4), Temporal (TC3 + TC4), Occipital (O1' + O2'), and Hemisphere (Left, Right).

Next, single-sample t-tests were used to determine whether the ERD at temporal and occipital electrode positions in the last 250 ms interval preceding the KR stimulus significantly differs from zero, i.e. whether there *is* a significant ERD over the auditory and visual cortices. In order to limit the number of t-tests, we averaged the ERD over response sides and hemispheres, since effects involving these factors were found to be caused exclusively by post-movement processes (see results section).

Third, we wanted to test for differences between conditions in the pre-stimulus ERD by means of an ANOVA. On the basis of previous results however, we expected a post-movement ERS at central electrodes which lasts until after the presentation of the KR stimulus, and which interferes with the pre-stimulus ERD (Bastiaansen et al., 1999a). In this previous study we therefore subtracted the ERD in the voluntary movement condition from the ERD in the time estimation conditions, leaving the stimulus-related ERD intact in the subtracted data. This approach proved to be a good way to solve the problem (see Bastiaansen et al., 1999a). However, such a subtraction can be done reliably only if the movement-related ERD is similar in all conditions. In order to verify this, we first performed an ANOVA on the movement-related ERD. We used three time intervals to assess differences between conditions in the movement-related ERD: an early and a late pre-movement interval, respectively corresponding to intervals from 1250 to 1000 ms and from 250 to 0 ms prior to movement onset, and the last 250 ms interval preceding stimulus presentation. For this ANOVA, we used only the ERD at central (C3' and C4') channels, where movement-related processes are most prominent. Factors were Frequency Band (8-10 Hz, 10-12 Hz), Time Interval (1250-1000 ms premovement, 250-0 ms pre-movement, 250-0 ms pre-stimulus), Condition (Voluntary Movement, KR Auditory Intact, KR Auditory Degraded, KR Visual Intact, KR Visual Degraded), Response Side (Left Hand, Right Hand), and Hemisphere (Left, Right).

For the analysis of condition differences in the pre-stimulus ERD, from 250 to 0 ms pre-stimulus, we used only temporal and occipital electrode positions. The reason for this is that visual inspection of the ERD maps indicated that there were no appreciable ERD/ERS effects at frontal electrode positions, while at central positions there is a large postmovement ERS;

therefore only the ERD at temporal and occipital channels is of interest. Factors were Frequency Band (8-10 Hz, 10-12 Hz), KR Modality (Auditory, Visual), KR Type (Intact, Degraded), Response Side (Left hand, Right Hand), Electrode Pair (Temporal (TC3 + TC4), Occipital (O1' + O2')) and Hemisphere (Left Hemisphere, Right Hemisphere).
For all ANOVA's that were performed, degrees of freedom were corrected using the Greenhouse-Geisser Epsilon (ε, Vasey and Thayer, 1987) when necessary, and significant interactions were clarified by breaking them down into simple effects.

9.4 Results.

Behavioral data.

Over subjects, the average window defining correct responses was 525 ± 84 ms (M ± SD). With respect to the quality of the time estimation, the ANOVA on the percentages too early, correct and too late responses reveals that subjects produce more correct responses (57%) than too early or too late responses (20 and 23 %, respectively; main effect of Response Category: $F_{2, 22} = 61.48$, $p < 0.0000$, $\varepsilon = 0.9859$). Furthermore, in conditions with auditory KR stimuli subjects performed poorer than in conditions with visual KR stimuli, as indicated by an interaction of KR Modality with Response Category ($F_{2, 22} = 9.62$, $p = 0.0024$, $\varepsilon = 0.88094$). In the conditions with auditory KR the distribution was 22% too early , 54% correct and 24 % too late responses, while in the visual KR conditions these percentages were 18, 60 and 22, respectively.
KR stimuli indicating that a response was too early or too late resulted, on the subsequent trial, in an average of 86 % of the cases in an adjustment of the RT in the desired direction. An interaction of KR modality with KR type ($F_{1, 11} = 7.37$, $p = 0.0201$) revealed that in the auditory modality, stimulus degradation affected the effectiveness of the KR stimulus (83 vs. 88 correct adjustments in the degraded and intact conditions, respectively, $F_{1, 11} = 9.66$, $p = 0.0100$). This is not the case in the visual modality (86 vs. 87% correct adjustments in the intact and degraded conditions, respectively, this difference is not significant).

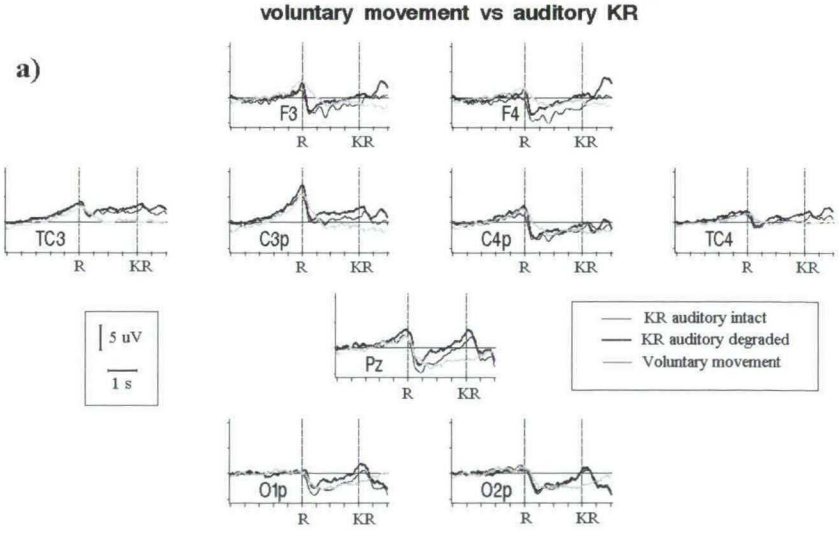

Figure 9.2a. Time courses of the grand average (N=12) slow potentials at selected channels. Data are from right-hand movements. Comparison between the auditory time estimation conditions and the voluntary movement condition.

Slow potentials.

Figure 9.2 presents the time courses of the slow potentials recorded during the voluntary movement tasks and the time estimation tasks, at selected channels. Preceding the movement a slow negative potential shift can be observed, which we identified as a Readiness potential (Kornhuber and Deecke, 1965). Preceding the presentation of the KR stimulus, a slow negative potential is present that we identified as a Stimulus-Preceding Negativity (SPN; Damen and Brunia, 1987). Figure 9.3 presents topographic maps of the average SPN in the last 100 ms interval preceding stimulus presentation.

Readiness Potential.

The ANOVA revealed that the RP has a central maximum (main effect of Electrode pair: $F_{3, 33} = 12.19$, $p = 0.0006$, $\varepsilon = 0.59$; mean amplitudes of -1,28, -4.46, -3.00 and –0.88 uV for Frontal, Central, Temporal and Occipital electrode pairs, respectively), and a contralateral dominance (interaction of Response Side and Hemisphere: $F_{1, 11} = 48.94$, $p < 0.0001$; simple effect of hemisphere for left-and right hand movements: $F_{1, 11} = 21.71$, $p = 0.0007$, and $F_{1, 11} = 13.75$, $p = 0.0035$, respectively). Moreover, this contralateral dominance is present at frontal, central and temporal sites, not at occipital electrode positions (interaction of Response Side with Electrode Pair and Hemisphere: $F_{3, 33} = 51.45$, $p < 0.0001$). The ANOVA did not reveal any differences between conditions in the RP.

Stimulus-Preceding Negativity.

The results of the ANOVA on the SPN amplitudes are summarized in Table 9.1. The main effect of Electrode Pair indicated that the SPN was maximal at temporal positions (Frontal: 0.83 uV; Central: -0.06 uV; Temporal: -1.54 uV; occipital: 0.08 uV).

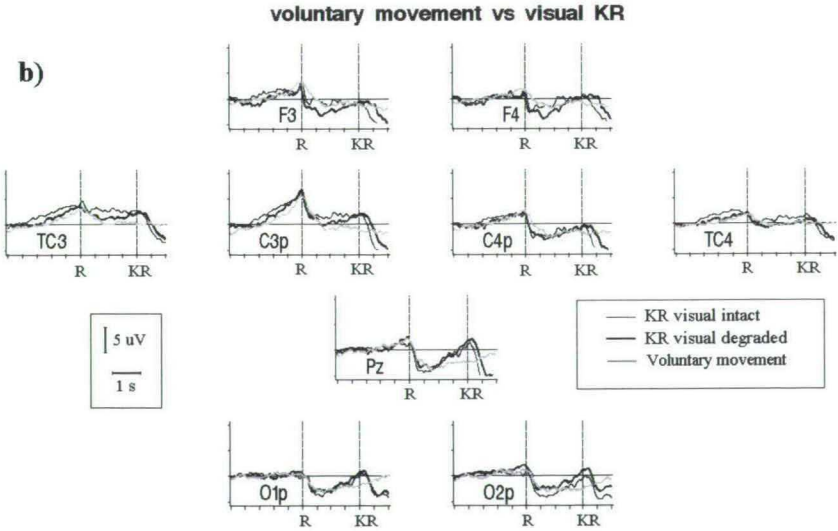

Figure 9.2b) Comparison between both visual time estimation conditions and the voluntary movement condition. Note (1) that the presentation of a KR stimulus results in a Stimulus-Preceding Negativity (SPN) that is not present in the voluntary movement condition; (2) that preceding auditory KR stimuli the SPN amplitude is larger when stimuli are degraded, and (3) that this effect is not present for KR stimuli in the visual modality.

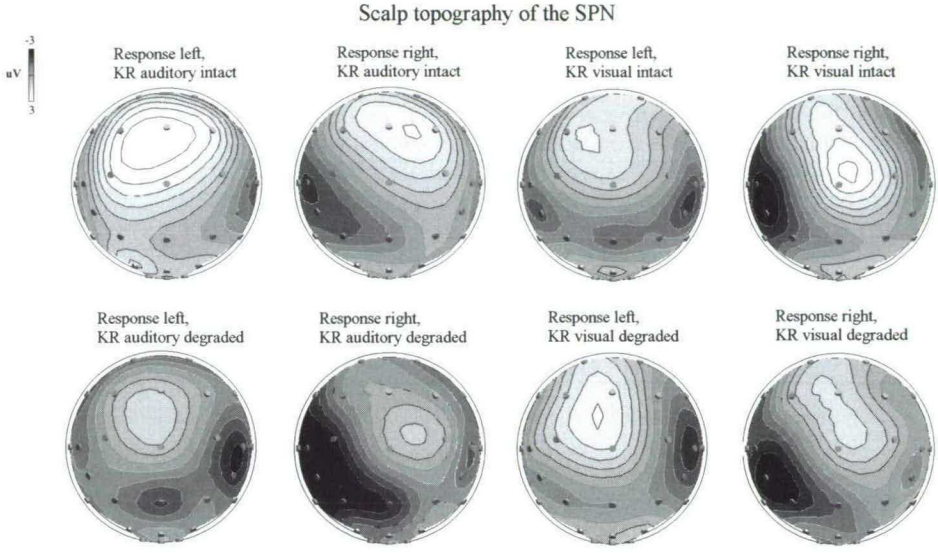

Figure 9.3. Topographic maps of the Stimulus-Preceding Negativity (SPN), averaged over the last 100 ms interval preceding stimulus presentation, in all time estimation conditions. Positivity is depicted as light gray surrounded by black isopotential lines; negativity is depicted as dark gray surrounded by white isopotential lines. Spacing of isopotential lines is 0.5 uV. Scaling as indicated in the figure. Note (1) that only in the auditory modality, the amplitude of the SPN increases with stimulus degradation, and (2) that the scalp distribution of the SPN is independent of stimulus modality.

The SPN was larger preceding degraded (-0.62 uV) than preceding intact (+0.28 uV) KR stimuli (main effect of KR Type). However, this amplitude enhancement as a result of stimulus degradation was only present preceding auditory KR stimuli, as indicated by a marginally significant interaction of KR Modality with KR Type (cf. Table 9.1). The underlying simple effects clearly support this interaction (simple effect of KR Type in the auditory modality: $F_{1, 11} = 7.75$, $p = 0.0178$; simple effect of KR Type in the visual modality: $F_{1, 11} = 0.09$, $p = 0.7721$). Furthermore, the interaction Modality * KR Type * Hemisphere revealed that the amplitude enhancement of the SPN as a result of stimulus degradation in the auditory modality was largest over the left hemisphere.
Finally, the SPN was largest over the hemisphere contralateral to the response side (interaction of Response Side with Hemisphere), but this effect was significant only at central and temporal channels (interaction R * E * H).

ERD.

Figure 9.4 presents topographic maps of the pre-KR ERD for all conditions. The pre-movement ERD follows the pattern of results usually reported (e.g. Pfurtscheller and Berghold, 1989). Starting from approximately 1250 ms prior to movement onset, an ERD can be observed over the contralateral motor cortex. This contralateral ERD shifts to a bilaterally symmetrical ERD just prior to movement onset. Prior to the presentation of the KR stimulus, at central channels a massive post-movement ERS can be observed over the contralateral motor cortex, as previously described by e.g. Pfurtscheller (1992). Prior to visual KR stimuli,

an additional occipital ERD is present, while prior to auditory KR stimuli no appreciable ERD is observed.

Table 9.1 Significant effects of the ANOVA on the Stimulus-Preceding Negativity. p-values are corrected with the Greenhouse-Geisser Epsilon (ε).

Effect	F	df	p	ε
KR Type (T)	6.83	1, 11	0.0239	
Electrode pair (E)	7.20	3, 33	0.0027	0.74
KR Modality (M) * KR Type	4.74	1, 11	0.0521	
Response Side (R) * Hemisphere (H)	44.60	1, 11	< 0.0001	
Modality * Type * Hemisphere	5.32	1, 11	0.0415	
Response Side * Electrode Pair * Hemisphere	18.32	3, 33	0.0001	0.56

Alpha power in the reference interval.

The ANOVA's on the level of absolute alpha power in the reference interval revealed that there were no differences in baseline power between conditions. A main effect of Electrode Pair (8-10 Hz band: $F_{3, 33} = 7.33$, $p = 0.0203$, $\varepsilon = 0.33$; 10-12 Hz band: $F_{3, 33} = 3.81$, $p = 0.0769$, $\varepsilon = 0.33$) indicated that the power was largest at occipital leads.. Furthermore, in both frequency bands a main effect of Hemisphere (8-10 Hz: $F_{1, 11} = 11.00$, $p = 0.0069$; 10-12 Hz: $F_{1, 11} = 5.43$, $p = 0.0399$) indicated that the power was larger in the right hemisphere (8-10 Hz: 327 A^2/m^2; 10-12 Hz: 487 A^2/m^2) than in the left hemisphere (8-10 Hz: 161 A^2/m^2; 10-12 Hz: 247 A^2/m^2). The absence of effects involving the factor Condition indicates that differences in ERD between conditions cannot be attributed to differences in the power in the reference interval.

Movement-related ERD.

The results of the ANOVA on the movement-related ERD are summarized in Table 9.2. The movement-related ERD is globally characterized by three effects, which are expressed in the interaction of Response Side with Time Interval and Hemisphere (R * I * H): First, at the early pre-movement time interval, there is a contralaterally dominant ERD (simple effect of R * H at this time interval: $F_{1, 11} = 5.15$, $p = 0.0444$). Second, at the late pre-movement time interval there is a bilaterally symmetrical ERD, which somewhat surprisingly displays a trend towards a larger ERD on the ipsilateral side (simple effect of R * H at this time interval: $F_{1, 11} = 3.71$, $p = 0.0802$). Third, at the post-movement time interval (which corresponds to the pre-KR interval in the time estimation conditions) there is a contralaterally dominant ERS (simple effect of R * H at this time interval: $F_{1, 11} = 15.52$, $p = 0.0023$). However, the contralateral dominance of the post-movement ERS is significant only following right-hand movements (simple effect of hemisphere in right-hand movement conditions at this time interval: $F_{1, 11} = 14.04$, $p = 0.0032$), whereas following left-hand movements the post-movement ERS is bilaterally symmetrical. This can be seen in Figure 9.4. Furthermore, the magnitude of the post-movement ERS following right-hand responses is such (an average of 143.37% power increase) that it also produces the main effects of Time Interval and Hemisphere, and the interaction of Time Interval with Hemisphere.

However, the effects contained in the R * I * H interaction only hold for the time estimation conditions, as indicated by the 4th order interaction Condition * Response Side * Time Interval * Hemisphere: the simple effect of R * I * H is significant in all four time estimation conditions (all p-values < .05) but not in the voluntary movement condition. This can be

attributed to the fact that in the voluntary movement conditions, the post-movement ERS is much smaller than in the time estimation conditions.

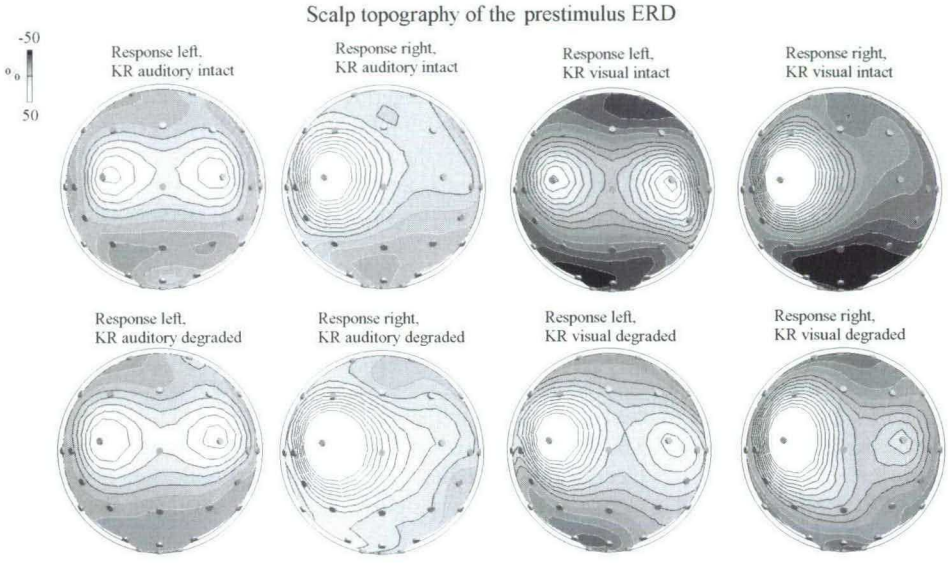

Figure 9.4 Topographic maps of the grand average (N=12) ERD in the last 250 ms interval preceding the presentation of the KR stimulus. Power increase (ERS) is depicted as light gray surrounded by black isopotential lines; Power decrease (ERD) is depicted as dark gray surrounded by white isopotential lines. Spacing of isopercentage lines is 5%. Scaling as indicated in the figure. Note (1) the strong post-movement ERS at central electrodes (2) that the ERD preceding the presentation of the KR stimuli (right-hand column) is dependent upon stimulus modality: preceding auditory stimuli no ERD is present, whereas preceding visual stimuli an occipital ERD is present, and (3) that the latter is larger preceding intact than preceding degraded stimuli.

Table 9.2. Significant effects of the ANOVA on the movement-related ERD. Reported p-values are corrected with the Greenhouse-Geisser Epsilon (ε).

Effect	F	df	p	e
Time Interval (I)	16.49	2, 22	0.0014	0.53725
Hemisphere (H)	5.71	1, 11	0.0359	
Response Side (R) * Hemisphere	12.65	1, 11	0.0045	
I * H	4.91	2, 22	0.0474	0.51355
R * I * H	16.42	2, 22	0.0014	0.54220
Condition * R * I * H	3.51	8, 88	0.0328	0.32520

The differences in post-movement ERS between the voluntary movement conditions and the time estimation conditions indicates that we cannot subtract the ERD in the voluntary movement task from the ERD in the time estimation task in order to eliminate the movement-related ERD from the pre-KR ERD. However, if we can demonstrate that the post-movement ERS at central channels is similar for all time estimation conditions, we can still validly

attribute differences in ERD at other channels to prestimulus processes. This was verified by an additional ANOVA on the post-movement ERS in the time estimation conditions at central channels in the pre-KR interval, with factors Frequency Band (8-10, 10-12), Condition (Auditory Intact, Auditory degraded, Visual Intact, Visual Degraded), Response Side (Left hand, Right hand) and Hemisphere (Left, Right). This ANOVA revealed no effects involving the factor condition. Significant effects were Response Side ($F_{1, 11} = 5.86$, $p = 0.0340$), indicating that the postmovement ERS was larger following right- than following left-hand responses (91 and 60 % power increase, respectively) and Hemisphere ($F_{1, 11} = 4.78$, $p = 0.0490$), indicating that ERS was larger in the left than in the right hemisphere ((133 and 38 % power increase, respectively). An interaction of Response Side with Hemisphere ($F_{1, 11} = 15.55$, $p = 0.0023$) further indicates that these effects are due to the fact that following right-hand responses, the ERS is present exclusively on the contralateral side (simple effect of hemisphere at Right Hand conditions: $F_{1, 11} = 12.74$, $p = 0.0044$), whereas following left-hand responses the ERS is bilaterally symmetrical. (simple effect of hemisphere at Left Hand conditions: $F_{1, 11} = 0.00$, $p = 0.9798$); see also Figure 9.4.

Pre-stimulus ERD.

Table 9.3 presents the results of the t-tests on the pre-stimulus ERD. As Table 9.3 reveals, prior to the presentation of visual KR stimuli there is a significant ERD at occipital electrode positions, but not at temporal electrodes. Preceding auditory KR stimuli there is no significant ERD; in the 10-12 Hz band there is even a significant ERS at temporal electrode positions preceding auditory degraded KR stimuli.

*Table 9.3. Results of the t-tests on the pre-stimulus ERD, averaged over response sides and hemispheres. In each cell the average percentage power change is given; negative values indicate a power decrease (ERD), positive values indicate a power increase (ERS). Significance levels of the t-test are coded as follows: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Note (1) that the prestimulus ERD is only significant at occipital electrodes preceding visual stimuli, both for the intact stimuli and for the degraded stimuli, and (2) that the ERD is larger preceding the intact than preceding the degraded stimuli. This difference is significant as revealed by the ANOVA (see Table 9.4).*

Freq. Band	8-10 Hz				10-12 Hz			
KR Type	Intact		degraded		intact		degraded	
KR Modality	AUD	VIS	AUD	VIS	AUD	VIS	AUD	VIS
Temporal Electrodes	10 (ns)	-1 (ns)	11 (ns)	11 (ns)	8 (ns)	2 (ns)	20 (*)	5 (ns)
Occipital Electrodes	-8 (ns)	-33 (**)	0 (ns)	-18 (*)	-4 (ns)	-31 (***)	-8 (ns)	-21 (*)

The differences in movement-related ERD between conditions prohibit a subtraction of the ERD in the voluntary movement conditions from the ERD in the time estimation conditions. Therefore the ANOVA on the pre-stimulus ERD was performed on the non-subtracted data. As a consequence, the results of the ANOVA on the pre-stimulus ERD (summarized in Table 9.4) show a number of effects that can be attributed to the post-movement ERS rather than to pre-stimulus processes: A main effect of Electrode Pair reveals that there is an ERD at occipital electrode positions (17.07 % power decrease) while at temporal electrode positions there is an ERS (8.66 % power increase). Visual inspection of Figure 9.4 supports the

interpretation of the latter as a post-movement ERS that extends from central to temporal electrode positions. Furthermore, the interaction of Response Side with Hemisphere (R * H) reveals that in right-hand movement conditions there is a significant ($F_{1,11}$ = 8.15, p = 0.0157) difference between the right (9.18 % power decrease) and left (-4.78 % power *increase*) hemisphere, which is not present in left-hand movement conditions. The interaction of Response Side with Electrode Pair and Hemisphere (R * E * H) indicates that this effect is restricted to temporal electrode positions. These effects (R * H and R * E * H) are probably produced by the fact that in right-hand movement conditions there is a strong contralaterally dominant ERS, while in left-hand movement conditions the post-movement ERS is bilaterally symmetrical. Finally, the interaction of Frequency Band with KR modality and Response Side indicates that in the 8-10 Hz band, following right-hand responses, there is a significant difference ($F_{1, 11}$ = 7.29, p = 0.0207) between the ERD preceding auditory (13.09 % power *increase*) and visual (13.51 % power decrease) KR stimuli, which is not present following left-hand movements. Although this does not interact with Electrode pair, it is probable that this effect is caused by the differences in post-movement ERS between right- and left hand responses.

The remaining two effects are not easily explained in terms of post-movement processes, and probably truly reflect pre-stimulus processes. First, a trend towards a main effect of modality indicated that the ERD tended to be larger preceding visual (10.30 % power decrease) than preceding auditory (1.89 % power *increase*) KR stimuli. Second, contrary to expectation, the ERD was smaller preceding degraded KR stimuli (1.75 % power *increase*) than preceding intact KR stimuli (9.16 % power decrease), as indicated by a main effect of KR type. Both effects can be seen in Figure 9.4.

Table 9.4 Significant effects of the ANOVA on the pre-stimulus ERD. Note that the main effect of KR Modality is only marginally significant.

Effect	F	df	p
KR Modality (M)	4.37	1, 11	0.0607
KR Type	8.34	1, 11	0.0148
Electrode pair (E)	13.76	1, 11	0.0034
Response Side (R) * Hemisphere (H)	10.96	1, 11	0.0069
R * E * H	7.19	1, 11	0.0214
Frequency Band * M * R	14.20	1, 11	0.0031

9.5 Discussion.

We investigated the stimulus-preceding negativity and the event-related changes of the power in the alpha frequency band (ERD/ERS) of the EEG related to the anticipation of auditory and visual stimuli, in a paradigm in which subjects performed a time estimation task and were informed about the quality of their time estimation by a KR stimulus. The perceptual anticipation was manipulated by presenting the stimuli either in intact or in degraded form. The modality of the KR stimulus did not influence the scalp topography of the SPN. However, the SPN was larger preceding degraded auditory KR stimuli than in the other three conditions. This coincided with a reduced effectiveness of the KR stimulus in guiding the behavior on the next trial in the former condition. In contrast, we found clear differences between modalities in the pre-stimulus ERD: preceding auditory KR stimuli no ERD was present, whereas the visual KR was preceded by an ERD over the occipital areas (cf. Table 9.3; Bastiaansen et al., 1999a, b). Contrary to expectation, the occipital ERD was smaller preceding degraded visual KR stimuli than when intact stimuli were presented.

In the following paragraphs we will first discuss the slow potentials and the ERD related to the anticipation of the KR stimulus, since this is the main focus of the present paper. Next we

will discuss in more detail the results of the slow potentials and the ERD related to movement execution, since the results are striking in some respects.

Pre-stimulus processes.

The SPN was larger preceding auditory degraded stimuli than preceding the other three types of KR stimuli (auditory intact, visual degraded and visual intact). In this respect it is interesting to note that the effectiveness of the degraded auditory KR stimuli was lower than for the other KR stimuli in guiding the behavior on the subsequent trial. This indicates that these stimuli were more difficult to recognize, and as a result the task was more difficult to perform. Despite the increase in task difficulty subjects performed equally well in the auditory intact and auditory degraded condition. Thus, apparently subjects counteracted the reduced effectiveness of the degraded auditory KR stimuli in some way, most probably by an increase in effort to accurately perform the task. Thus, our data are in agreement with previous studies (Chwilla and Brunia, 1991b, 1992), which have shown that SPN amplitudes increase with increasing task difficulty. This was explained by the fact that increased task difficulty motivates the subjects to maintain performance at a high level. In sum, our data (further) strengthen the interpretation of the pre-KR SPN as reflecting anticipation of the affective-motivational aspects of Knowledge of Results rather than the perceptual anticipatory attention that is described by our neurophysiological model (Brunia, 1999).

In general terms the results of the pre-stimulus ERD, that is, an occipital ERD prior to visual KR stimuli and an absence of ERD prior to auditory stimuli, are a replication of the results of previous experiments (Bastiaansen et al., 1999a, b; Bastiaansen et al., 2000). We have explained the absence of a bilateral temporal ERD in the EEG in terms of a differential sensitivity of EEG and MEG for rhythmic activity originating from the auditory cortex (Bastiaansen et al., 1999b), which has been partly confirmed by the results of a subsequent study combining EEG and MEG (Bastiaansen et al., 2000). In addition, we have tentatively interpreted the occipital ERD prior to visual stimuli as reflecting anticipatory attention (Bastiaansen et al., 1999a, b). As we pointed out in the introduction, the latter interpretation would gain strength if the pre-KR ERD would be influenced by stimulus parameters. In the behavioral pilot experiment we have established that it took subjects more time to classify the degraded stimuli than the intact stimuli, which strongly suggests that the former were more difficult to perceive. We have reasoned that in such a situation anticipatory attention would be more prominent than in a situation in which stimuli are easily perceived. Therefore, if the pre-stimulus ERD is a correlate of a perceptually based anticipatory attention process, we would expect it to be larger preceding degraded stimuli than preceding intact stimuli. Although the finding of the present experiment that stimulus degradation results in a *smaller* ERD (although still significantly different from zero) does indicate a sensitivity of the anticipatory ERD to stimulus parameters, the direction of the effect is opposite to what we expected. It is unclear at present how to interpret this effect.

Movement-related processes.

The RP that was observed prior to movement execution did not show any differences between conditions. However, the analyses of the movement-related ERD indicated that although the premovement ERD was similar for all conditions, there was a marked difference in the magnitude of the ERS at central positions following the movement between the time estimation task and the voluntary movement task: in the former task the ERS was much larger than in the latter. It seems unlikely for several reasons that such a synchronization at central electrode positions can be attributed to the anticipation of the KR stimulus. First, it is largest over the contralateral motor cortex. Second, the central ERS is also present in the voluntary movement task, although it is much smaller. Third, although post-movement

synchronization is usually most prominent in the beta frequency ranges, it has also been reported in the alpha band (e.g. Pfurtscheller et al., 1996).

This leaves us with the question of what might have caused the difference in post-movement ERS between the time estimation task and the voluntary movement task. Post-movement ERS usually varies with movement parameters such as moving body part (Arroyo et al., 1993; Toro et al., 1994; Salmelin et al., 1995; Pfurtscheller et al., 1998), speed (e.g. Stancak and Pfurtscheller, 1995) and force (e.g. Stancak et al., 1997). The latter authors also noted that post-movement ERS, at least in the beta band, might also characterize subjects' difficulty of performing the motor task. Since we did not explicitly control the different movement parameters in the experiment, one possible explanation is that there were systematic differences in movement parameters between both tasks. The consequence then is that there is some inherent difference between simply performing a voluntary movement, and performing the same movement within the context of a time estimation task. One might therefore argue that the enhanced post-movement ERS in the time estimation task is caused by the fact that the movement has to be carefully timed, which of course imposes additional constraints upon movement execution itself, although such an interpretation is rather speculative. Another interpretation might be that, from the generally accepted interpretation of post-movement synchronization as a correlate of the transition of cortical activity to cortical idling (e.g. Pfurtscheller, 1992), it follows that such a transition process was more prominent in the time estimation task than in the voluntary movement task. It is unclear however why this should have been the case. Finally, it must be noted that our findings in this respect contrast with the results of a previous study, where we did not find any differences in movement-related ERD/ERS between both tasks (Bastiaansen et al., 1999a). Further research would be needed to clarify this issue.

In conclusion, in the main our results support a clear dissociation between the SPN and the anticipatory ERD. Our present data provide further support for the notion that the pre-KR SPN is a reflection of the affective-motivational anticipation of a stimulus that evaluates past performance, in that it is larger in the more difficult condition. In addition, although the exact functional significance of the anticipatory ERD needs to be investigated by further delineating its antecedent conditions, the results globally support the idea that the anticipatory ERD is related to perceptual anticipatory attention because it was influenced by stimulus degradation.

Chapter 10: Does event-related desynchronization reveal anticipatory attention in the somatosensory modality?

10.1 Abstract.

In previous studies anticipatory attention has been studied with a technique know as Event-Related Desynchronisation (ERD). The results of these studies partially support the notion that anticipatory attention in the auditory and visual modalities is accompanied by an ERD over the temporal and occipital cortices, respectively. In order to establish a firmer basis for the more general notion that anticipatory attention for an upcoming stimulus manifests itself as an ERD that is restricted to that part of the sensory cortex that corresponds to the modality of the anticipated stimulus, an experiment was performed in which the ERD preceding somatosensory stimuli was investigated. 12 Subjects performed a time estimation task, and were informed about the quality of their time estimation by a stimulus providing Knowledge of Results (KR), that could be either visual or somatosensory. Preceding the visual KR the previously found occipital ERD was replicated; Preceding the somatosensory KR a marked reduction in postmovement event-related synchronization (ERS) was found at the postcentral midline, which corresponds topographically to the cortical representation of the stimulated body part in the somatosensory cortex. The results are interpreted to be in line with the notion that anticipatory attention is manifest as a prestimulus activation of the cortical area corresponding to the modality of the anticipated stimulus.

10.2 Introduction.

Man has five sensory modalities. Up to now, only two of them have been investigated in this thesis, that is, the auditory and visual modalities. For the reasons pointed out in Section 1.4, olfaction and taste are not considered in this thesis. The remaining modality is the somatosensory modality; therefore the present chapter will investigate the ERD preceding somatosensory KR stimuli.

The reason that most of the experiments described in this thesis have used auditory and visual KR stimuli is that the cortical areas involved in the processing of these sensory modalities are relatively far in space from the motor cortex. This reduces the chances that, in the time estimation paradigm that has been employed throughout this thesis in order to induce anticipatory attention in subjects, postmovement activity is confounded with prestimulus activity. The spatial proximity of the somatosensory and motor cortices may pose a problem for separating these two processes when somatosensory KR stimuli are used. This holds not only for the analysis of the anticipatory ERD, but also for the Stimulus-Preceding Negativity (SPN; Damen and Brunia, 1987). This has led researchers interested in the pre-KR SPN to avoid the use of somatosensory KR stimuli. Thus, there are as yet no experimental data on the SPN and on the ERD preceding somatosensory KR stimuli.

However, for the ERD analyses of the present experiment there are in principle two ways of separating post-movement effects from prestimulus effects. First, the ERS that is usually observed following movement offset (e.g. Pfurtscheller, 1992) has a maximum over the motor cortex contralateral to the movement side. Therefore, incorporating response side as an independent variable in the design of the experiment will yield an interaction of response side with hemisphere for the postmovement ERS. If somatosensory KR stimuli are applied to one

location on the body irrespective of which hand is used for producing the response, the ERD that we expect to find preceding these stimuli will be independent of response side. In this way, the ERD or ERS effects that are found during the pre-KR interval can be attributed either to postmovement activity or to prestimulus activity depending on whether or not an effect interacts with response side and hemisphere. Such a procedure is probably not very useful for the slow potential data, since the pre-KR SPN typically contains a response side * hemisphere interaction (cf. Damen and Brunia, 1994). Second, the location of the prestimulus ERD will be correspond to the cortical representation area of the stimulated body part. In the present experiment somatosensory stimuli will be applied to the subject's right calf (m. gastrocnemeus medialis). The cortical representation area of this part of the body lies in or around the interhemispheric fissure. Therefore ERD effects related to anticipatory attention for these stimuli are expected to occur over the postcentral midline, while postmovement effects are expected to occur at more lateral positions, i.e. over the cortical hand representation area. Third, recent experimental evidence suggests that somatosensory and motor processes can be distinguished in the ERD on the basis of frequency. It appears that the central mu rhythm, that has traditionally been related to somatomotor activity (e.g. Gastaut, 1952), is not a unitary phenomenon. Its arch-like shape suggests that it is built up of a 10-Hz component and a 20-Hz component. Results of recent MEG experiments suggest that there may be a qualitative difference between these two components. By means of source analysis of the 10- and 20-Hz components, Salmelin and Hari (1994; Salmelin et al., 1995) have provided evidence for the notion that the 20-Hz component has generators mainly in the precentral gyrus (and a few in the postcentral gyrus as well). This is in agreement with intracortical recordings performed by Jasper and Penfield (1954), who recorded 20-Hz oscillations in their patients during the preparation for voluntary movements. On the other hand, Salmelin and Hari (1994; Salmelin et al., 1995) found that generators of the 10-Hz component are confined to the postcentral gyrus. Together, these data suggest that the 10-Hz component of the mu rhythm is somatosensory in nature, while the 20-Hz component is a motor rhythm (see also section 3.3.1). On the basis of these results the anticipatory ERD preceding somatosensory stimuli is expected to be present in the 10-Hz band, and not in the 20-Hz band.

The main purpose of the experiment reported in this chapter is to further investigate the modality-dependence of the anticipatory ERD. To this end, an experiment was carried out in which subjects were asked to perform a time estimation task, and were subsequently informed about the quality of their time estimation by a KR stimulus. The KR stimulus could be either somatosensory or visual. If the prestimulus ERD we have previously reported is a true index of perceptual anticipatory attention, and reflects the prestimulus activation of the sensory cortex corresponding to the modality of the anticipated stimulus, one would expect somatosensory stimuli to be preceded by a postcentral ERD, and visual stimuli by an occipital ERD. Additionally, we will investigate the SPN preceding somatosensory stimuli, since it has as yet not been recorded preceding stimuli in this modality. If the pre-KR SPN is a reflection of the anticipation of the affective-motivational value of a stimulus, as has been suggested previously (cf. sections 4.2.1 and 9.4), one would expect the scalp distribution of the SPN in the present study to be independent of stimulus modality.

10.3 Methods.

Subjects.

13 healthy, right-handed subjects, 5 male and 8 female, participated in the experiment. The subjects, with ages ranging from 18 to 22 years (M=19,5) were all undergraduate students. They either received course credits or were paid fl. 7.50 (about 3.4 US $) an hour for their

participation. The data of two subjects were discarded from further analysis because of the presence of excessive eye movements during the EEG recordings, that could not be reliably corrected for by means of an EOG correction algorithm. The data of an additional subject were discarded from further analysis because of the absence of clear 10 Hz peaks in the frequency spectrum of the EEG, which makes ERD analyses meaningless (c.f. Lopes da Silva and Pfurtscheller, 1999a). The final subject pool consisted of 3 males and 7 females, aged 18-22 (M=19.8).

Design and procedure.

Subjects were seated in a dimly illuminated, sound-attenuating chamber. The experiment consisted of two tasks: a voluntary movement task and a time estimation task. In the voluntary movement task, subjects were instructed to produce rapid self-paced unilateral flexions of index finger and thumb at a slow pace (4-6 movements per minute), with either the left or the right hand. Trials were discarded from further analysis if the inter-response interval was shorter than 8.5 s. A total of 80 behaviorally correct trials were recorded for each response side.

In the time estimation task, subjects were instructed to produce a rapid unilateral flexion of index finger and thumb, 4000 ms after the onset of an auditory warning stimulus (WS; 910 Hz, 53 dB, 200 ms). Two seconds after response onset subjects were informed about the correctness of the estimated time interval by either a visual or a somatosensory KR stimulus (see below). The KR stimulus indicated whether the response was too early, correct or too late. After two initial training blocks (one with somatosensory KR and one with visual KR), the window defining a correct response was individually adjusted in two additional training blocks (one with somatosensory KR and one with visual KR), according to the algorithm described by Wetherill and Levitt (1965), so as to obtain about 60 % correct responses. This window was used in the remainder of the experiment. The time-out was set at 4750 ms after WS onset, and was followed by a KR corresponding to a response too late. Trials in which the estimated time interval was shorter than 3500 ms or longer than 4500 ms were discarded from further analysis.

A total of 80 behaviorally correct trials was recorded for each condition. The order of the 4 time estimation conditions (2 response sides * 2 KR modalities) was randomized over subjects. The 2 voluntary movement conditions (one for each response side) always preceded the time estimation conditions, in order to prevent carry-over effects from the time estimation task to the voluntary movement task.

Responses were recorded by force transducers, mounted on both arms of the chair. The criterion force was defined as 20 % of the subject's maximum voluntary force, which was determined prior to the experiment during a unilateral tonic contraction of 3 s duration, separately for the left and right hand. Response onset was defined as the moment the criterion force was reached.

KR stimuli.

The information conveyed by the KR stimuli was encoded by the number of presentations of the (visual or somatosensory) stimulus. This could be either 1, 2 or 4 times, corresponding to an estimated interval that was either too short, correct or too long, respectively. The visual KR stimulus consisted of a white vertical bar (length 4 cm, width 1 cm) against a black background, presented on the computer screen placed 1,3 m in front of the subject. The visual stimulus appeared on the screen for 30 ms. The inter-stimulus interval in the case of multiple presentations (for correct and too long time estimations) was 120 ms. For the somatosensory KR stimuli electrical pulses were used. These pulses generated by means of a Grass S88 Stimulator, connected to the subject in series with a SIU5 isolation unit and a CCU1A

constant current unit. The pulses (duration 10 ms, and, in the case of multiple presentations, an inter- pulse-interval of 140 ms) were administered through 2 electrodes placed on the subjects' calf muscle (m. gastrocnemius medialis). The intensity of the pulses was individually determined, and was set at two times the perception threshold. This was subjectively described as clearly discriminable and not uncomfortable, certainly not painful.

Electrophysiological recordings.

For the EEG-recordings 27 non-polarizing Beckman 8 mm Ag-AgCl electrodes were affixed to the scalp, most of them placed according to the international 10-20 system. Standard positions were Fp1, Fp2, F7, F3, Fz, F4, F8, T3, T4, T5, T6, P3, Pz, P4, O1, Oz, and O2. Non-standard positions were C3', Cz', C4' which are 1 cm anterior to C3, Cz, C4 respectively; C1' and C2' were placed halfway between C3' and Cz' and between Cz' and C4' respectively; C3'', Cz'', C4'' were placed 2 cm posterior to C3, Cz, C4 respectively; C1'' and C2'' were placed halfway between C3'' and Cz'' and between Cz'' and C4'' respectively. This electrode montage was designed to cover the scalp above the entire brain with an increased spatial resolution over the primary motor and somatosensory cortices. Electrode impedance was kept below 5 kΩ. Software-linked mastoids served as a reference. The EEG was amplified with a 30 s time constant, and a 70 Hz (-42 dB / octave) lowpass filter. Epochs of 3000 ms pre-movement to 3000 ms post-movement were digitized with a sampling frequency of 256 Hz, and stored for offline analysis.
The horizontal EOG from the outer canthi, and the vertical EOGs of both eyes were recorded, and an off-line EOG correction was performed (Van den Berg-Lenssen et al., 1989). Subsequently, a semi-automatic artifact detection was performed, discarding trials containing spikes and large drift.

Data reduction and analysis.

Behavioral data.

Two behavioral measures were derived from the reaction time (RT) data. First, the quality of time estimation was monitored by computing the percentages of too fast, correctly timed or too slow responses. These data were analyzed by an ANOVA with KR Modality (visual, somatosensory), Response side (left, right) and Response category (too early, correct, too late) as repeated measures. Second, the effectiveness of the KR stimulus was assessed as follows: for trials with too early or too late responses, we computed the percentage of subsequent trials for which the RT changed in the desired direction (that is, an RT decrease following a trial with a too late response, and an RT increase following a trial with a too early response). These data were analyzed by an ANOVA with KR Modality (visual, somatosensory) and Response side (left, right) as repeated measures.

Slow potentials.

For the computation of the slow potentials, artifact-free trials, from 3000 ms pre-movement to 3000 ms post-movement were averaged, and the data were baseline-corrected from 2750 to 2000 ms prior to movement onset. The Stimulus-Preceding Negativity (SPN, Damen and Brunia, 1987) was quantified as the average amplitude in a 100 ms window preceding the presentation of the KR stimulus. The SPN was subjected to an ANOVA with factors Condition (Visual KR, Somatosensory KR, Voluntary Movement), Response Side (Left hand, Right Hand), Electrode Position (Frontal (F3 + Fz + F4), Postcentral (C3" + Cz" + C4"), and Occipital (O1 +Oz + O2')) and Laterality (Left Hemisphere, Midline, Right Hemisphere).

ERD.

The ERD was computed as follows. First, the surface Laplacian of the recorded potentials was estimated by means of spherical spline-based Scalp Current Density fields (Perrin et al., 1987; 1989). Next, the EEG was bandpass filtered using an FFT filter in three frequency bands: 8-10 Hz, 10-12 Hz and 17-23 Hz, corresponding to the lower and upper alpha bands and the beta band, respectively. The data then were transformed into power values by squaring the amplitudes. Intervals of 64 consecutive samples were averaged, giving rise to 24 time intervals of 250 ms each. For each subject data were averaged over trials, and ERD was computed as the percentage power increase (ERS) or decrease (ERD) for a particular time interval in a particular frequency band, relative to the reference interval from 2750 to 2000 ms pre-movement. The end of this reference interval corresponds to the point in time when movement-related ERD starts (e.g. Pfurtscheller and Berghold, 1989). The prestimulus ERD was calculated from 250 to 0 ms preceding the presentation of the KR stimuli in the time estimation conditions; this corresponds to the interval of 1750 to 2000 ms postmovement in the voluntary movement condition.

For the statistical analyses we were mainly interested in condition differences in the prestimulus ERD. However, we first wanted to determine whether the ERD at postcentral and occipital electrode positions in the last 250 ms interval preceding the KR stimulus significantly differs from zero, i.e. whether there *is* a significant ERD over the somatosensory and visual cortices. This was verified with single-sample t-tests. In order to limit the number of t-tests, we averaged the ERD over response sides, since effects involving this factor are most probably caused by post-movement processes.

For the analysis of differences in the pre-stimulus ERD between experimental conditions, an ANOVA was performed with factors Frequency Band (8-10 Hz, 10-12 Hz, 17-23 Hz), Condition (Visual KR, Somatosensory KR, Voluntary Movement), Response Side (Left hand, Right Hand), Electrode Position (Frontal (F3 + Fz + F4), Postcentral (C3" + Cz" + C4"), and Occipital (O1 +Oz + O2')) and Laterality (Left Hemisphere, Midline, Right Hemisphere).

For all ANOVA's that were performed, degrees of freedom were corrected using the Greenhouse-Geisser Epsilon (ε, Vasey and Thayer, 1987) when necessary, and significant interactions were clarified by breaking them down into simple effects.

10.4 Results.

Behavioral data.

With respect to the quality of the time estimation, the ANOVA on the percentages too early, correct and too late responses reveals that subjects produced more correct responses (54%) than too early or too late responses (22 and 24 %, respectively; main effect of Response Category: $F_{2, 8} = 40.48$, $p < 0.0000$, $\varepsilon = 0.97$). There were no significant effects involving Response Side and KR Modality.

KR stimuli indicating that a response was too early or too late resulted, on the subsequent trial, in an average of 87 % of the cases in an adjustment of the RT in the desired direction. Furthermore, a main effect of Response Side ($F_{1, 9} = 14.18$; $p = 0.0046$) indicates this percentage was larger when subjects responded with the left hand (89%) than when they responded with the right hand (86%).

Stimulus-Preceding Negativity.

Preceding the presentation of the KR stimulus a slow negative-going shift could be observed that was identified as the SPN. Figure 10.1 presents the time courses of the slow potentials at selected electrode positions.

Visual inspection of Figure 10.1 shows that the KR stimuli are preceded by a negative-going slow potential shift, which can be identified as an SPN. However, the
SPN does not reach above baseline, and is not well-developed compared to other SPN studies (e.g. Damen and Brunia, 1987; Chapter 9, this thesis), although this is not uncommon (e.g. Böcker et al., 1994c). Furthermore, in the voluntary movement condition a negative-going shift appears to be present following movement execution, but again this is not uncommon (e.g. Böcker et al., 1994c; Damen and Brunia, 1994).
The SPN is maximal over occipital electrode positions (main effect of Electrode Position: $F_{2, 18} = 3.90$; $p = 0.0401$, $\varepsilon = 0.98$; amplitudes at frontal, postcentral and occipital positions are 0.80, -0.52 and -0.64 uV, respectively). Furthermore, the SPN has a right-hemisphere preponderance (main effect of Laterality: $F_{2, 18} = 11.48$, $p = 0.0012$, $\varepsilon = 0.86$; amplitudes over the right hemisphere, midline and left hemisphere are -0.22, 0.74 and -0.87 uV, respectively). However, interactions of Response Side with Laterality ($F_{2, 18} = 22.00$; $p = 0.0004$, $\varepsilon = 0.62$) and Response Side * Electrode Position * Laterality ($F_{4, 36} = 22.61$; $p < 0.0001$, $\varepsilon = 0.69$) indicate that the right-hemisphere preponderance of the SPN is present at all electrode positions regardless of response side, except at postcentral electrode positions following right-hand movements, where it is larger over the left hemisphere.
The absence of effects involving the factor Condition in the ANOVA on the SPN indicates (1) that the SPN is independent of the modality of the KR stimulus, and (2) that the negative shift following the response in the voluntary movement condition is in the same order of magnitude as the negative shift preceding KR stimuli. It may be argued however that this is due to the fact that the post-movement positivity (that might be related to reafferent activity) is much larger in the time estimation conditions than in the voluntary movement condition. As a result, the SPN starts on a large positivity and although it is negative-going it does not reach above baseline. Since this postmovement positivity is much less pronounced in the voluntary movement condition, the negative shift following movements in this condition reaches amplitudes that are similar to those in the time estimation conditions. In order to verify whether the absence of condition effects is due to differences between conditions in reafferent postmovement activity, a new baseline was calculated in the interval of 500 to 700 ms postmovement. The resulting time courses are presented in Figure 10.2, and an additional ANOVA was performed on the resulting data, with the same factors as the ANOVA on the SPN with premovement baseline.
This ANOVA yields results that are highly similar to those of the ANOVA on the SPN with a premovement baseline. A main effect of Electrode Position ($F_{2, 18} = 4.14$; $p = 0.0419$, $\varepsilon = 0.51$) revealed that the SPN is maximal at occipital electrode positions (amplitudes at frontal, postcentral and occipital positions are 0.20, -0.38 and –1.76 uV, respectively). A main effect of Laterality ($F_{2, 18} = 6.80$; $p = 0.0151$; $\varepsilon = 0.64$) indicated that the SPN has a right-hemisphere preponderance (amplitudes are -0.16, -0.8 and –0.9 for electrodes overlying the left hemisphere, the midline and the right hemisphere, respectively). An interaction of Response Side * Electrode Position * Laterality ($F_{4, 36} = 11.97$; $p = 0.0004$; $\varepsilon = 0.51$) again indicated that the right-hemisphere preponderance of the SPN is present at all electrode positions regardless of response side, except at postcentral electrode positions following right-hand movements, where it is larger over the left hemisphere. Most importantly for this analysis however, is the absence of effects involving the factor Condition. This indicates that the absence of condition effects in the ANOVA on the SPN with premovement baseline cannot be attributed to differences in reafferent postmovement activity. The absence of a condition effect reveals the following. First, there is a negative shift following the response in the voluntary movement condition. The amplitude of this negative shift is comparable to the amplitude of the SPN. Second, the SPN in the time estimation conditions is independent of stimulus modality.

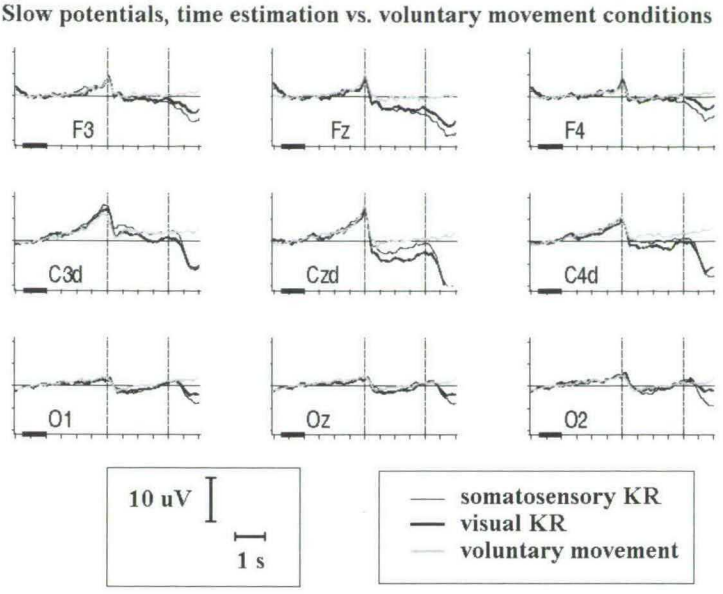

Figure 10.1 Grand average (N=10) slow potentials in all three conditions. Vertical bars indicate onset of response and KR stimulus. Data are from right-hand responses. Marked area on the x-axis corresponds to baseline interval. Note the (unexpected) presence of a negative shift following voluntary movements.

ERD.

Figure 10.3 presents topographic maps of the ERD at the interval of 250 – 0 ms prior to the presentation of the KR (in the voluntary movement condition this corresponds to the interval of 1750-2000 ms post-movement, since no KR was presented in this condition), in all three conditions and for all three frequency bands studied. The results of the ANOVA on the prestimulus ERD are summarized in Table 10.1; the results of the t-tests on the prestimulus ERD are presented in Table 10.2.

The t-tests on the prestimulus ERD (cf. Table 10.2) indicate that a significant, (or in some cases marginally significant), ERS can be observed at central electrode positions in all frequency bands (see also Figure 10.3), which can be identified as a postmovement ERS (Pfurtscheller, 1992). As can be seen in Figure 10.3, this postmovement ERS at central positions differs strongly between conditions. Therefore, a subtraction of the ERD in the voluntary movement condition from the ERD in the time estimation conditions, that would serve the goal of eliminating postmovement activity from prestimulus activity, is not warranted with the present data. Furthermore, in the 8-10 Hz and 10-12 Hz bands a significant ERD is present at occipital electrode positions preceding visual KR stimuli, which is not present in the voluntary movement and somatosensory KR conditions. Finally, it should be noted that in the voluntary movement condition there is a small, although non-significant ERD at the postcentral midline (see also Figure 10.3). In the somatosensory KR condition there is a small, non-significant ERS at this lead.

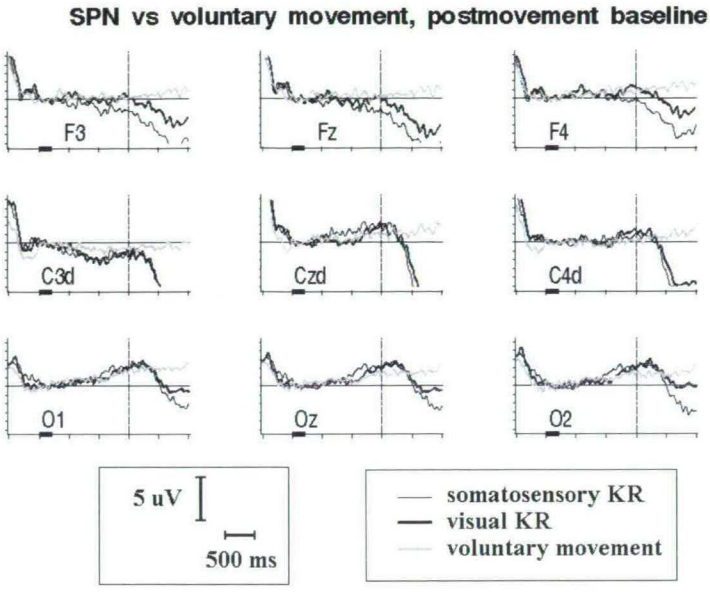

Figure 10.2 Grand average (N=10) slow potentials following movement in all three conditions, with a postmovement baseline (marked on the x-axis). Time 0 corresponds to movement onset; Vertical bars indicate the onset of the KR stimulus. Data are from right-hand responses.

Table 10.1 Main and interaction effects of the ANOVA on the prestimulus ERD. Both significant ($p < 0.05$) and marginally significant ($p < 0.10$) effects are included. Reported p-values are corrected with the Greenhouse-Geisser ε.

Effect	F	Df	P	ε
Condition (C)	4.24	2, 18	0.0473	0.77
Electrode Position (P)	4.08	2, 18	0.0647	0.59
Laterality (L)	5.13	2, 18	0.0201	0.93
Frequency Band (B) * L	3.89	4, 36	0.0228	0.70
C * P	2.81	4, 36	0.0704	0.63
C * P * L	2.41	8, 72	0.0791	0.42
Response Side (R) * L	7.65	2, 18	0.0198	0.53
P * L	3.12	4, 36	0.0629	0.55
R * P * L	5.02	4, 36	0.0395	0.31
B * R * P * L	3.10	8, 72	0.0528	0.32

The ANOVA on the prestimulus ERD (cf. Table 10.1) shows a main effect of Laterality, which reveals that on the average there is a larger ERS at lateral recording sites (18 and 17 % power increase over the left and right hemispheres, respectively) than over the midline (6 % power increase). The interaction of Frequency Band with Laterality further reveals that this effect is restricted to the 8-10 Hz and 10-12 Hz bands (simple effects of Laterality at 8-10 Hz: $F_{2,18} = 6.27$; $p = 0.0100$, $\varepsilon = 0.94$; at 10-12 Hz: $F_{2,18} = 4.33$; $p = 0.0304$, $\varepsilon = 0.98$; at 17-23 Hz: $F_{2,18} = 2.50$; $p = 0.1319$, $\varepsilon = 0.71$).

On the average, there is a clear ERS at postcentral electrodes (33 % power increase), and a much lower ERS at frontal and occipital leads (4 and 3 % power increase, respectively), as indicated by the main effect of Electrode Position. This postcentral ERS is maximal over the hemisphere contralateral to the movement side, as indicated by the interactions of Response Side * Laterality and Response Side * Electrode Position * Laterality (Simple effect of Laterality in left hand conditions: $F_{2, 18} = 8.67$; $p = 0.0085$; $\varepsilon = 0.66$; in right-hand conditions: $F_{2, 18} = 4.92$; $p = 0.0449$; $\varepsilon = 0.59$. Simple effect of Response Side * Laterality at postcentral electrodes: $F_{2, 18} = 6.85$; $p = 0.0267$; $\varepsilon = 0.51$; this simple effect is not significant at frontal and occipital electrodes). Furthermore, the four-way interaction Frequency Band * Response Side * Electrode Position * Laterality indicates that the contralateral dominance of the postmovement ERS is strongest in the 17-23 Hz band (see also Figure 10.3). Finally it should be noted that although Figure 10.3 suggests that the postmovement ERS is stronger in the somatosensory KR conditions than in the other two conditions, the absence of an interaction Condition * Response Side * Laterality (or Condition * Response Side * Electrode Position * Laterality) indicates that this difference is not statistically significant. Preceding visual KR stimuli there is an occipital ERD that is not present in the other conditions. This effect, that can be observed in Figure 10.3, is expressed in the interaction Condition * Electrode Position: in the visual KR condition there is a significant difference between postcentral electrodes (24 % power increase, or ERS) and occipital electrodes (24 % power decrease, or ERD; simple effect of Electrode Position in the visual KR condition: $F_{2,18} = 6.83$; $p = 0.0139$, $\varepsilon = 0.73$), while in the other conditions there is ERS both at postcentral and occipital electrodes (simple effects of Electrode Position in these conditions are not significant). The occipital ERD in the visual KR condition also produced the main effect of Condition, which indicated that on the average there is an ERS in the voluntary movement (19 % power increase) and somatosensory KR (22 % power increase) conditions, but not in the visual KR condition (0.5 % power decrease).

In the somatosensory KR condition there is a significant reduction in the ERS at the postcentral midline as compared to the lateral postcentral electrodes (cf. Figure 10.3). This effect is not present in the visual KR condition, whereas in the voluntary movement condition it appears to be present but it is not significant (in Table 10.2 the corresponding percentages ERD and ERS are presented separately for the three frequency bands). This effect is expressed in the interaction Condition * Electrode Position * Laterality: the simple effect Position * Laterality is significant only in the somatosensory KR condition ($F_{4, 36} = 4.34$; $p = 0.0179$; $\varepsilon = 0.65$), and the simple effect of Laterality in the somatosensory KR condition is significant only at postcentral electrodes ($F_{2, 18} = 5.55$; $p = 0.0159$; $\varepsilon = 0.92$). Furthermore, the interaction Position * Laterality also points to this effect: the simple effect of Laterality is significant only at postcentral electrodes ($F_{2, 18} = 5.55$; $p = 0.0159$; $\varepsilon = 0.92$).

10.5 Discussion.

We investigated the stimulus-preceding negativity (SPN) and the event-related changes of the power in the alpha and beta frequency bands (ERD) of the EEG related to the anticipation of somatosensory and visual stimuli, in a paradigm in which subjects performed a time estimation task and were informed about the quality of their time estimation by a KR stimulus. The present experiment is the first report on the SPN and the anticipatory ERD preceding somatosensory KR stimuli.

For the SPN the usual pattern of results was found, that is, a right-hemisphere preponderance, which is larger following left-hand movements than following right-hand movements (see e.g. Damen and Brunia, 1994). It should be noted however that the SPN in the present study is rather small, and it is virtually absent over frontal leads, as opposed to the usually reported frontal negative plateau (see e.g. Böcker and Van Boxtel, 1997, for a review of the SPN). It is

unclear why this frontal plateau is absent from the SPN in the present experiment. Most importantly for the present purpose however, is the finding that the SPN is independent of stimulus modality. This has previously been demonstrated for the visual and auditory modalities (Böcker et al., 1994c; Bastiaansen et al., 2000). The present results extend this finding to the somatosensory modality, and therefore support the notion that the SPN does not primarily reflect perceptual anticipatory processes, as has been put forward elsewhere (Bastiaansen et al., 2000, Chapter 9 of this thesis; see also section 4.2.1 of this thesis).

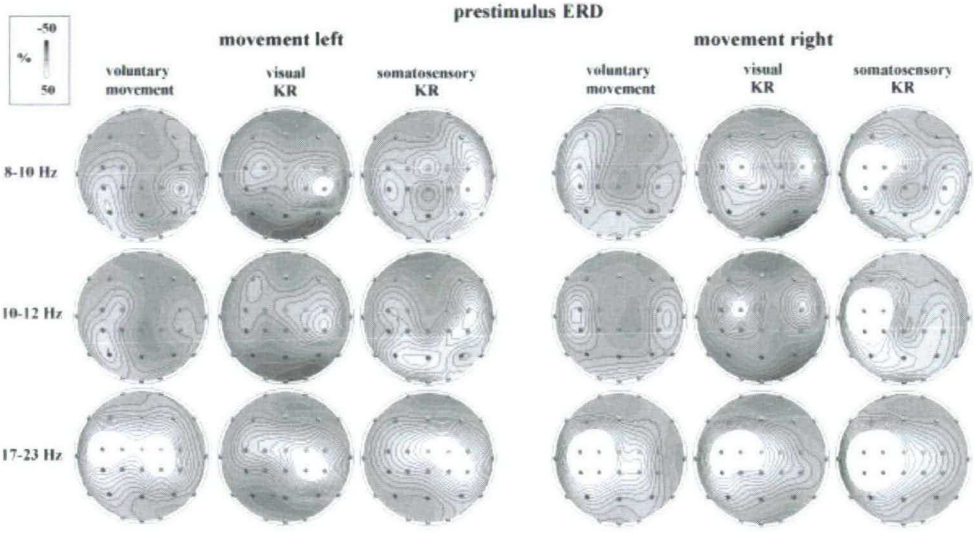

Figure 10.3 Grand average (N=10) topographic ERD maps at the pre-KR interval in all three conditions and all three frequency bands. Note (1) the presence of an occipital ERD in the 8-10 and 10-12 Hz bands preceding visual KR stimuli, (2) the presence of a postcentral ERD in the 8-10 and 10-12 Hz bands in the voluntary movement condition, and (3) a reduction of the post-movement ERS at the postcentral midline in the 8-10 and 10-12 Hz bands preceding somatosensory KR stimuli.

Preceding visual KR stimuli an occipital ERD was found, that is present neither in the voluntary movement condition nor in the somatosensory KR condition. This is in agreement with previous studies (Bastiaansen et al., 1999a, b, 2000; see Chapters 6, 7 and 9 of this thesis, respectively). Preceding somatosensory KR stimuli the results are less straightforward. In this condition there is a postmovement ERS at central electrode positions, which is stronger than in the other two conditions (to be discussed later in this section). However, at the postcentral midline there is a significant reduction in the postmovement ERS that is not present in the other two conditions. It may be hypothesized that this reduction in ERS is in fact an ERD that is superimposed on the strong postmovement ERS.

There are a number of arguments in favor of such an interpretation. First, the reduction in ERS is localized to the postcentral midline, which corresponds to the representation of the leg in the somatosensory cortex. Second, the reduction in ERS is present irrespective of response side. As pointed out in the introduction, an effect that is caused by postmovement processes is usually characterized by an interaction with response side and hemisphere, as in the case of the postmovement ERS at lateral postcentral electrodes. Therefore the reduction in ERS at the postcentral midline cannot be attributed to postmovement processes. Third, the reduction in

ERS in the present experiment is present in the 8-10 Hz band and (although to a lesser extent) also in the 10-12 Hz band, but not in the 17-23 Hz band. This is in agreement with the proposition, put forward by several authors, that the 10-Hz component of the mu rhythm originates from the somatosensory cortex, whereas the 20 Hz component of the mu rhythm originates mainly from the motor cortex, as I noted in the introduction (Salmelin et al., 1995; Pfurtscheller et al., 1998).

*Table 10.2. Results of the t-tests on the pre-stimulus ERD, averaged over response sides. Significance levels of the t-test are coded as follows: ns: $p > 0.10$; +: $p < 0.10$; *: $p < 0.05$; **: $p < 0.01$. In each cell the average percentage power change is given; negative values indicate a power decrease (ERD), positive values indicate a power increase (ERS). Note that in the voluntary movement condition, no KR stimulus was presented, so the pre-KR interval corresponds to 1750 to 2000 ms postmovement in this condition. LH = left hemisphere, ML = midline, RH = right hemisphere.*

Voluntary movement (no KR)									
Band	8-10 Hz			10-12 Hz			17-23 Hz		
Laterality	LH	ML	RH	LH	ML	RH	LH	ML	RH
Frontal Electrodes	14 ns	0 ns	8 ns	5 ns	0 ns	7 ns	15 ns	3 ns	9 ns
Postcentral Electrodes	42 *	-3 ns	23 *	32 +	-6 ns	23 +	53 *	34 +	31 **
Occipital Electrodes	13 ns	3 ns	24 ns	18 ns	15 ns	17 ns	5 ns	6 ns	5 ns
Somatosensory KR									
Band	8-10 Hz			10-12 Hz			17-23 Hz		
Laterality	LH	ML	RH	LH	ML	RH	LH	ML	RH
Frontal Electrodes	18 ns	5 ns	12 ns	11 ns	1 ns	5 ns	11 ns	2 ns	2 ns
Postcentral Electrodes	52 *	6 ns	54 **	56 *	23 ns	57 *	71 **	47 +	52 *
Occipital Electrodes	8 ns	12 ns	21 ns	10 ns	2 ns	16 ns	4 ns	0 ns	5 ns
Visual KR									
Band	8-10 Hz			10-12 Hz			17-23 Hz		
Laterality	LH	ML	RH	LH	ML	RH	LH	ML	RH
Frontal Electrodes	-3 ns	-6 ns	3 ns	1 ns	-10 ns	3 ns	7 ns	-4 ns	-4 ns
Postcentral Electrodes	23 +	18 ns	43 *	1 ns	-1 ns	14 ns	33 +	37 *	38 *
Occipital Electrodes	-26 *	-32 *	-33 **	-27 +	-31 *	-33 *	8 ns	13 ns	16 ns

A problem with this interpretation of the reduction in postmovement ERS is that it is paralleled in the voluntary movement condition by the postcentral ERD that is present in the interval of 1750 to 2000 ms postmovement (and which corresponds to the interval preceding the presentation of the KR in the time estimation conditions, see Figure 10.3). Admittedly, such a postcentral ERD is usually not found in the postmovement ERD. However, the postcentral ERD in the voluntary movement condition is very small and statistically non-significant, and can therefore be attributed to mere chance. Most importantly, the difference between lateral postcentral electrodes and the postcentral midline electrode is not significant in the voluntary movement condition, whereas it is significant in the somatosensory KR

condition (this is expressed in the three-way interaction of condition * electrode position * laterality). This suggests that in the latter condition a component is present (a postcentral prestimulus ERD that 'rides' on top of the postmovement ERS) that is not present in the voluntary movement condition.

In conclusion, the present results support the notion that the SPN does not mainly reflect perceptual anticipatory attention, since its scalp topography is not affected by the modality of the KR stimulus. It should be added however that results from a recent experiment in our laboratory indicate that there are small but significant differences in the scalp topography of the SPN preceding auditory and visual KR stimuli, which go in the expected direction. These findings leave room the possibility that a small part of the SPN does reflect perceptual anticipatory processes. With respect to the prestimulus ERD, the results confirm the findings of previous experiments, in that the anticipation of a visual stimulus is accompanied by an occipital ERD. In addition, the present results suggest that anticipating a somatosensory stimulus is accompanied by a postcentral ERD, although because of the paradigm that has been used in this experiment the postcentral ERD is hidden in a postmovement ERS. With respect to the latter it should be added that the temporal overlap between postmovement processes and prestimulus processes one the one hand, and the spatial proximity of the somatosensory and motor cortices on the other hand, hinders the identification of the postcentral ERD preceding somatosensory stimuli as a separate component. In future studies the overlap between postmovement and prestimulus processes might be avoided by increasing the temporal separation of movement execution and stimulus presentation. Since postmovement ERS in the alpha frequency range may last for over three seconds (e.g. Bastiaansen et al., 1999), stimulus presentation should follow movement execution no sooner than four seconds. In this way it may be established whether the postcentral ERD preceding somatosensory KR suggested by the present data is truly an independent component.

Chapter 11: Summary and conclusions.

11.1 Summary of the thesis.

Anticipatory behavior leads to a faster and/or more efficient processing of the anticipated event once this event occurs. In Chapter 1 it is noted that two components of anticipatory behavior can be distinguished. If anticipatory behavior is directed at an upcoming movement, the process is termed motor preparation; if it is directed at an upcoming stimulus, the process is termed anticipatory attention. This thesis is aimed at gaining a better understanding of the latter process. It is argued that physiological measures such as EEG or MEG are most adequate for studying anticipatory attention, since these measures are continuous and may yield information about the ongoing process instead of its post-hoc effects, while behavioral measures such as Reaction Time (RT) or error percentage can only yield information about the outcome of the process. The central question of this thesis is whether anticipatory attention for an upcoming stimulus is realized at the neurophysiological level as a prestimulus activation of the sensory cortex corresponding to the modality of the anticipated stimulus. This central research question is based on a thalamocortical gating model that proposes a neurophysiological mechanism of anticipatory attention.

Chapter 2 describes the state-of-the art thinking on the genesis of rhythmic EEG/MEG activity with a frequency of about 10 Hz. 10-Hz rhythms originate in thalamic circuits involving thalamo-cortical relay (TCR) nuclei and the reticular (RN) nucleus of the thalamus, which can fire either in burst mode (when high-frequency spike bursts recur periodically with a frequency of 10 Hz) or in tonic mode. Tonic mode firing of cells in a TCR nucleus is associated with the transmission of information from sensory afferents or subcortical structures to the cortex. The presence of rhythmic (burst mode) firing in a specific TCR nucleus is associated with the disruption of information transmission from sensory afferents or subcortical structures to the cortical projection area of that TCR nucleus. Burst mode firing in TCR cells most probably also produces a 10-Hz rhythm in the cortical projection area of the TCR nucleus, although the exact relationship between thalamic 10-Hz activity and 10-Hz activity in the corresponding projection area is not fully understood.

The modulation of 10-Hz rhythms in the EEG or MEG, insofar as it is related to an event, can be quantified by means of a technique known as Event-Related Desynchronization (ERD, discussed in Chapter 3). ERD analyses focus on the non-phase-locked part of the EEG or MEG signal. Therefore these analyses contain information that is not present in the widely used and more traditional analyses of Event-Related Potentials (ERPs), which only contain information that is both time- and phase-locked to the event in question. The spatiotemporal analysis of the ERD thus provides another means of analyzing the EEG or MEG, and can be used in addition to ERPs.

During the last decades different models have been proposed that describe which neurophysiological processes may underlie anticipatory attention. These models are presented in Chapter 4. Although the different models show significant differences in their account of anticipatory attention, they all assign an important role to the (thalamic) TCR and RN nuclei. More specifically, these nuclei are thought to play a role in the selection, or gating, of the relevant sensory modality: sensory afferent input in a modality that is anticipated easily reaches the cortex because of a facilitation of the relevant TCR nucleus, while sensory input in a modality that is not anticipated does not easily reach the cortex because of an inhibition

of the relevant TCR nucleus. This mechanism is termed thalamocortical gating. In the second part of Chapter 4 a brief review is presented of the EEG and MEG research that has addressed anticipatory attention. Anticipatory attention for an upcoming stimulus has been investigated mainly with two types of ERPs, slow potentials and evoked potentials (EPs) to probe stimuli. During anticipatory attention for an upcoming stimulus a negative slow potential can be measured that has been termed the Stimulus-Preceding Negativity (SPN, Damen and Brunia, 1987). However, parametric research on the SPN suggests that the SPN primarily reflects the presetting of cortical areas that are involved in the execution of the task at hand rather than the perceptual anticipatory process that is described by the thalamocortical gating model. EPs to probe stimuli, applied during the foreperiod of a forewarned reaction time task, are expected to show increased amplitudes relative to control EPs (evoked by probes when the subject is at rest) when the probes are of the same modality as that of the imperative stimulus, and decreased amplitudes when probe and imperative stimulus are of a different modality. The results of probe studies are equivocal, in that in- and decreases of EP amplitudes are not systematically dependent on whether the probe and imperative stimulus are of the same or of a different modality.

In sum, the results of ERP studies have not provided support for the prediction of the thalamocortical gating model that anticipatory attention is realized as a prestimulus activation of the relevant sensory cortex. As noted in Chapter 5, this thesis uses a different approach: ERD has been used as a dependent measure in order to establish whether anticipatory attention for an upcoming stimulus is accompanied by a prestimulus activation of the sensory cortex corresponding to the modality of the anticipated stimulus. For two reasons it may be argued that ERD analyses are better suited to study anticipatory attention than ERPs. First, because of the similarities between the proposed neurophysiological generator mechanisms of rhythmic 10-Hz activity on the one hand, and the thalamocortical gating mechanism on the other hand, it may be argued that ERD analyses, which are essentially a quantification of event-related variations in rhythmic EEG/MEG activity, are particularly suited to investigate anticipatory attention. Second, ERD analyses extract information from the EEG or MEG that is not contained in ERPs (i.e., the time-but not phaselocked event-related changes). Finally, it is argued that the time estimation paradigm, in which subjects are informed about the quality of their time estimation by a stimulus providing Knowledge of Results, is well suited to study the anticipatory ERD. The experimental part of this thesis describes parametric research, in which the modality and the discriminability of the KR stimulus are varied systematically in a number of experiments.

Chapter 6 describes the first experiment in which the ERD prior to auditory and visual KR stimuli has been investigated. The main finding from this experiment is that preceding visual KR stimuli an ERD is present which is maximal over occipital electrode positions, while preceding auditory KR stimuli no appreciable ERD was found. Furthermore, it was found that there is a clear temporal overlap between the postcentral ERS that can be observed following voluntary movements (Pfurtscheller, 1992) and the prestimulus ERD. Postmovement processes were separated from prestimulus processes by subtracting the movement-related ERD recorded in a control condition, in which subjects were simply asked to produce voluntary movements at a slow rate, from the ERD in the time estimation tasks. Note that the occipital ERD preceding visual KR stimuli only reached significance after this subtraction procedure.

A possible explanation of the absence of the expected bilateral temporal ERD preceding auditory stimuli might be that rhythmic activity from the auditory cortex cannot be measured with scalp-recorded EEG, as has been demonstrated by Niedermeyer (1990, 1991, see also Niedermeyer, 1997 for a review). Instead, with MEG it is possible to record such a rhythm, which has been termed the tau rhythm (Tiihonen et al., 1991; Lehtelä et al., 1997; see Hari et

al., 1997, for a review). If this is the reason for the absence of an ERD over the auditory cortex preceding the auditory KR, then this effect should be present in MEG data. This question is addressed experimentally in Chapter 7, where the ERD is investigated both on EEG and on MEG data during the anticipation of auditory and visual KR stimuli. The occipital ERD preceding auditory KR stimuli was replicated for all subjects, both in the EEG and in the MEG. Additionally, in two out of the five subjects studied we found a bilateral temporal ERD preceding auditory KR stimuli in the MEG that was not present in the EEG. These two subjects also had a larger level of absolute power at the MEG sensors overlying the auditory cortex than the other three subjects, suggesting a well-developed tau rhythm only for the two subjects displaying the temporal ERD. Therefore, it is concluded in Chapter 7 that this study provides at least partial evidence for anticipatory attention in the auditory modality.
Chapter 8 addresses a methodological issue that is important when computing ERD on MEG data recorded with axial gradiometers, as is the case for the MEG data described in Chapter 7. A problem with the straightforward computation of ERD on this kind of data is that because of the orientation of the (axial) gradiometers, field extrema are measured at sensors located at either side of a neuronal generator instead of at sensors directly above the source. This is problematic since ERD relies on a correspondence between the signal maximum and the location of the neuronal generator. In Chapter 8 a new method is presented that is based on computing spatial derivatives of the MEG data. Conceptually this comes down to transforming the 'axial' MEG into a signal that is similar to the MEG that would have been recorded with planar gradiometers. Simulations showed that this method has some limitations. First, fewer channels reduce accuracy and amplitude. Second, it is less suitable for deep or very extended sources. Third, multiple sources can only be distinguished if they are not too close to each other. Finally, the signal-to-noise ratio of the data should be relatively high, although this is dependent on the number of sources, their location, and the number of channels. Applying the method in the calculation of ERD on experimental data led to a spatial enhancement of the resulting ERD maps as compared to the straightforward calculation of ERD on the axial MEG. The new method was tentatively applied to the MEG data presented in chapter 7, but this yielded uninterpretable results. Most probably this is due to the relatively poor spatial sampling in this dataset (only 64 MEG channels were used), combined with a low signal-to-noise ratio. It is important to note however that this does not invalidate the results presented in Chapter 7: although the ERD on MEG data can be spatially enhanced by applying the method presented in Chapter 8, the condition differences in the ERD on the MEG data in Chapter 7 are macroscopic effects, in the sense that they involve comparisons between the spatially distant temporal and occipital cortices.
Chapter 9 addresses the effects of stimulus degradation on the ERD preceding auditory and visual KR stimuli. As expected, preceding auditory KR stimuli no ERD was present, while preceding visual stimuli an occipital ERD was found. Contrary to expectation however, the latter was larger preceding intact than preceding degraded stimuli. An unexpected finding in this experiment is that the postmovement ERS is much larger in the time estimation conditions than in the control condition, in which subjects were simply asked to perform selfpaced voluntary movements. This difference is tentatively explained by the fact that the time estimation task poses additional constraints on the movement (i.e., the timing of it). The consequence of these differences in postmovement ERS between conditions is that a subtraction of postmovement processes from prestimulus processes, as has been successfully carried out in the experiment reported in Chapter 6, could not be performed in the present study. The SPN was also analyzed in this experiment, and it was found that its amplitude varied with task difficulty. Auditory degraded KR stimuli were less effective than other KR stimuli in guiding subsequent behavior, and were preceded by a larger SPN. Thus, these data demonstrate a clear dissociation between the anticipatory ERD and the SPN. It is concluded

that the data support the interpretation of the pre-KR SPN as a reflection of the anticipation of the affective-motivational value of KR stimuli, and of the pre-stimulus ERD as a perceptually based anticipatory attention process, although it is unclear why stimulus degradation results in a smaller prestimulus ERD.

Finally, in Chapter 10 both the ERD and the SPN preceding visual and somatosensory KR stimuli is investigated. In the past, somatosensory KR stimuli have been avoided because of the spatial proximity of the motor and somatosensory cortices, which makes the separation between postmovement processes and prestimulus processes more difficult. Again it was found that the scalp topography of the SPN was not influenced by the modality of the KR stimulus. The postmovement ERS appeared to show differences between the experimental (time estimation) and control (voluntary movement) conditions, as was the case in the experiment reported in Chapter 9. Although these differences were not statistically significant, they were sufficiently apparent to avoid a subtraction of the postmovement ERS from the prestimulus ERD. Therefore both processes are simultaneously active at the pre-KR interval, as we will see below. With respect to the prestimulus ERD, the results again show the occipital ERD prior to visual KR stimuli. Prior to somatosensory stimuli, there is a marked reduction in the postmovement ERS at the postcentral midline. For three reasons this reduction in ERS may be interpreted as a prestimulus ERD which is superimposed on the postmovement ERS. First, the reduction in ERS is localized to the postcentral midline, which corresponds to the representation of the leg in the somatosensory cortex. Second, the reduction in ERS is present irrespective of response side. Since an effect that is caused by postmovement processes is usually characterized by an interaction with response side and hemisphere, the reduction in ERS at the postcentral midline cannot be attributed to postmovement processes. Third, the reduction in ERS in the present experiment is present in the 8-10 Hz band and (although to a lesser extent) also in the 10-12 Hz band, but not in the 17-23 Hz band. This is in agreement with the proposition, put forward by several authors (Salmelin et al., 1995; Pfurtscheller et al., 1998), that the 10-Hz component of the mu rhythm originates from the somatosensory cortex, whereas the 20 Hz component of the mu rhythm originates mainly from the motor cortex (see also section 3.3.1). In sum, it is difficult in the somatosensory condition to separate the prestimulus ERD from the postmovement ERS, as was expected. However, the results seem to indicate that in this condition a separate component is present (i.e., a postcentral prestimulus ERD) that is related to the anticipation of the somatosensory KR stimulus. Therefore it is concluded that although the results are certainly not decisive, they may be interpreted to reflect modality-specific anticipatory attention in the somatosensory modality.

11.2 Conclusions.

Taken together, the results of the different experiments show one robust effect, that has been found in all the subjects of all the experiments: this effect is the occipital ERD preceding visual KR stimuli. Therefore, it can be concluded that anticipatory attention for a visual stimulus is accompanied by an activation of the visual cortex. In the auditory modality, there is no bilateral temporal prestimulus ERD in the EEG data; this finding has been replicated in all three EEG experiments that used auditory KR stimuli. However, in the MEG such a bilateral temporal prestimulus ERD was found in two out of the five subjects studied, which fits well into the results of other research groups who found that rhythmic activity originating from the temporal cortex can be measured with MEG, but not with scalp-recorded EEG. In sum, the data only partly support the notion that anticipatory attention for an auditory stimulus is accompanied by an activation of the auditory cortex. In the only experiment in which the somatosensory modality was used it has been difficult to separate movement-related processes from prestimulus processes. However, the data suggest that anticipatory

attention for a somatosensory stimulus is accompanied by an activation of the somatosensory cortex.

A possible explanation for the fact that the clearest results were obtained in the visual modality may be that rhythmic 10-Hz activity originating from the visual cortex (i.e., the alpha rhythm) dominates the EEG/MEG of most individuals, whereas the 10-Hz rhythms from the auditory and somatosensory cortices (the tau and mu rhythms, respectively) are much less prominent. This is probably due to the fact that the visual cortex covers a larger part of the scalp than the somatosensory or auditory cortices. Therefore, the effects in these modalities may be less sizeable than in the visual modality, and as a result the detectability of these effects at the scalp may be more dependent, as compared to the effects in the visual modality, on factors that were not explicitly controlled for. Such factors may be for example the signal-to-noise ratio of the measurements, the general level of alertness of subjects, the exact orientation of the sensory cortices relative to the EEG or MEG sensors, etc.

Nevertheless, the general pattern of the results clearly points to a modality specificity of the prestimulus ERD. Thus, the data are in line with the hypotheses that were formulated in Chapter 5. Therefore, the answer to the general research question, *"is anticipatory attention for an upcoming stimulus realized at the neurophysiological level as a prestimulus activation of the sensory cortex corresponding to the modality of the anticipated stimulus?"*, can be answered positively. Recall from Chapter 1 that this question was based on a prediction of the thalamocortical gating model. Therefore it can be concluded that, although the present data do not allow for a direct test of this model (cf. section 1.3) they provide clear, albeit indirect, support for it.

In Chapter 4 it was noted that there are two different views of how selectivity is brought about in the thalamocortical gating system. Some authors (e.g. Skinner and Yingling, 1977; Brunia, 1993, 1997) have suggested that selectivity is mediated through the activating influence of the frontal cortex on those sectors of the RN nucleus that overly (and inhibit) the irrelevant TCR nuclei. Others (e.g. Laberge et al., 1992; Suffczynski et al., 1999) have proposed that selectivity is introduced at the thalamic level by virtue of the lateral inhibitory properties of the RN nucleus. It should be noted again here that EEG/MEG data can only indirectly support either one or the other claim, since these measures reflect only cortical activity. However, in none of the experiments presented in this thesis an ERD was found at frontal recording sites, although it was explicitly tested only in two experiments (presented in Chapters 6 and 10). Thus, our ERD data do not support an active role of the frontal cortex in selecting one of the sensory modalities, and therefore these results can be considered to be in favor of selectivity at the thalamic level. However, the ERP data that have been collected over the years do point to a contribution of the (pre)frontal cortex in the execution of the time estimation task, which might be partly related to between-channel selection. In sum, the ERD and ERP data are contradictory in this respect. Therefore the available evidence does not allow for any firm conclusions with respect to how and where selectivity is realized.

It is interesting to note that in this thesis a clear functional dissociation is present between the prestimulus ERP (i.e., the SPN) and the prestimulus ERD. It has been argued (cf. section 4.2.1) that in general SPN reflects the presetting of cortical areas that are involved in the execution of the task at hand. The fact that, in the time estimation paradigm that has been used in this thesis, the pre-KR SPN most probably reflects the anticipation of the affective-motivational properties of the KR stimulus (the SPN results presented in Chapter 9 provide additional evidence for this notion) is in line with this general interpretation of SPN. On the other hand, the prestimulus ERD that has been computed on the same data most likely reflects perceptual anticipatory attention, as has been argued above. In Chapter 3 it was noted that at the signal-analytic level, with ERD analyses different information is extracted from the EEG or MEG signal, i.e., the non-phase-locked part of the signal than when ERPs are

computed, since the latter only focus on the phase-locked part of the signal. The dissociation between SPN and prestimulus ERD strongly supports the idea that the signal-analytic differences between ERPs and ERD are not mere theoretical constructs. Instead, different psychophysiological processes can be uncovered by these different dependent measures. The important implication of the functional dissociation between ERPs and ERD that was found in the present thesis is that it may be advantageous to use both ERD and ERP measures in the analysis of EEG/MEG recordings. While most EEG/MEG researchers use either ERPs or ERD as a dependent measure, the results obtained in this thesis warrants the general recommendation to use both measures.

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Samenvatting (Dutch summary)

Anticipatoir gedrag leidt tot een snellere en/of meer efficiënte verwerking van een geanticipeerde gebeurtenis, op het moment dat deze optreedt. Aan anticipatoir gedrag kunnen twee componenten kunnen worden onderscheiden. Als anticipatoir gedrag gericht is op een in de nabije toekomst uit te voeren beweging, dan noemt men het proces *motorische preparatie*. Anticipatoir gedrag gericht op een stimulus die in de nabije toekomst in het centraal zenuwstelsel zal arriveren, wordt *anticipatoire aandacht* genoemd. Dit proefschrift is gewijd aan het verkrijgen van een beter inzicht in het tot stand komen van het laatstgenoemde proces. In Hoofdstuk 1 wordt beargumenteerd dat fysiologische maten als het Electro-EncephaloGram (EEG) en het Magneto-EncephaloGram (MEG) zeer bruikbaar zijn bij het bestuderen van anticipatoire aandacht, omdat deze maten continu zijn en informatie kunnen opleveren over het proces zelf. Gedragsmaten zoals reactietijd of foutenpercentages daarentegen leveren alleen informatie op over de uitkomst van het anticipatoire proces. De centrale vraagstelling van dit proefschrift is, of anticipatoire aandacht voor een stimulus van een bepaalde modaliteit (bijvoorbeeld auditief, visueel, somatosensorisch) op neurofysiologisch niveau wordt gerealiseerd als een prestimulus activatie van de sensorische gebieden die corresponderen met de modaliteit van de stimulus. Deze centrale vraagstelling is gebaseerd op een neurofysiologisch model van anticipatoir gedrag, namelijk het thalamo-corticale poortmodel.

In Hoofdstuk 2 wordt een overzicht gegeven van de huidige inzichten in het totstandkomen van ritmische EEG/MEG activiteit met een frequentie van ongeveer 10 Hz. Deze zogeheten 10 Hz ritmes vinden hun oorsprong in thalamische circuits, waarvan thalamo-corticale *relay* (TCR) cellen en de Nucleus Reticularis Thalami (NRT) de belangrijkste schakels vormen. Deze cellen kunnen vuren in twee verschillende modi: in *burst* modus treden hoogfrequente spike bursts periodiek op met een frequentie van 10 Hz, terwijl dit in de tonische modus niet het geval is. Het vuren van TCR cellen in de tonische modus wordt geassocieerd met de transmissie van neurale informatie van sensorische afferenten of van subcorticale motorische structuren naar de relevante corticale gebieden, terwijl het vuren van TCR cellen in *burst* modus wordt gerelateerd aan het onderbreken van deze informatie-transmissie. Elke TCR kern heeft zijn eigen corticale projectiegebied(en), en onder bepaalde omstandigheden produceert een TCR kern die in *burst* modus vuurt een 10-Hz ritme in 'zijn' corticale projectiegebied(en), hoewel de precieze relatie tussen thalamische 10-Hz activiteit en 10-Hz activiteit in het corresponderende corticale projectiegebied niet volledig begrepen wordt.

De modulatie van 10-Hz ritmes, voor zover deze systematisch gerelateerd is aan een (interne of externe) gebeurtenis, kan worden gekwantificeerd door middel van een techniek die Event-Related Desynchronisatie (ERD) wordt genoemd. Deze techniek, alsmede de rationale voor het gebruik ervan, worden in Hoofdstuk 3 gedetailleerd beschreven. ERD analyses richten zich op het niet-fase-*locked* gedeelte van het EEG of MEG signaal, en bevatten daarom informatie die niet aanwezig is in de veelgebruikte en meer traditionele Event-Related Potentials (ERPs). Deze laatste zijn namelijk per definitie opgebouwd uit EEG of MEG activiteit die zowel een vaste tijdsrelatie als een vaste faserelatie heeft tot de gebeurtenis in kwestie. De spatiotemporele analyse van de ERD is dus een alternatieve manier van het analyseren van *event-related* ('gebeurtenis-gerelateerde') EEG of MEG activiteit, en kan worden gebruikt als aanvulling op ERP analyses.

Gedurende de laatste decennia heeft men verschillende modellen geopperd die beschrijven welke neurofysiologische processen mogelijk ten grondslag liggen aan anticipatoire aandacht. Deze modellen worden uiteengezet in het eerste gedeelte van Hoofdstuk 4. Ondanks de aanzienlijke verschillen die er bestaan tussen deze modellen kennen ze allen een belangrijke rol toe aan de (thalamische) TCR en NRT kernen. Met name wordt van deze kernen gedacht dat ze een rol spelen in de selectie van de relevantie sensorische modaliteit, met andere woorden dat ze een poortwerking hebben: sensorische afferente input in een modaliteit die wordt geanticipeerd kan gemakkelijk de hersenschors bereiken omdat er in de relevante TCR nucleus facilitatie optreedt (de 'poort' is open), terwijl sensorische input in andere modaliteiten minder gemakkelijk de cortex bereikt omdat deze corresponderende TCR kernen ge?nhibeerd worden (de 'poort is dicht'). Dit mechanisme wordt het thalamo-corticale poortmechanische genoemd. In het tweede gedeelte van Hoofdstuk 4 wordt een overzicht gegeven van het bestaande EEG/MEG onderzoek dat gericht was op het verwerven van een beter inzicht in de neurofysiologische basis van anticipatoire aandacht. Dit proces is hoofdzakelijk bestudeerd met behulp van twee soorten ERPs, de zogeheten langzame potentialen en de evoked potentials (EPs) opgeroepen door *probe* stimuli. Tijdens anticipatoire aandacht voor een opkomende stimulus kan een negatieve langzame potential worden gemeten in het EEG die de Stimulus-Preceding Negativity wordt genoemd. Echter, de resultaten van 10 jaar parametrisch onderzoek aan deze SPN suggereren dat de SPN eerder een reflectie is van het 'klaarzetten' van de corticale gebieden die nodig zijn voor het uitvoeren van de betreffende taak, dan van het perceptuele proces van anticipatie zoals dat door het poortmodel wordt beschreven. EPs, opgeroepen door *probe* stimuli tijdens de voorperiode van een reactietijdtaak, worden geacht grotere amplitudes te vertonen dan EPs opgeroepen in een rustsituatie als de stimuli worden aangeboden in de zelfde modaliteit als de imperatieve stimulus. Zijn de probe stimuli van een andere modaliteit dan de imperatieve stimulus, dan verwacht men kleinere amplitudes dan tijdens rust. De resultaten van EP studies zijn echter niet eenduidig, in de zin dat af- en toenames van EP-amplitude niet systematisch afhangen van de overeenkomst tussen probe en imperatieve stimulus.
Kortom, de resultaten van ERP studies vormen geen duidelijke steun voor de voorspellingen die op basis van het poortmodel zijn gedaan. In Hoofdstuk 5 wordt uiteengezet dat in dit proefschrift een andere aanpak wordt gevolgd: ERD zal worden gebruikt als afhankelijke maat om vast te stellen of anticipatoire aandacht voor een stimulus op neurofysiologisch niveau gerealiseerd wordt door een prestimulus activatie van de relevante sensorische hersenschors. Er zijn twee redenen om te veronderstellen dat ERD analyses geschikter zijn voor het bestuderen van anticipatoire aandacht dan ERP analyses. Ten eerste zijn er grote overeenkomsten tussen de mechanismen die 10-Hz activiteit genereren enerzijds, en de mechanismen die worden beschreven in het thalamo-corticale poortmodel anderzijds. Daarom zou men *a priori* kunnen argumenteren dat ERD analyses bij uitstek geschikt zijn voor het bestuderen van anticipatoire aandacht. Ten tweede wordt met ERD analyses informatie uit het EEG of MEG signaal geëxtraheerd die niet aanwezig is in ERP analyses. In het laatste deel van Hoofdstuk 5 wordt uitgelegd waarom voor het operationaliseren van de anticipatoire aandacht gekozen is voor een tijdschattingstaak, waarbij proefpersonen worden geïnformeerd over de kwaliteit van hun tijdschatting door middel van een stimulus die Kennis van Resultaten (KR) overbrengt.

Het experimentele gedeelte van dit proefschrift beschrijft parametrisch onderzoek, waarin de modaliteit en waarneembaarheid van de KR stimuli systematisch zijn gevarieerd in een aantal experimenten. Hoofdstuk 6 beschrijft het eerste experiment, waarin de ERD werd geanalyseerd voorafgaand aan auditieve en visuele KR stimuli. De belangrijkste uitkomst van deze analyses was dat voorafgaand aan de visuele KR een ERD werd gevonden die maximaal

was boven de occipitale cortex, terwijl er voorafgaand aan de auditieve KR geen ERD waargenomen werd. Verder werd geconstateerd dat er een overlap bestond tussen de Event-Related Synchronisatie (ERS, de tegenhanger van ERD) die optreedt na het uitvoeren van een beweging, en de prestimulus ERD. De post-beweging ERS werd gescheiden van de prestimulus ERD door de bewegings-gerelateerde ERD/ERS die gemeten was tijdens een controleconditie (waarin proefpersonen alleen een vrijwillige beweging maakten) te subtraheren van de ERD in de tijdschattingstaak. Deze subtractie leidde tot een duidelijker beeld van de occipitale ERD voorafgaand aan visuele stimuli.
Een mogelijke verklaring van de afwezigheid van de verwachtte bilaterale temporale ERD voorafgaand aan auditieve KR stimuli zou kunnen zijn dat ritmische activiteit die zijn oorsprong heeft in de auditieve cortex niet kan worden opgepikt door scalp elektroden. Hiervoor zijn duidelijke aanwijzingen in de literatuur (zie Niedermeyer, 1990, 1991, 1997). Met MEG daarentegen kan deze activiteit wel worden opgepikt, en dit ritme wordt doorgaans het tau ritme genoemd. (Tiihonen et al., 1991; Lehtelä et al., 1997; Hari et al., 1997). Als dit de reden is voor de eerder genoemde afwezigheid van ERD boven de auditieve cortex voorafgaand aan de auditieve KR stimuli, dan zou dit laatste effect wel zichtbaar moeten zijn in de ERD analyses op MEG data. Dit werd onderzocht in het experiment beschreven in Hoofdstuk 7, waar de ERD zowel op EEG als op MEG data werd berekend tijdens de anticipatie van auditieve en visuele KR stimuli. De occipitale ERD voorafgaand aan visuele KR stimuli werd gerepliceerd voor alle onderzochte proefpersonen, zowel in de ERD op MEG als in de ERD op EEG data. Daarenboven werd voorafgaand aan auditieve KR stimuli bij twee van de vijf proefpersonen een bilaterale temporale ERD gevonden voor de MEG data, die niet aanwezig was in de ERD op EEG data. Deze twee proefpersonen vertoonden tevens een hogere absolute *power* dan de resterende drie op de MEG sensoren die boven de auditieve cortex gesitueerd waren, hetgeen suggereert dat allen deze proefpersonen een goed ontwikkeld tau ritme hebben. Geconcludeerd wordt dat deze resultaten ten minste ten dele een ondersteuning vormen voor anticipatoire aandacht in de auditieve modaliteit.
In Hoofdstuk 8 beschrijft een methodologische studie, waarin is onderzocht hoe men de ERD op MEG data gemeten met axiale gradiometers (zoals het geval is in Hoofdstuk 7) kan optimaliseren. Een probleem met het berekenen van de ERD op axiale MEG data is dat vanwege de (axiale) oriëntatie van de gradiometers, de extrema van de magnetische flux worden gemeten aan weerszijden van de neurale generator in plaats van recht erboven. Omdat ERD afhankelijk is van een redelijke overeenkomst tussen het signaalmaximum en de locatie van de generator vormt dit een probleem. Een nieuwe methode wordt uiteengezet in Hoofdstuk 8, die is gebaseerd op het berekenen van spatiele afgeleiden van de MEG data. Conceptueel komt dit neer op het transformeren van het gemeten signaal naar een signaal zoals dat gemeten zou zijn door een MEG met planaire gradiometers. De mogelijkheden en beperkingen van de methode werden onderzocht door middel van een aantal simulaties, en de methode werd toegepast op daadwerkelijk gemeten MEG data. Een vergelijking tussen de 'oude' en de nieuwe ERD methode toonde aan dat de ERD een hogere (en dus betere) spatiele resolutie heeft bij gebruik van de nieuwe methode. De nieuwe methode werd vervolgens toegepast op de MEG data die in Hoofdstuk 7 zijn beschreven, maar dit leverde oninterpreteerbare resultaten op. Dit is zeer waarschijnlijk het gevolg van het lage aantal MEG sensoren dat in deze laatste studie was gebruikt, gecombineerd met de relatief slecht signaal-ruisverhouding. Hierbij moet worden opgemerkt dat dit niet tot gevolg heeft dat de resultaten beschreven in Hoofdstuk 7 niet betrouwbaar zijn, omdat de effecten die daar werden gerapporteerd macroscopische effecten zijn in die zin dat ze vergelijkingen betroffen tussen spatieel ver van elkaar verwijderde gebieden (temporaal versus occipitaal).
In Hoofdstuk 9 worden de resultaten beschreven van een experiment waarin de waarneembaarheid van de KR stimuli is gemanipuleerd door middel van stimulus degradatie.

Zoals verwacht werd voorafgaand aan de auditieve KR stimuli geen ERD gevonden, terwijl voorafgaand aan de visuele stimulus wederom een occipitale ERD optrad. Echter, tegen de verwachting in was de occipitale ERD kleiner voorafgaand aan gedegradeerde KR stimuli dan voorafgaand aan intacte KR stimuli. Een andere onverwachte bevinding was dat in tegenstelling tot wat in het experiment beschreven in Hoofdstuk 6 werd gevonden, de post-beweging ERS veel groter was in de tijdschattingstaak dan in de controleconditie, waarin proefpersonen waren geïnstrueerd om vrijwillige bewegingen te maken. Dit verschil werd tentatief verklaard door het feit dat aan de beweging die moest worden uitgevoerd in de tijdschattingstaak meer eisen gesteld werden (namelijk de *timing* ervan). Als gevolg van de verschillen in post-beweging ERS kon de subtractie, van de bewegingsgerelateerde ERD, van de ERD in de tijdschattingstaak zoals die in Hoofdstuk 6 is uitgevoerd hier niet worden gedaan. In het huidige experiment werd ook de SPN geanalyseerd, en de bevinding was dat de SPN amplitude varieerde als functie van met taakmoeilijkheid. Auditieve, gedegradeerde stimuli waren minder effectief in het sturen van het gedrag op de volgende trial dan de andere soorten KR stimuli, en juist in eerstgenoemde conditie was de SPN amplitude het grootst. Samen genomen demonstreren deze resultaten een duidelijke dissociatie tussen de anticipatoire ERD en de SPN. De data ondersteunen de interpretatie van de SPN als zijnde een reflectie van de anticipatie van de affectief-motivationele eigenschappen van de KR stimulus, en van de prestimulus ERD als zijnde een reflectie van een perceptueel anticipatoir aandachtsmechanisme, hoewel het onduidelijk is waarom stimulus degradatie resulteert in een kleinere anticipatoire ERD.

In Hoofdstuk 10 werden zowel de anticipatoire ERD als de SPN onderzocht voorafgaand aan stimuli in de visuele en de somatosensorische modaliteit. In het verleden is de somatosensorische modaliteit vermeden door onderzoekers vanwege het feit dat de motorische en de somatosensorische cortices aan elkaar grenzen, hetgeen de interpretatie van effecten als zijnde zuiver post-motorisch of zuiver pre-stimulus bemoeilijkt. Wederom was de topografie van de SPN onafhankelijk van stimulus modaliteit. De post-beweging ERS vertoonde dezelfde conditieverschillen als die gevonden werden in Hoofdstuk 9. Ondanks dat deze verschillen niet statistisch significant waren, waren ze voldoende duidelijk zichtbaar om een subtractie van bewegings-gerelateerde ERD/ERS van de ERD in de tijdschattingstaak te vermijden. Het gevolg hiervan was dat een strikte scheiding tussen post-beweging ERS en prestimulus ERD bemoeilijkt werd. Voorafgaand aan visuele KR stimuli werd andermaal een occipitale ERD gevonden. Voorafgaand aan somatosensorische stimuli werd een statistisch significante reductie in post-beweging ERS gevonden, die om drie redenen kan worden geïnterpreteerd als een prestimulus ERD die gesuperponeerd is op een post-beweging ERS. Ten eerste is de reductie in ERS beperkt tot de postcentrale midline elektrode, waarvan de locatie overeen komt met het corticale projectiegebied van het gestimuleerde been. Ten tweede is de reductie in ERS onafhankelijk van responszijde, hetgeen pleit tegen een interpretatie in termen van post-beweging activiteit. Ten derde is de reductie in ERS wel aanwezig in de 8-10 Hz band en (in mindere mate) in de 10-12 Hz band, maar niet in de 17-23 Hz band. Dit is overeenkomstig met de suggestie dat centrale 10-Hz ritmes overwegend hun oorsprong hebben in de somatosensorische cortex, terwijl 20 Hz ritmes overwegend gegenereerd worden door de motorische cortex (Salmelin et al., 1995; Pfurtscheller et al., 1998). Concluderend kan worden gesteld dat, ondanks dat het moeilijk is om post-beweging ERS te scheiden van prestimulus ERD, de resultaten erop lijken te duiden dat voorafgaand aan somatosensorische stimuli een afzonderlijke component kan worden onderscheiden die kan worden gerelateerd aan anticipatoire aandacht in de somatosensorische modaliteit.

Conclusies.

Samengenomen vertonen de resultaten van de verschillende experimenten een robuust effect, dat optrad bij alle proefpersonen in alle experimenten, namelijk de occipitale ERD voorafgaand aan auditieve stimuli. Daarom kan worden geconcludeerd dat anticipatoire aandacht voor een visuele stimulus gepaard gaat met een activatie van de visuele cortex, zoals werd voorspeld door het thalamocorticale poortmodel. In de auditieve modaliteit treedt er geen prestimulus ERD op in de EEG data; dit is gerepliceerd in alle drie de experimenten waarbij auditieve stimuli zijn gebruikt. Daarentegen werd wel een prestimulus ERD gevonden voorafgaand aan auditieve stimuli in de MEG data, hetgeen past in de bevindingen van andere onderzoeksgroepen dat ritmische activiteit van de auditieve cortex alleen met MEG kan worden gemeten. De voorlopige conclusie is dat de resultaten slechts ten dele de notie ondersteunen van anticipatoire aandacht in de auditieve modaliteit. Tenslotte, in het enige experiment waar somatosensorische stimuli werden gebruikt bleek het moeilijk om een duidelijk onderscheid te maken tussen post-beweging processen en prestimulus processen. Daarom luidt de voorlopige conclusie op dit vlak dat de data slechts suggereren dat anticipatoire aandacht in de somatosensorische modaliteit gepaard gaat met prestimulus activatie van de somatosensorische cortex.

Desalniettemin duidt het algemene patroon van resultaten op een modaliteits-specificiteit van de prestimulus ERD. Daarmee zijn de resultaten globaal in overeenstemming met de hypothesen die in Hoofdstuk 5 werden geformuleerd. De centrale vraag van dit proefschrift, "wordt anticipatoire aandacht voor een stimulus die in de nabije toekomst zal arriveren op neurofysiologisch niveau gerealiseerd als een prestimulus activatie van de sensorische cortex die correspondeert met de modaliteit van de stimulus?", kan dan ook positief worden beantwoord.

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