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Time-frequency domain EEG activity during the preparation of task sets and movements

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Contents

Chapter 1

Introduction

1.1 Foundations

Walle! walle,
Manche Strecke!
Daß, zum Zwecke,
Wasser fließe
Und mit reichem, vollem Schwalle
Zu dem bade sich ergieße.

Stehe! stehe!
Denn wir haben
Deiner Gaben
Vollgemessen! -
Ach, ich merk es! Wehe! wehe!
Hab ich doch das Wort vergessen!

From Der Zauberlehrling, J. W. von Goethe.

(Sweep! sweep // do not stop, // To reach my goal // let water flow // so streams and torrents // fill the bath.
Stop! stop! // for we have // your gifts // in plenty! - // Oh, I see! Woe! woe! // I no longer know the word!) Author's translation.

When the sorcerer's apprentice lost control over the demonic broom, the situation he had himself created continued regardless of his changing desires. Something similar happens when we try to change the way we respond to our environment. The existing state of mind seems to resist being overwritten. Once we start sweeping, there is a tendency to keep at it, even if we would really prefer to stop and do something else. But eventually the sorcerer is called back to use the magic word and stop the task to which we had set the brooms of our mind.

The main question this thesis aims to explore is what the magic word is. What allows us to change the way we react to the world? The studies described in the Experiments section are explorative attempts to provide information on this and related questions. In these experiments, analyses were done of the oscillatory behavior of the electric potentials generated by brain cells while subjects perform a variety of tasks. The reasons why such data might help understand how we change our mind are provided in the introduction. First, the concepts of information, control and encoding will be explained. These concepts are used in many if not all of the cited studies, but also provide an unambiguous way to talk and think about complex behavioral processes. Second, the main experimental paradigm of the experiments will be introduced: task switching. In this section, behavioral studies will be discussed. The following section is concerned with the organization of the brain and how that relates to task switching. Studies of brain activity look at the processes between the external events of stimuli and responses, and so could help understand behavioral results concerning relations between stimuli, responses and experimental manipulations. In following sections results on oscillatory neural behavior are discussed, organized by the three frequency bands of interest in the experiments. These sections, taken together with the foundational concepts, behavioral results and principles of brain organization, provide a framework from which tentative hypotheses arise and within which empirical data can be interpreted.

1.1.1 Information

Intuitively, information is a measure of how much a message tells you about something. For instance, if I tell you that a loaf of bread costs between two and three euros, I tell you less than if I tell you that it costs precisely 1.35 euros. If every time Pinochio lies, his nose grows by x cm, then the length of his nose tells you something about how many lies he's told. If Pinocchio tells you a loaf of bread costs 1.35 euros, you know less if his nose grows at that point than if it doesn't. A similarly intuitive idea of information processing is that that is what happens when you use what a message tells you. For instance, if you know the price of bread, you would make sure to bring at least that amount of money to the shop to buy a loaf. Information can also be communicated: messages can be passed along and maybe change their form. For instance, I could receive a letter by post, tell my neighbour what it says, and he could tell someone else via e-mail. Such ideas about information are relevant to the kind of self-control described above. The information conveyed by stimuli must be processed by the brain to eventually be used to choose an appropriate response. How the information is processed determines what response we choose. So, when we try to change the way we respond to events, we are actually trying to change the way we process information. But in the face of the complexity of behavioral patterns and neural organization, such intuitive ideas seem too vague to be of much use. Almost anything could be described as ”information processing” - so by itself the term says very little.

A more rigorous theory of information was developed by Shannon [209] and Wiener [240]. This theory defined information in such a way that it became a formally defined entity and a precisely computable quantity. This allowed, for instance, the informativeness of two kinds of messages to be compared, even if their generation was complex and the differences subtle. It also allows the reduction of many kinds of mechanisms, capabilities, requirements, changes over time and patterns of activity to their characterization in terms of information processing, with sufficient detail to distinguish between and define specific cases. For instance, the brain contains on the order of 10^9 neurons. To demand each individual neuron and synapse to be described in all its uniqueness makes no sense and would bring neuroscience to a grinding halt. To describe each neuron too simplistically - as a point in space for example - would provide no understanding of how they subserve what the brain does. Considering the neuron as a precisely definable type of information processing unit is one of the steps that allows work towards an understanding of the principles of brain behavior. Information theory is in a sense a new language in which we can talk about patterns for which natural languages have insufficient words and rules of grammar. Because of its rigor, a statement made in information theoretical terms has immediate and unavoidable consequences that can be tested. Because of the power of the mathematical language, intuition-surpassing extrapolations and inferences can be made - for instance from one neuronal unit to many.

So at least a rudimentary understanding of information seems desirable, if not necessary, to try to understand what the brain does. Fortunately, the basic theory is simple to understand, needing only three building blocks: probability, surprise and entropy. Probability is a measure of how often a certain event occurs, expressed as a number between 0 and 1. For instance, when adding the values of two six-sided D6 dice, the event ”the sum is smaller than 4” is fulfilled in three of the 36 possible outcomes. So, if all the outcomes occur equally often, the probability is $\frac{3}{36} = \frac{1}{12}$. The measure of surprise is directly mapped to a probability p by the function $-^2 \log p$. So, when an event has a probability of 1, the surprise when it happens is 0. The closer the probability of an event gets to zero, the larger the surprise when it does in fact happen. The entropy, symbolized by S, is the weighted sum of surprises over a set of events: $S = \sum_{\text{event}} p(\text{event}) * \text{surprise}(\text{event})$.

This provides the expected value of surprise when an event occurs, that is, the average surprise over a large number of events drawn from the set. For all exhaustive and distinct sets of events (of which one must and only one may occur at a time), the summed probability is 1. Entropy, in contrast, provides a distinction between such event sets. The surprise, or uncertainty, involved in tossing a coin works out as $\frac{1}{2} + \frac{1}{2} = 1$bit, bits being the unit of entropy. The entropy of rolling a four-sided die is 2 bits. For an eight-sided die the entropy is 3 bits, which shows the meaning of the bit measure: an increase in entropy by one bit is equivalent to doubling the number of alternatives of the set.

The formal definition of information is: the reduction of entropy due to a message. Once you see that the tossed coin is heads, the probability distribution becomes "p(heads) = 1", with an entropy of zero, so that 1 bit of entropy is lost. Rolling the eight-sided die reduces uncertainty by 3 bits, and so forth. For messages that are not 100 % reliable, the conveyed information is reduced by the remaining entropy following a response, averaged over responses.

1.1.2 Coding

Coding is the form of the message that is used to convey information. For instance, consider the intensity of light falling on a receptive cell. Even if it is known that the cell transmits the information, it could do so in different ways. Its firing rate could increase, by some monotonic function, with intensity. It could fire sooner after stimulation (this is an example of a time, or temporal code). It could fire a burst of increasing length or frequency. If the cell connects to a group of cells, the proportion of cells in the group that start firing could also encode the intensity. The firing rate of specific cells is a very well-studied code in the brain (the in vivo studies of section 1.3.2 all look at this code). However, so-called population [29] and temporal [235] codes are also used in the brain.

First, note that distributed and population coding are not synonymous. A distributed code involves multiple messengers, or signals. The abstract event "7, 3" could be encoded into a single value by a coding scheme of the form "message = (10 * number 1) + number 2", combining the information into a single message. It could also be encoded into two messages, one for the first and one for the second number. As illustrated in this example, while distributed coding requires more messages, the complexity of the encoding per message can be kept simpler. The neurons in our central nervous system are of course the instance of distributed coding of most interest to this text. An example of distributed coding is the representation of whisker deflections in rat somatosensory cortex [179] [180]. Each whisker is mapped, via the thalamus (see section 1.5.4), to a specific cellular unit (or cortical column [160], see 1.3.2) but also evokes activity in neighbouring units. The response to whisker deflection is initially restricted to the central unit but spreads to neighbouring units during the 10 ms following stimulation. Which stimulus has been presented can be reconstructed from the messages of the neighbouring units alone, indicating a spread of information over the population [179]. Extra information is provided by the timing of the first post-stimulus spikes [180]: the more central the cell, the quicker the first spike. The transmission of information in this way - by spike timing - is an example of a temporal code. Another form of temporal coding, synchrony, has been shown to play a distinct role from rate coding. Synchrony is a form of temporal coding in which neural events provide the reference time, as opposed to external stimuli. In motor cortex, the modulation of rate and spike synchronization have been shown to be differently related to motor functions [195]. Monkeys were trained to perform a delayed-response hand movement task, containing a preparatory signal and a response signal, presented after a delay of 600, 900, 1200 or 1500 ms. Each delay was equally probable. Neurons in primary motor cortex showed an increase in synchronization, independently from changes in firing rate, around the delay times, even when no response signal was given. Rate modulation was found around actual responses. Thus, spike synchronization was related to internal, behaviorally relevant events (i.e. expectation and preparation), while rate modulation was related to producing a movement.

A population of neurons that responds to a stimulus by a distributed code does not, by itself, imply the use of a population code. A population code requires synergy [29]: the population response must convey more bits of information than the summed non-redundant information of the separate signals. This happens when the relationship between spikes of different neurons defines the events carrying information. For instance, in a population of four neurons, cells 1 and 3 could fire in response to stimulus A, and cells 1 and 4 to stimulus B, and so forth. "Reading" cell 1 could then not distinguish between stimuli A and B, while reading the combined response could unambiguously distinguish stimuli. In the rat somatosensory data, the late spikes in the neighbouring units could be due to any whisker with a neighbouring central unit. It is their pattern - around a given central, fast-spiking unit - that uniquely determines to what whisker they are responding, although in this case, the late-spiking pattern supplied no more information that the fast, central spike. In the antennal lobe of locust olfactory cortex, the response to odors consists of stimulus-dependent, spatially distributed spiking patterns [127]. Whether this is due to information encoded independently in spiking patterns over time for each cell individually, or whether "reading" the whole pattern is necessary to reconstruct stimulus information, was not tested directly. The data do, however, at least illustrate the feasability of population codes.

Population coding leads to the superposition problem, which can be overcome using temporal coding, in particular synchronization [212]. For instance, stimuli in the environment do not occur one at a time or in isolation, and so their presence must be encoded simultaneously. How are the distributed signals that encode the component parts of different stimuli separated from each other? The superposition problem can be solved by combining population coding with an extra coding dimension for encoding set membership; this combination has been termed assembly coding [212] [196]. The precise timing of neurons' spikes may be used to define sets, as neurons are sensitive to the precise (millisecond scale) timing of their inputs. This sensitivity is due to coincidence detection [10]: the peak of the superimposed post-synaptic potentials is higher for synaptic events that occur closer in time. A set-coding dimension that uses spike timing would separate a population of active neurons into subsets, the elements of which would fire with a specific phase difference relative to each other. If that phase difference is zero, then the set coding dimension is synchrony. Synchrony has been argued to be well-suited for assembly coding: set membership is communicated quickly - one synchronous burst would be sufficient - and the number of overlapping assemblies is limited only by the time needed to separate the post-synaptic effects of such bursts [212]. Assembly coding using synchrony has been shown to arise in visual cortex. In monkey visual cortex, two sets of neurons were selected with different preferred orientation of light bars, but with overlapping receptive fields [123]. When a single bar with an orientation to which both sets of neurons responded was presented, all measured neurons fired synchronously. When two light bars were superimposed, one at each preferred orientation, the neurons in the two groups fired synchronously with each other, but lost their synchrony with the other group. In cat visual cortex [56], a similar study has been performed using either a single vertical bar moving across the screen, or two smaller vertical bars moving in opposite directions. Neurons with receptive fields through which the bars passed showed synchronous activity for the single bar, but unrelated spike timing for the separate bars.

These findings agree with a phase-coding solution to the superposition problem.

One form of temporal coding is phase coding. In this case, coding time is defined relative to some reference oscillation. Phase coding has been used to establish relations between representations other than only set membership. In a study on proposition representation (in an abstract system not intended to be very similar to the brain), statements such as "John loves Mary" and "Mary loves John" were separated from each other by the timing of the elements' activation [94]. During cycles similar to musical measures, terms such as "beloved" and "lover" were activated at different times, and names such as "John" and "Mary" were active during the active phase of one or the other term. In the locust olfactory system, cells in the mushroom body, to which neurons of the antennal lobe project, fire in a specific phase region relative to a 20 Hz oscillation of the local field potential [178]. Only input to the mushroom body that is correctly timed to this window of opportunity can contribute to further spikes. Thus, while a complex spatiotemporal pattern of spikes encodes the odor, the phase of spikes encodes the salience of different parts of that pattern.

All in all, population and temporal coding have the potential to be an important part of information processing in the brain. Evidence exists, at least for primary sensory cortices, for a richer repertoire of coding mechanisms than only rate coding. Later sections will review studies of distributed and temporal coding at larger scales than the in vivo studies above.

1.1.3 Information and working memory

Many studies cited in this thesis refer to working memory, which has been defined as "the temporary storage of information that is being processed in any of a range of cognitive tasks" [11]. In this definition, working memory is an act - "storage" as opposed to "storage space". The existence of such acts can be inferred from the performance of tasks with suitable demands, e.g. "remember the following random list: ...". However, working memory has also been defined as a system, comprising a "central executive", "visuospatial sketch pad" and "phonological loop", each of which assigned functions involved with, respectively, attentional control, the temporary storage and manipulation of visual and spatial information and the maintenace of items in subvocal speech [12]. So it is not clear whether "working memory" should be conceived of as the act of temporary storage, the place where information is temporarily stored, or the systems operating on such information. Many variations of the definition also exist, e.g. "the ability to transiently hold and manipulate goal-related information to guide forthcoming actions" [54].

The reason working memory was postulated was as an elaboration of a unitary short-term memory, which could not explain dissociations in neuropsychological findings within the set of short term memory dysfunctions [12]. It seems likely that working memory defined as an ensemble of systems would have to be upgraded to include every modality introduced by new tasks (e.g. comparing two smells, determining whether a sequence of touches is a sensory palindrome, and so forth). The underlying idea of working memory concepts appears to be the existence of distributed short term memories combined with at least one and possibly a unitary organizing structure. A different kind of definition of working memory can be given in terms of task demands, in contrast with the inferred structures and processes involved in performing those tasks. Working memory tasks, such as those listed above, involve a certain type of demand: the processing of temporarily stored information [11]. In this text, unless otherwise stated, "working memory" refers to the task demands of temporary information storage and the manipulation of such information.

What does it mean to say that a task demands the temporary storage of information? Take the following two situations. First, let two events A and B occur at time t0. Then information of the type "A == B" might need to be encoded into a response. Next, let an event A occur at time t0 and be encoded in some form at place p0. What happens if at a later time t1 a new event B occurs and the task still demands the encoding of the event A == B? The information of event A occurring must be communicated over time to t1, when it can be processed together with event B to produce the desired response. So, storage of information will be defined here as communication over time. Temporary storage occurs when stored information is lost after some duration or processing step. Note that this actually encodes a specific kind of information, namely timing: if the information is still active, it must be due to a recent event. The complementing kind of storage, long-term storage, encodes what has happened at some point, or over some period, in the past. Prefrontal cortex has been shown to play an important role in communication over time and in goal-directed changes in how information is processed, as discussed in section 1.3.2.

1.1.4 Neural channels for communication over time

The temporary storage and manipulation of information requires a certain kind of encoding. After a stimulus is encoded into a neural pattern, that pattern must communicate itself to a future point in time. At that point, the information can be processed further, e.g. when more information becomes available. The typical example of such temporal communication is when a cue is given that must be combined with a subsequent stimulus, presented after a delay, to encode the event "the cue was (or consequent context is) X and the stimulus is Y". Similarly, since manipulation of information takes time, an enduring encoding is a prerequisite for that second aspect of working memory. What form could such encoding take? Two mechanisms which have been used in neurocomputational models of working memory [54] are recurrent excitation and cellular bistability. The ideas involved in these mechanisms may help understanding task switching and its underlying brain activity.

Recurrent excitation involves a pattern of activity feeding back onto itself in such a way that it converges to a stable state over time (or iterations) [90] [83]. Note that communicating information via a distributed pattern of activity is a form of population coding. Other terms for recurrent excitation are reverberation [6], autoassociation [83] and attraction [6]. Hopfield networks [90] are a well-known example of a system of recurrent excitation [54] [6], which illustrate three important concepts: convergence, stability and temporal tuning. Hopfield networks consist of interconnected elements, termed neurons, which compute whether their weighted input exceeds a threshold. There is no direction in the structure of a Hopfield network, as in a neural network with an input and output layer connected either directly or via hidden layers; only time provides direction, in the way described below. Each element has a state variable, its activation, which is either one or zero. The connection, termed synapse, from a neuron i to a neuron j specifies the weight neuron j applies to neuron i's activation value when it determines its input. The biological terminology was based on an analogy with the firing rate of a neuron as a function of the effect of synaptic events on its membrane potential. The elements are allowed to independently and stochastically determine at which times they summate their input and perhaps change their activation. The network encodes information through its convergence to one of a number of patterns, stored in the synaptic weights. The storage algorithm bases the weight between two neurons on the co-occurrence of their activations over a set of activation patterns to be stored. This choice of weights can be learned by the network through Hebbian learning, and once instantiated, leads to convergent network behavior. Convergence means that changes in the activation pattern remain low after a sufficient period of time following a given starting pattern, during which the eventual non-changing, or stable, pattern is reached. The converged pattern is said to have low energy, the energy of the network at a certain time point being defined as a measure of how much the activation pattern will change in the next iteration, or over the following time period. Low energy therefore means that the activation pattern remains the same. The stored patterns on which the synaptic weights are based become stable patterns. If a pattern of activation is imposed on the network, it only has to be sufficiently similar to one of the stored patterns for the network to converge to the full stored pattern. This kind of pattern retrieval is termed content-addressable memory.

Note that in Hopfield networks the only direction is time, not any kind of flow from input to output layers within the network. As described in 1.3.1, this kind of "inwards-looking" processing may be an important part of coordinative brain function. Further, the abstract, computational neurons in the network could be hypothesized to represent meaningful functional units of the brain, implementing e.g. stimulus processing or response generation. Pattern completion in the network would in that case translate to stimulus - response mapping, and since various patterns can be stored, such a mapping of stimuli to responses would be flexible. The question of how task switching works in computational terms might then be related to the question of whether and if so how pattern completion involving sensory and motor regions is performed by the brain. If pattern completion is the underlying process involved when subjects prepare to perform an upcoming task, certain questions arise. First, something must determine a starting point for the network, which determines its nearest stable state. Note that the tendency to converge provides control as well as information storage and manipulation. Second, even if the end-state is determined, a period of time is required for convergence to take place. Third, if the same network is used for subsequent patterns, interference may occur, and the energy of the network must be increased sufficiently to break out of established stable states. Hopfield believed that the convergence behaviour in his networks would generalize to other specific implementations, and in line with that belief these questions about pattern-recognition, although inspired by the general behaviour of Hopfield networks, do not rely on their details.

Neuronal delay activity measured from cortex using single-unit recordings has been modelled using an attractor model [6]. In the experiment [155], visual stimuli were presented in a fixed sequence during training. Unexpectedly, delay activity for different stimuli was correlated with how close they were to each other in the learning sequence. The temporal closeness had been encoded into spatial similarity. An attractor model was built using excitatory integrate-and-fire neurons. The derivative of a neuron's current was a function of the weighted sum of the firing rates of the other neurons and a decay term. Patterns were presented as an additional term in the equation for the current derivative. A nonlinear current-to-rate transduction function was used. Unstructured inhibitory feedback was provided that led to an overall hyperpolarization driven by the mean activity in the pool of excitatory neurons. The synaptic matrix was learned using a periodic sequence of patterns. Weights w_{ij} between neurons i and j were 0, a or 1. If a pattern exists in which both neuron i and j are active, then $w_{ij} = 1$. If a consecutive pattern exists in which neuron i and j are active, one in pattern n and the other in pattern $n + 1$, then $w_{ij} = a$. Otherwise, the weight is zero. This kind of learning algorithm allowed the network to learn sequences and exhibit the same behavior as that found in the empirical data. When pattern n is presented and then removed, the network stays active in that pattern, but also activates the surrounding patterns, which in turn activate their neighbours. The learning parameter a determines the breadth of temporal tuning, i.e. the tendency of pattern n to evoke patterns that are nearby in terms of sequence position, or more generally, time. Note that, the stronger neighbouring patterns become activated, relative to the relevant pattern, the less specific the networks response is to the actual stimulus, so that a trade-off appears to exist between the precision of representation and breadth of temporal tuning. This trade-off may play a role in the organization of prefrontal cortex (section 1.3.2). Another similarity between this model and prefrontal cortex is the ability of cells to code retrospectively and prospectively, that is, bidirectionally in time, just as was achieved by a non-zero temporal tuning parameter.

A problem with the specific Hopfield network as a model for working memory is that the synaptic weights must be learned for the network to function, while novel information should be able to be encoded in working memory with no or a minimal learning phase. If Hopfield networks are to play a role in working memory, it seems that either a) a large number of patterns must already be stored, or some further mechanism exists which either b) allows fast, transient changes in synaptic weights within the Hopfield network or c) flexibly connects the neurons in a central Hopfield network to peripheral, content-providing neurons (e.g. for perception and action), changing the meaning of the central patterns. However, no task is performed without either training (especially in animal studies) or an available analogue in long-term memory (especially in human studies), which may be important for this problem.

In cellular bistability models, oscillation due to the dynamics of realistic model neurons combined with recurrent inhibition is the key to memory maintenance [237]. As will be shown later (in 1.4, 1.5 and 1.6), neural oscillations are extensively involved in cognition, so such oscillatory mechanisms are of special interest. Recurrent inhibition provides a robust mechanism for the generation of oscillations [237]. The basic recurrent inhibition model reciprocally connects neurons belonging to two groups: one excitatory and one inhibitory. Excitation of the excitatory group results in spikes that cause the inhibitory neurons to fire. They in turn inhibit the excitatory pool, thus depriving themselves of input. Now the excitatory pool can fire again, and the oscillation enters its second period. The continuation of the oscillation requires either a continuous depolarization of the excitatory neurons, or long-lasting depolarizing current, such as caused by NMDA channels [237]. In the latter case, when spiking occurs in an interconnected group of excitatory neurons, both a post-synaptic depolarization within the excitatory group and recurrent inhibition are initiated. The depolarization may last long enough to still be able to reach spiking threshold after the inhibitory phase is over, which starts the cycle again. Recurrent inhibition causes synchronization because if neurons fire at all, that must occur in the time window between two inhibitory phases.

The presence of oscillations provides the potential for phase coding, as the effect of incoming excitations may be dependent on the phase of the oscillation, as shown in olfactory cortex in the locust [178]. The phase coding in locust olfactory systems has further been shown to be generated by recurrent GABA inhibition from lateral horn interneurons [178]. Recurrent inhibition has been argued to be part of the cause of the encoding of tones by single spikes in auditory cortex [51]. A further example of the importance of the timing of synaptic input relative to rhythmic inhibition will be shown in section 1.5.4 on thalamocortical behavior.

Cellular bistability provides a short-term memory mechanism: a pattern of activity can remain after a stimulus is no longer present, encoding the past event, and the memory lasts only as long as the oscillation, with no changes in synaptic weights. Oscillatory activity in post-synaptic potentials has also been associated with assembly coding, as a method to make patterns of synchrony within a network robust by coupling the precise timing of discharges to the oscillation and not to the perhaps noisy timing of individual synaptic events [212] [196]. Cellular bistability could play a further role in maintaining an assembly code over time. If bistable elements are part of a Hopfield network, pattern completion and temporal tuning could be added to a network of such elements' capabilities. The channels provided by attractors and cellular bistability, together with assembly coding, provide a computational framework for thinking about cognitive control in reductionist terms, and will recur in the discussion of various fields of research.

1.1.5 Control and cognitive control

Similarly to information, control has an intuitive and a rigorous meaning. Intuitively, control is the ability to either change or stabilize something in accordance with our desires. A more rigorous development was initiated by Wiener in his book on cybernetics [240]. Wiener identified control with negative feedback applied to error signals. This idea contains four important elements. First, an error signal implies both information on some variable and a target or goal, deviations from which define the error. So control, as intuited, involves goals. Second, the negative feedback means that during control, such actions are taken that result in a decrease in error. Again, this formalizes an intuition: control should not let errors persist, and certainly not increase them - at least not as the final result. Third, an intimate relation with information is implied. The error signal must be communicated to the control system, but there is also a deeper identification. Control can also be described as the encoding of error signals into reactions, via such a coding that negative feedback occurs. In this way, control mechanisms implement this special kind of information processing.

The fourth consequence of defining control as negative feedback is the least obvious. When there is no error signal, no action is required; the situation could be described as satisfaction. The idea of dissatisfaction, or unpleasure, leading to action, is the basis of Freud's distinction between the primary and the secondary process [60]. The most primitive form of cognition, according to Freud, consists of the generation of random actions in response to unpleasant stimulation. The action leading to removal of the stimulus would become associated in memory with both the stimulus and the pleasure (e.g. of reducing hunger or pain). This primitive cognition could then fall into the trap of achieving a hallucinatory pleasure via such associations between thoughts instead of by responding adaptively to the environment. The primary process of the mind is this activation of ideas solely on the basis of associatively reaching pleasurable memories. The secondary process was suggested to have evolved to prevent primary process thinking from leading the organism into hallucination. In other words, it had to prevent pleasure from being achieved in a way that did not take reality into account. To do this, new rules for associating ideas had to be imposed. While the primary process simply spreads activation along lines of association until pleasure-nodes are reached, the secondary process must block those lines that would work less well in reality than in fantasy. So, at the basis and the pinnacle of thought, lies control. Primary process thinking starts by responding to an error signal; secondary process thinking controls hallucinatory pleasure seeking via the inhibition or biasing of primary process activity.

It is interesting to note that these ideas were published in 1900, in "The Interpretation of Dreams" - that is, before information theory, control theory, behaviorism (especially operant conditioning) and computation in neural networks, and in the same period as the establishment of the neuron theory, the cellular theory of the nervous system. Yet such important ideas were not only foreshadowed but combined, in such a way as to also link simple underlying processes to motivation and emergent patterns of thought (e.g. condensation). While this text will not delve further into the original psychodynamics, it should be noted that well-known cognitive dual-process hypotheses (discussed next) and an organizing function of prefrontal cortex (section 1.3.2) on which the experiments in this thesis are based, seem to lie close to the primary and secondary process described above.

Dual-process hypotheses emphasize differences between two ways in which people can process information. In Schneider and Shiffrin's two-process theory of human information processing, controlled processing is defined against the background of a long-term memory consisting of broadly defined units or nodes [204] [205]. These units are abstract representations of mental events, including perceptions and actions but also complex mental events, such as action sequences or shifts of attention. Information processing is defined, again at a high level of abstraction, as the activation of a sequence of such units. The claim of the theory, initially based on visual search experiments using a Sternberg task, is that sequences of nodes can be activated in two ways. Sequences can be initiated and completed regardless of current goals, if they are sufficiently well-learned. Such activations are termed automatic processing. Automatic processing describes the pattern of behavior when subjects consistently search for the same set of stimuli in a display: under such consistent mapping conditions, detection times are independent of the memory and probe set. Controlled processing is the activation of a sequence that is temporarily set up to perform a task; this does not require the sequence to be part of long term memory itself, but does require attention. Under varied-mapping conditions, when subjects had different memory sets on each trial and so could not automatize processing, increased probe and set size caused longer response latencies. Note that the metaphor of activation sequences in connected nodes are a geometric abstraction of successive instances of encoding, or chains of communication, and not a direct description of spreading activation in a neural network. In visual detection, Posner et al. contrasted orienting and detection in an analagous way to controlled and automatic search [190]. Orienting was defined as both overt behavior bringing sensory and motor systems into an advantageous position (e.g. moving the eyes towards objects), as well as inferred covert preparation. Detection, in contrast, concerned the arrival of sensory input into an information processing system that could output arbitrary (e.g. experimenter-determined) responses. Orienting, based on pre-stimulus cues, was shown to occur before detection. This led to the suggestion that habitual responses, such as orientation to locations, can occur independently from the nonhabitual responses involved in detection. Thus, again, sequences of mental events were proposed to occur either because they are well-learned, or because they are specified by a current, flexible goal concerning stimulus - response mappings. The same basic distinction, although stated in terms of systems instead of processes, is made in Norman and Shallice's model of schemata and the supervisory attentional system [167]. Schemata are abstractions based on experience, including habitual behavioral patterns in response to stimuli. Since people do not always respond in their most habitual manner - for instance when asked to perform a Stroop task - competition between schemata, termed contention scheduling, does not seem to provide a full explanation for behavior. A supervisory attentional system was proposed to exist, and to be able to bias contention scheduling when such competition was inadequate to achieve desired performance. Again, it could be said that an important difference between the two systems is the degree to which current goals concerning external behavior govern internal processes.

Controlled and automatic processing have been implemented in a hybrid symbolic - connectionist architecture called CAP2 [205]. This architecture consisted of a modular data matrix and a control system. Automatic processing is the basic information transmission by the autoassociative, connectionist modules, based on the coding of the priority of their input. Controlled processing occurs when a module that would otherwise not transmit information is provided with an output gain signal by the control system. The model involves various subdivisions and signals, but a perhaps important point about its structure is the separation of the data matrix and control system. Note that controlled *processing* does not happen in the control *system*: controlled processing happens in the data matrix, modulated by the control system. Such a separation of organization and representation will resurface in the discussion of the function of prefrontal cortex (section 1.3.2).

So, in the dual-process models, information has a default, robust way of being processed, based (in these models, but see below) only on learned associations, but the way information is processed can be changed, using temporary, goal-directed associations. In terms of control, the error signal that arises during controlled processing is the deviation of the desired activation sequence and the actually activated pathway. Since the long-term associations do not disappear when undesired, control must be exerted to inhibit escapes from the goal-related sequence. This kind of control is termed cognitive control. In neural terms, cognitive control is the control of the way information is or will be processed in the brain, where error is caused by some form of automatic processing. Task switching is an instance of cognitive control that occurs around the time the target is changed, and so a previously satisfactory state becomes encoded as an error. So, however the control is implemented, it must lead to such negative feedback that a previously stable state is replaced by a new state of how information will be processed. The processes of overcoming stability and reconfiguring the chains of communication, and how these processes occur in response to changing goals, are the themes of task switching research, as discussed below. In task switching, automatic tendencies or biases are not due to habits or well-learned memories, but to transient states due to recent task performance. What remains of the controlled - automatic distinction is not so much the habitual - arbitrary dichotomy, but whether activity is or is not a consequence of goals at the level of stimulus - response mappings.

1.2 Task switching

What happens when subjects change the goal of cognitive control? If the basic characteristics of control hold in this situation, then the chains of communication that were previously being stabilized will now provide an error signal, and some form of negative feedback will replace those chains with the new target. This change of cognitive control goal and subsequent changes in cognition is called task switching.

This cybernetics-based approach to cognitive control pays off when reading task-switching literature. Effects on reaction time and accuracy due to switching tasks in a variety of experimental setups may be due to a variety of influences. How much time does the change in goal take? Does the change always take place at all? Given that a new goal is encoded, how long does it take for the negative feedback to realize the target chain of communication? What is necessary for that realization to be completed, in the specific situation in which it takes place?

1.2.1 Proactive interference 1: task set inertia

Allport et al. [3] studied seven situations in which subjects had to switch between different tasks. Their initial expectation was to find increases on reaction time when subjects had to switch to more difficult tasks, or had to perform a more complex switch. After all, switching was conceived to be an example of executive control, so such difficulty manipulations should have such an impact on switching. Allport et al. describe how, over the course of their experiments, their basic assumptions about task switching were reversed.

In their first experiment, stimuli were a group of one to nine numbers, all of which had the same value (again, one to nine). This provided two stimulus dimensions - group size and numerical value - with which subjects were required to perform two types of judgement: whether the relevant number was odd or even, or whether it was more or less than five. Stimuli were presented in lists, with only one stimulus visible at a time, and the time to complete the list was used as the dependent variable. Responses were given vocally. Three kinds of switch condition were presented in which subjects had to a) switch between relevant stimulus dimension, keeping the judgement type the same; b) switch between judgement types, while the same stimulus dimension remained relevant; and c) switching between both judgement type and stimulus dimension. In these conditions, the task alternated each trial. The reaction times of these conditions were compared with the average completion time of the tasks being switched between, when those tasks were performed in isolation. The results showed that odd - even judgements were slower than more - less judgments, and that judgements based on group size were slower than those based on numerical value. For all types of switching, switch conditions had higher completion times than the baseline conditions. This difference is the cost of switching between tasks in this experimental context. The size of these switch costs was not different for the different types of switching - stimulus dimension, judgement and both stimulus and judgement switches.

In the second experiment, task difficulty was manipulated. Now, two number groups were presented adjacently. The left and right values and group sizes all differed from one another. The two judgment tasks were 1) to declare whether the left or right number, based on the relevant stimulus dimension, was greatest, and 2) to name the greatest number. Difficulty was manipulated by the difference in numbers on the left and right stimuli. Near stimuli differed by one to three, far stimuli by three to five units. It is unclear why this overlap in distances was used in preference to simply not using a distance of three, as the overlap would apparently reduce differences between the near and far groups. Regardless, the manipulation was effective in that difficulty caused a significant increase in list-completion reaction time. Switch costs, calculated between the shift stimulus dimension and shift response switch conditions and their baselines, were also found. There was no interaction of switch costs with difficulty.

In the third experiment, stimuli were either a number group or a Stroop word. The tasks involved naming the value or the group size for the number groups, and reading the word or naming the color for the Stroop words. Uniform lists with only one stimulus type were presented on which subjects alternated between tasks or performed each task in isolation. Also, mixed lists were presented with alternated number group and Stroop word stimuli. These lists were performed using either the dominant (value and word) or nondominant (group size and color) tasks. Results showed smaller switch costs for mixed than for uniform lists (230 ms against 440 ms per item). No interaction of dominance with switch cost was found on either the uniform or mixed lists.

These first three experiments had been expected to show effects on switch costs based on some form of limited capacity attributed to the supervisory attentional system. No such effects were found - due to multiple stimulus dimensions to be switched between, task difficulty or task dominance - that suggest that switch costs are sensitive to increasing demands on a unitary, limited-capacity central executive. Three further experiments were performed to explore the contrasting idea that control is distributed amongst subsystems.

The fourth experiment was aimed at explaining the persistence of switch costs in mixed lists, which was in contrast to the expectation, based on Spector and Biederman [217], that switch costs should not occur when the stimulus unambiguously cues the response. In the mixed lists of the third experiment, stimuli were actually associated with both the dominant and nondominant task, even though only one of those was "officially" relevant in a specific condition. In this experiment, the order in which subjects were introduced to the tasks associated with the stimuli was manipulated. In the first block, subjects completed mixed lists using only either the dominant or the nondominant tasks. Baseline lists were only performed for the tasks to be used in the mixed list. In the second block the tasks were switched, and in the third block, switched back. So, in the third block, the only difference compared to the first block was that the stimuli had been contaminated by the other tasks. Each block contained eight runs of three lists (two baselines and the mixed list). The results were as follows. Dominant tasks were faster than nondominant tasks. Strong switch costs were found on the first one or two runs of the second two blocks, but not the first block. Switch costs on subsequent runs remained small but significant in blocks two and three, but were zero in block one. This evidence of proactive interference led to the task set inertia hypothesis: switch costs are due to competing stimulus-response mappings associated with the same stimuli used in performing a different task on previous trials. This interference persisted for a time of the order of one minute.

The task set inertia hypothesis predicted that increasing the intertrial interval, allowing subjects more time to prepare for the new task, will not reduce switch costs. In the experiment to test this hypothesis, the interval between a response and the next stimulus was manipulated. Stimuli were incongruent Stroop words or neutral stimuli: color words displayed in black and colored rows of x's. The stimuli in the lists were now presented in pairs. After the first response, a delay of 20, 550 or 1100 ms was placed before the next stimulus was presented. The delays were kept constant within lists and blocked over eight lists, the order of the blocks being counterbalanced over subjects. Two instructions were given for completing the alternating lists, differing on the order of tasks: either word reading, then color naming, or the reverse. Alternating lists were presented using either the incongruent Stroop stimuli or the neutral stimuli. The dependent variable was the reaction time to the second stimulus. On incongruent lists, stimulus type did not cue the task. In these lists, switch costs were found only for the word reading task. These costs seemed to decrease as the response-stimulus interval was increased, but this was nonsignificant. The costs remained present (around 140 ms) even at the longest interval of 1100 ms. For neutral stimuli, switch costs were also present, but they were not different for the color naming and word reading tasks. Differences between reaction times for incongruent and neutral stimuli - Stroop interference - were also studied. On baseline lists, a large Stroop effect was found for color naming, as expected, but also a reverse Stroop effect: word reading was also influenced by the incongruent color. On alternating lists, the reverse Stroop effect was larger, converging to the normal (color naming) Stroop effect at the longest response-stimulus interval. The important points of this experiment were, first, that increasing response-stimulus interval did not remove or even significantly reduce switch costs. Second, no switch costs were found for the color naming task, even at short intervals. If this reflects a complete endogenous switch, how could that take so much longer for the word reading task? Finally, word reading was influenced by a different task associated with the Stroop stimuli, even when that task was performed on a different list, as shown by the unexpected reverse Stroop effect on baseline lists. That is, subjects did not seem (able?) to disengage the irrelevant task from the Stroop stimuli. Such effects could be explained by task set inertia. The more difficult task (color naming) requires strong biasing for its action schema to be associated with a stimulus feature, which causes more proactive interference (e.g. due to inhibition of irrelevant but dominant tasks), so that the easier task (word reading) suffers higher switch costs.

Two final experiments studied switching in a different context, namely rapid sequential visual presentation. In these tasks, sequences of words were presented one after another. The words were taken from three semantic categories. One or two of the words in the list were from a target category; subject had to detect and subsequently, after the list presentation, report these words. The sequence could change position on screen, and this spatial shift cued a switch in target category. In the first of these experiments, accuracy following a switch decreased and gradually, over the course of seven stimuli or, equivalently, 1100 ms, returned to the pre-switch baseline. The final experiment was aimed at understanding whether it was time or the number of stimulus presentations that caused the decay of switch costs. Now, a fast and a slow sequence were presented. The switch cost decay was shown to be slower for the slow sequence when plotted against time, but was exactly the same in the two lists when plotted against the number of presentations. Spatial shifts without a semantic shift were also included, and were shown to have much smaller effects on accuracy, with the effect gone after one or two items.

Allport et al. conclude that this evidence points to a dependence on external stimuli of task set control. Of an endogenous / autonomous, unitary, limited-capacity central executive concept, they conclude

> As we have seen, the stimulus-independent autonomy of such control operations must be seriously questioned. If the metaphor of a limited-capacity central executive can, in other respects, provide so little guidance - still less any testable predictions - for experiments of this kind, it may be time to look for a better metaphor.

1.2.2 Task set reconfiguration

Rogers and Monsell [197] established a number of task variations that influence switch costs. They varied trial-type - switch or non-switch - within blocks using an alternating runs design. In this design, tasks A and B are presented in an order of the form AABBAABB... The first presentation of a task in a run thus requires a switch from the other task, while the second presentation does not. AABB is of course not the only possible scheme, and Rogers and Monsell also used a AAAABBBB scheme, to test a prediction they derived from the proactive interference hypothesis on switch costs. The use of alternating runs - more generally, of any within-block presentations of switch and non-switch trials - avoided the problems in comparing an alternating block with a pure block as in [103], [217] and [3]. In such studies, only the alternation block involves keeping two tasks instead of one task in mind and this may have influenced differences between the alternation and pure blocks. The task was cued exogenously (which was in principle redundant) by the location in which stimuli were presented. The screen was divided into four quadrants (in the AABB) design or eight slices (in the AAAABBBB) design. Stimuli were presented in a clockwise circuit, and tasks were assigned to locations so that the desired task scheme had to performed. The time between a response and the next stimulus was manipulated experimentally. The tasks used were a vowel - consonant letter task, and an even - odd digit task. Trials involved the presentation of two stimuli, the left or right (randomly over trials) of which belonging to the relevant task, close together. Crosstalk and no-crosstalk conditions were created based on what the irrelevant stimuli was: a member of the set belonging to the other task, or a non-alphanumeric character. In the crosstalk condition, the stimulus could be congruent or incongruent depending on whether the associated response was the same as the correct response, based on the relevant character.

Using a variety of these alternating runs experiments, the following results were found for crosstalk and preparation interval. Crosstalk increased reaction time for both switch and non-switch trials, but more for switch trials. Within the crosstalk condition, incongruent characters slowed reaction time for both switch and non-switch trials, but more for switch trials. Switch costs declined as the response-stimulus interval was increased, but only if that interval was kept constant within a block. Switch costs at long (1200 ms) response-stimulus intervals were still present (around 40 ms), even in a no-crosstalk condition. These switch costs were termed residual switch costs. Three final effects were found that further constrained switch costs as they occurred in Rogers & Monsell's spatially-cued task-sequence paradigm. In the AAAABBBB scheme, only the first trial of a run of tasks showed a switch cost, and the subsequent three trials did not differ from each other. Adding a warning signal 500 ms before stimulus presentation reduced reaction time and increased error rate but did not affect switch costs. Only non-switch trials benefitted from response repetition.

The results led to the following main conclusions. First, a residual switch cost exists that endogenous control cannot remove. Switching between tasks has an exogenous component that requires the presentation of a stimulus to complete. Second, task sets - or action schemas [167] - can be cued by stimuli associated with that task, as shown by the effect of crosstalk stimuli. Third, proactive interference was expected to cause a gradual decline in reaction time after a switch. However, no such pattern was found. A single trial was sufficient to achieve an apparently asymptotic non-switch condition. Some perhaps apparently more basic effects were found: a) switch costs did decrease with increased response-stimulus interval, under the right conditions, b) switch costs were not sensitive to a manipulation (the warning signal) that influenced the general state of preparedness, and c) switching disrupted the positive proactive effect of response repetition. Such effects are in line with a general idea that switch costs reflect - at least in part and under certain conditions - some kind of ”executive” reconfiguration prior to stimulus presentation.

Meiran [149] specified two conditions that must be fulfilled for switch costs to reflect an executive process, in the sense of Norman and Shallice's model [167], of reconfiguration. He described a task switch as a combination of control processes and lower-level processes. Control processes shift the task and subsequently reconfigure the lower level processes which, once configured, automatically perform it. An executive reconfiguration process must 1) be specifically related to shifting the task, and 2) be proactive, preceding actual performance. So, for switch costs to reflect such a process, they must must decay with preparation time, as this would reflect proactivity, and this decay must be specific to switch trials. Meiran held the inter-trial interval constant while manipulating preparation time by presenting an explicit task cue at different distances in time from the imperative stimulus (the stimulus demanding a response). Thus, proactive interference was assumed to be held constant over different preparation intervals, in contrast to the Rogers and Monsell study, in which preparation time and decay time were confounded. Meiran found that shift costs did decrease at a longer cue-stimulus interval, although it turned out that instructions and / or training were essential in finding the effect. The effects of pratice were also studied, from the perspective that practice would strengthen the cue-task association (in Norman and Shallice's terms, automatize the schema selection process). It was found that practice reduced switch costs only for the short cue-stimulus interval, that is, when switch costs were interpreted to be due to incomplete reconfiguration. The residual switch costs, at cue-stimulus intervals that were so long (more than twice the mean reaction time) that reconfiguration could, in terms of duration, have been completed, remained even after practice.

An important contrast between the studies by Meiran and Rogers and Monsell is that Meiran found effects of preparation interval when that was varied within-block. Meiran attributed this to the potency of his cues in comparison with the spatial locations. Meiran further noted that effects of the cue-stimulus interval were found for both switch and non-switch trials, and switch costs were still found at long cue-stimulus intervals, which were argued not to be due to reconfiguration. It was the specific interaction of switch - non-switch and (non-confounded) preparation interval on performance that suggested that task switching involves an executive process involving some form of reconfiguration that is only necessary for switch trials.

1.2.3 Modelling versus interpretations

In their AAAABBBB scheme, Rogers and Monsell [197] showed that reaction time following a switch does not gradually decline, but shows a peak for the first trial and subsequently a level reaction time for the following three non-switch trials. But does such a result prove that an endogenous switch with an exogenous component is responsible for switch costs, as opposed to proactive interference? A modelling study by Gibert and Shallice, using a parallel distributed processing model, suggested that this is not the case [70]. They extended an existing model for Stroop interference [38] so that the state of the model at the end of a trial influenced the state at the start of the next trial. The essence of the model was that task-demand units biased mutually inhibitory "word" and "color" responses. These responses were activated by their respective stimulus dimensions. Differences in the weights between the word and color stimulus-dimensions and their responses made color naming require biasing from the task-demand units to win the response competition. In the extended model, a proportion of the activation of the task-demand units (which was specified as desired by the modeller to determine which task should be performed) persisted. So, on the trial following a color-naming trial, the color-naming task-demand unit would still have a high activation due to its required role on the previous trial. In contrast, the word-naming task-demand unit was not needed to bias the already favorable stimulus - response connections. Switching from a color-naming to a word-reading trial therefore resulted in more interference than the reverse switch, since the color-to-word switch involves higher persistent activation of the incorrect task-demand unit. By the time a (correct) response can be given, however, the correct task-demand unit has regained dominance. Subsequent trials - as in the AAAABBBB scheme - are thereby protected from proactive interference, despite that the switch costs on the first trial are due to proactive interference. Furthermore, preparation was shown to reduce switch costs, preparation involving simply an advance activation of the task-demand units (as could occur either following a response [197] or a cue [149]). The essential point is that a computational model can be formulated in which precisely the same top-down process prepare for switch and hold trials, and important patterns found by Rogers and Monsell and Meiran on switch costs follow purely from the current state of the network, as determined by interference from the previous trial. It was emphasized by Gilbert and Shallice that their point was not that no endogenous switching process exists - it clearly does, and in their model simply exists as a change in which top-down unit gets activated - but that such a process may not determine switch costs.

1.2.4 Residual switch costs and the mixture model

While the endogenous part of switch costs was being suggested to actually reflect an exogenous process, the exogenous part was being suggested, by the failure-to-engage hypothesis, to actually reflect an endogenous process, or more precisely, its intermittent failure. The failure-to-engage hypothesis [47] is an explanation of residual switch costs that is based on reaction time distribution rather than average reaction time. The residual switch costs found when subjects are provided with the opportunity to prepare for a switch in task prior to stimulus onset have been found to have a distribution that consists of a mixture of reaction times drawn from two other distributions: those when subjects were already prepared and those when subjects had not had a chance to prepare [47, 163]. Residual switch costs may not, therefore, be due to an effect present on every trial when a switch must be performed, but to the proportions of prepared and unprepared trials. According to the failure-to-engage hypothesis, the intention to engage in advance preparation (note that this refers specifically to the context of switch trials) can or can not be activated by an internal or external cue. This activation was argued to be effortful and controlled, as shown by results that suggested that subjects engage in advance preparation less often when they were confronted with long blocks of trials. This effect on the proportion of prepared trials was found even if subjects only were aware that they might have to perform such blocks, but knew that they were at the moment performing a short block. The mixture model of the reaction-time distribution for residual switch costs can be used to estimate trial-by-trial preparation odds based on reaction time. In one of the experiments described in this thesis, these odds were used to define conditions for EEG analyses. Further details will be given in section 2.1.

1.2.5 Proactive interference 2: the retrieval hypothesis and backwards inhibition

After the publication of Rogers and Monsells task set reconfiguration paper, Allport and Wylie [4] again used Stroop stimuli to study task switching, but now in an alternating runs paradigm as in [197]. Three types of stimuli were used: colored words, words in black and colored rows of x's. Colored words were always incongruent: the color designated by the word and the color of its letters never matched. The tasks were to name the word or name the color. Three conditions were used.

In an all-neutral conditions, only black words and colored x's wer presented. This removed any incongruity from the stimuli, and also removed crosstalk: each stimulus was only relevant for one of the tasks. In a color-neutral condition, colored words were presented instead of black words for the word-naming task. Color naming was still done using colored x's. So in the color-neutral condition, only words were incongruent while color stimuli only allowed one task. The stimuli for tasks are still unique: no crosstalk occurs. In the final all-stroop condition, all stimuli were incongruent color words. Crosstalk in that case is complete. Only one response-stimulus interval of one second was used.

Results showed switch costs and reverse Stroop effects (slowing of word-reading due to an incongruent color) that were due to proactive interference from previous tasks. First, reaction times for word reading in the all-neutral and color-neutral (that is, word reading incongruent) conditions were not different, but word reading was slowed in the all-stroop relative to the color-neutral condition. That is, the reversed Stroop effect occurred only when the color-naming task involved the same incongruent, colored words stimuli as the word-reading task. Second, the switch costs for word reading were higher in the all-stroop task than the color-neutral condition. So, the effect of switching to the word-reading task, as opposed to repeating it, was influenced by the task being switched from: if the other task involves the same, incongruent stimuli, then switch costs are higher. Third, switch costs for color naming did not increase from the color-neutral to the all-stroop condition, despite a change from neutral to incongruent Stroop stimuli for that task. The word reading task, however, was the same in these conditions, just as color namings switch costs. Together, the results indicate that switch costs in this situation are due to the characteristics of the task being switched from, not the task being switched to.

Two further experiments were run which enabled the time course of proactive interference to be studied. Now, conditions were presented continually in mini-blocks of 6 cycles, a cycle being a run of 4 tasks in an AABB scheme. In the first of these experiments, only the color-neutral and all-stroop conditions were used. Conditions were cued by high or low tones at the beginning of each cycle in a mini-block. The results were as follows. Word-reading responses became faster over the course of the color-neutral mini-block, but became slower over the course of the all-stroop mini-block. Switch costs for word reading did not change over cycles in either the color-neutral or all-stroop mini-blocks. The responses for color naming also became faster during the color-neutral mini-block, but now an interaction occurred: the overall reaction time improvement was due to decreasing switch costs. The same pattern occurred in the all-stroop block: reaction times for repeat trials remained the same, while reaction times for switch trials decreased. Now, in contrast to Rogers and Monsell's results, a gradual effect of interference from a previous task was found: the presence of the color-naming task in all-Stroop mini-blocks decreasingly influenced word reading in color-neutral mini-blocks. In the discussion of these effects, Allport and Wylie noted that the original task set inertia hypothesis could not explain why there were switch costs at all on word-reading reaction times within the color-neutral mini-block. Performing the color-naming task in these mini-blocks did not require biasing the word-reading task-set, so why should there be switch costs?

The retrieval hypothesis was formulated to account for these within-mini-block switch costs: subjects learn specific stimulus-response associations as they perform the tasks, and these associations are triggered automatically when the stimuli they were based on are presented again. This idea was applied to the results of the mini-block experiment. During color-naming in all-Stroop mini-blocks, associations were learned between colors and a naming response, and between words and a null response. Subsequent word-reading would then suffer interference because the stimuli trigger the associations relevant to the color-naming response. After a change to a color-neutral mini-block, the colored words are only associated with the word-reading response. It was proposed that the color-naming stimulus-response associations would then become less associated with the colored words (Stroop) stimuli, while the word-reading stimulus-response associations were still being used and learned. This could explain the improvement in reaction time for word reading in the color-neutral condition. The retrieval hypothesis also explains the gradual increase in reaction time for word reading on switch trials in all-Stroop mini-blocks. In all-Stroop mini-blocks, colored words become associated with the color naming task, after a color-neutral mini-block in which colored words were unambiguously related to the reading response, and the color naming task was associated with other stimuli. The colored-words to color-naming association is (re-)learned during the all-Stroop mini-block, so that interference with word reading increases due to the increasingly learned retrieval of the color-naming task on the presentation of a colored stimulus.

A third experiment was performed to test the retrieval hypothesis. Now, a new condition was used instead of color-neutral, namely word-neutral. In the word-neutral condition, color-words are presented in an outlined font. Subjects now always encounter Stroop stimuli for the color-naming task, but alternate between neutral and Stroop stimuli for the word-reading task. They thus have more opportunity to learn the colored-word to color-naming task than in the previous experiment, so that the interfering effects of retrieval should be greater. This was the case: switch costs on the word-reading task in the all-Stroop mini-blocks were greater now that the Stroop stimuli were likely to be more strongly associated with the color-naming task.

Two points were brought forward in this paper. First, repeat trials in the alternating runs paradigm are not fully prepared, as shown by comparisons to pure blocks and by gradual effects in mini-blocks. Second, switch costs can be due to characteristics of the task being switched from, as opposed to the task being switched to. Switch costs, it was concluded, might then not be a good way to index the amount of executive control involved in switching between tasks.

A different kind of proactive interference is the backwards inhibition of task sets [142, 143]. Consider a sequence of three tasks, taken from the set of tasks A, B and C. It was shown that reaction times are slower for the third trial in the sequence A-B-A than the sequence C-B-A. That is, when a switch trial involves switching back to a task performed two trials ago, reaction times are higher than when the trial being switched to was performed more than two trials ago. This backwards inhibition effect was not sensitive to preparation interval, and was not modulated by the repetition of stimulus values or responses, or by negative priming conditions. Thus, the effect seemed to concern the abstract task set as opposed to its perceptual or motor components. Backwards inhibition was sensitive to the top-down control of the task set. This was shown by comparing subjects who received a cue informing them of the stimulus dimension (color, orientation and movement) with subjects who recevied no cue, but had to detect the deviant stimulus dimension from the display. For both groups, the task was to respond to indicate which of four displayed stimulus was deviant. Thus, both groups performed sequences of tasks including the A-B-A and C-B-A sequences, but only the cued subjects showed backwards inhibition. Residual switch costs at the long (650 ms) cue-stimulus interval were found to be much higher (127 ms versus 26 ms) when the switch was to the recent (lag-2) task set, than when the switch was to a less recent task set. Finally, backwards inhibition was also found when sequences of four tasks were cued at once, so that cues had to be retrieved from memory instead of being presented externally. The existence of backwards inhibition was related to the need to balance flexibility and stability.

Backwards inhibition was proposed to play a part in that balance by allowing us to move away from an initially highly activated (or stable, or dominant) task set, without a kind of weapons race of activations of subsequent task sets.

1.2.6 Task switching and task memory

Altmann [5] manipulated the interval between task-cue and imperative stimulus (100 or 900 ms), and looked at the effect of this manipulation when it was done between or within subjects. A further variable was how many trials were cued. In one-trial experiments, each trial was cued, and the cue remained available during the trial. In multiple-trial experiments, a single cue was followed by a run of, on average, seven trials during which the cue was only available in memory. The tasks involved judging the width or height of a rectangle. The results showed, first, decreasing switch costs over cue-stimulus interval, but only when the interval was varied within subjects. In the multiple-trial experiments, reaction time increased over the course of a run. Within the between-subject interval manipulations, a significant main effect of interval was only found for the multiple-trial experiment. Altmann emphasizes two results. First, whether switch costs decrease as preparation interval increases depends on the exposure of the cognitive system to multiple intervals. So, the preparation effect is limited to certain situations, and models of a switching process should predict this situational dependence. Second, the reaction time of the first trial in a run was a) higher than the single-trial reaction times, and b) sensitive to interval in both the within- and between-subject design. This effect was attributed to memory as opposed to a switch process. Prior to a run, the activation of the task in memory was conceived to be more important than when cues were present continually, and the effect of cue-stimulus interval suggests that this activation process is time-consuming. In these experiments, it would then seem that task activation is a more robust explanation for phenomena than task switching. Further, a methodological problem was claimed to exist in the alternating runs paradigm, as switch costs would always be based on comparisons between the first and second trials in a run, confounding switching with the (re-)activation of the memory of the task on the first trial of the run.

Logan [134] also studied task switching in the context of the activation of task-memories, using the task span procedure. In this procedure, subjects had to memorize a list of one to ten tasks, and then either actually perform the sequence of tasks (performance sequences) or simply indicate what the sequence was (recall sequences). A further condition was performing a sequence of only one task. Stimuli were numerals and number words from one to nine, and the tasks were judgements of parity (even or odd), magnitude (greater or less than five) and form (number or word). The dependent variables were accuracy (chance of correctly completing the sequence) plotted against list length, accuracy against time to retrieval ($t = 0$ being the start of the test sequence, which began 1 sec after end of the presentation of the sequence for memorization) and reaction time against position in the sequence. Accuracy was shown to decrease with list length, with the performance and recall sequences strongly overlapping, thus suggesting that there was no trade-off between sequence storage and task performance in working memory. The performance and recall accuracy decreases were no longer similar when plotted against time, suggesting that the sequence information was lost as a function of item-interference as opposed to decay-time. This conclusion was strengthened by manipulating response-stimulus interval, which resulted in overlapping accuracy curves against list length (over both interval and sequence-type conditions) but not against time. Reaction times showed increases at list positions where subjects were expected to retrieve a chunk of information from long-term memory. The time needed for task-set reconfiguration was estimated by the difference between the reaction times for a) the perform condition (which involve, in Logan's terms, retrieval of task goals, their translation into an effective representation that specifies the task rules, and the subsequent communication of these control settings to subordinate processes) and b) the sum of the recall and single-task sequences. Except at the first position in the list, 480 ms of increased reaction time was unaccounted for by the recall + single-task reaction times. Note that this measure of switch-related discrepancy controls for artefacts of task activation or run position [5]. In further contrast to the previous study, Logan found response-stimulus interval effects that suggested that the effects of interval duration are partially influenced by task switching, and not only memory activation. For one of the sequence sets used, the effect of interval duration was greater for the performance than the memory sequences. Subjects were presented with one of two sets of sequences: either of length 2, 4, 6 and 8, or of length 2, 3, 6 and 9. Sequences were created by concatenating subsets of permutations of the three tasks. The goal of these sequence sets was to determine the expected moments of chunk-recall, but in terms of understanding task switching, this interaction with response-stimulus interval seems at least as interesting. Unfortunately, the effect was not further discussed. It was only the 2n-length sequences that showed an effect of interval on switch costs, not the 3n-length sequences. Due to the concatenation procedure, repeat trials would often occur (1/3 of the time) at the expected chunk-retrieval times for the 3n-length sequences. For the 2n-sequences, chunk-retrieval would often definitely coincide with a task switch (at positions three and five), and only on position seven would there be a 1/3 chance of a repeat. Could this coincidence of retrieval and switching have caused the response-stimulus effect on the switch discrepancy for the 2n-sequences alone?

Retrieval of task cues from memory was compared with externally cued tasks in a study by Koch using an alternating runs design [118]. In this study, a short and long response-stimulus duration was varied between blocks, and subjects were divided into a group who had to perform the sequence (AABB...) from memory, and a group who also were presented with redundant cues. Only the group with external cues showed a reduction of switch costs with increasing preparation interval. One consequence of this is that decay of proactive interference could not have been the cause of the reduced switch costs, as that should be the same for both groups. Koch decomposes advance preparation for task switching to account for the cue x switch cost interaction. First, a task "goal" must be selected, and second, the task-specific stiulus-responses rules must be retrieved. Since the no-cue group did not have low accuracy scores, Koch suggests that the task selection process is not problematic with internal cues. However, the second, specific rule-retrieval process was considered to be possibly sensitive to the salience of cues. This division of preparatory work seems to fit well with Logan's results, in which performing tasks involving a switch required more time than the sum of performing the task and retrieving the task identifier.

Mayr and Kliegl [144] present a somewhat similar decomposition of task set reconfiguration. First, a cue must initiate the retrieval of task rules from long-term memory. This is termed the retrieval stage. Only one task set was proposed to be able to be active at once. Second, in the application stage, the task rules are automatically applied to a stimulus (either presented or imagined). The question posed by Mayr and Kliegl was whether switch costs result from changes in the task, or changes in the retrieval path (from cue to task rules). Their study used an information-reduction paradigm, in which a single task could be cued by two different cues. Thus, cues could be made to switch independently from tasks, providing two pure cost variables: a cue-switch cost (cue switch - no-switch) and a task-switch cost (task switch - cue switch). The results were as follows. First, switching cues while repeating tasks was found to result in cue-switch costs. Thus, in other studies in which task switches and cue switches were confounded, part of the switch cost may have been due to long-term memory retrieval, as opposed to reconfiguration. Second, response-repetition benefits were found following cue changes but not task changes. Changing the cue thus does not seem to disturb the task set configuration in the way that changing the task does. Third, practice only reduced the cue switch cost, but not the task-switch cost. Fourth, when response-cue and cue-stimulus intervals were manipulated (so that preparation and decay periods could be manipulated independently, as argued for by Meiran), the only interval-related cost reduction was a reduction of the cue-switch cost due to an increased cue-stimulus interval. So the task-switch cost was not reduced either by increased decay or preparation interval. Finally, backwards inhibition was found to occur even when the cues changed, so that backwards inhibition is linked to the application but not the retrieval stage.

1.2.7 Conclusion

From a control perspective, task switching would be expected to involve a change in goal and a subsequent process of error reduction. The broad literature concerning the various kinds of switch costs can be understood in these terms. The studies by de Jong, Logan, Koch and Mayr and coworkers provide information on goal changes. Goals appear to be decomposable into an identifier component and an effective-goal component, and so goal changes also may show effects specific to one or the other components, or their interaction. The identifier, serving as an internal cue to the goal-memory, plays a part in Logan's recall sequences and Koch's internally cued switched. The effective component, that results in a steering of neural chains of communication towards the goal state, seems to be what was manipulated by cue switching in Mayrs studies. The negative reinforcement part of the control perspective is very similarly to Mayr and Kliegl's automatic application of task rules. Mayr and Kliegl do not seem to make the identifier - effective goal distinction of Logan and Koch. De Jongs mixture model and failure-to-engage hypothesis fits well with the identifier - effective goal decomposition, suggesting that the effective goal can be retrieved but may not be, even if the identifier (the "ineffective" or "unengaged" intention) is in fact retrieved. People may want to switch in an abstract, unspecified way, but the intention may not be concretely or specifically realized so as to change the chains of communication, in other words, to reconfigure. The state of "wanting to switch" may conceivably be present in the brain, while for instance the effective goal "map 'X' to left index finger, map 'O' to right index finger", such that negative feedback could occur, is not at all present. Notably, the actual stimulus, of which the representation is part of this goal memory, seems quite likely to help activate an effective goal, which is perhaps the kind of exogenous process hypothesized to exist by Rogers and Monsell. A final point is that, if goal retrieval is a controlled process, it should actually be expected to be fallible [47] and sensitive to context [5], motivation [47] and strategy [149]. That is, in contrast to claims that the lack of preparatory switching under certain conditions is problematic for a general controlled-processing conceptualization of task switching [5], it would seem to be precisely what such an idea would predict.

The various kinds of proactive interference - task set inertia, the retrieval hypothesis and backwards inhibition - can be seen as affecting the second part of control, namely the negative feedback phase. It is actually this phase which may most deserve the term reconfiguration, as argued for by Mayr based on its wiping-out of the response-repetition benefit. This is a notable departure in conceptualization and terminology from earlier studies, in which reconfiguration was assumed to be the proactive process. It seems likely, however, that the proactive process is task retrieval (both task identifier and effective task goal), while reconfiguration is a subsequent automatic process of negative feedback. This automatic reconfiguration process is however the aspect of control specific to task switching as opposed to task preparation in general. Failures to retrieve an effective task goal, proactive interference and a simple lack of sufficient preparation time could all preclude or interfere with reconfiguration.

All in all, it would seem that a cooperative stance between results and hypotheses would be reasonable in studying task switching. Unfortunately, so far many studies seem to be geared towards verifying generalized claims concerning task switching or switch costs - that costs are or are not due to proactive interference or advance reconfiguration or cue retrieval for instance. This seems likely to have suppressed potentially interesting cross-studies, for instance, concerning the effects of proactive interference on the odds of the retrieval of an effective task goal. A second problem is a lack of data. Not in the sense of a lack of paradigms, effects, interpretations and contradictions, but in terms of data dimensions, or data types. Behavioral data has the inherent limitation that it reflects the end product of all the inferred systems and processes that are in no way directly measured, or even measurable without some kind of more precise, physical specification. Physiological data can to some extent imply theoretical consequences on mediating processes and structures, as described in subsequent paragraphs.

1.3 Brain activity involved in task switching

An overview of results and hypotheses regarding brain function will be given in the following sections, to provide a context for the studies on task switching and oscillatory activity discussed later.

1.3.1 Distributed processing

At multiple levels of aggregation, processors distributed over the brain independently communicate information that is local to them, but in such a way that functional behavior emerges at a relatively global level. Taking a somewhat arbitrary starting point, membrane channels encode the membrane potential into their opening or closing (and thus recursively into a new membrane potential). Combining many such channel-computers, a neuron maps a history of information, communicated via synaptic events, onto spiking behavior. Neurons are organized in chains of one to two hundred elements, extending vertically over layers II to VI of the cortex, called minicolumns. Minicolumns are recognizable by the cell-sparse zones separating them [161]. Minicolumns are organized into cortical columns or modules, which contain on the order of 100 minicolumns, connected through short-range horizontal synapses. Groups of cortical columns create a distributed system [160]. Such a system may compute ever more complex functions, mapping implicit information in its combined receptive fields to an explicit neural code, to be used as input by other groups or returning back to the same area. Importantly, the flow of information through such a system may follow different pathways. Temporary, goal-directed changes in the flow would appear to be the physical form of controlled processing.

At large scales, functional specialization in the brain arises from the long-term structure of columnar connections, e.g. occipital regions specialize in various kinds of visual processing, central regions in movement generation, and so forth. This specialization appears to hold regardless of the complexity of ongoing cognition, or whether processing is automatic or controlled. For instance, in an fMRI study, the regions that were active (that is, that required increased blood oxygen [135]) during the simple perception of visual and auditory stimuli, were also observed to increase their activity when responses had to be given to targets in the relevant modality [104]. The same regions showed a further increase in activity when auditory and visual stimuli were presented together, so that processing involving the relevant modality had to be selected over any automatic processing caused by the irrelevant stimulus. Decreases in activation were found in irrelevant sensory areas, and these decreases became more pronounced as the relevant activations increased. So, looking at those specialized areas involved in sensory processing, as control demands increased those same areas showed adjustments in their activity, as opposed to passively passing on their results to "higher levels" of short term memory where control happens. In another study, auditory regions (the superior temporal gyri) showed increased activation when a word was covertly generated at higher frequencies [210]. During working memory maintenance involving faces as stimuli, correlations of activity fluctuations were found between distributed brain areas and a seed area, the fusiform face area, known to be involved with the perception of faces [67]. The areas correlated with the face area included prefrontal cortex, anterior cingulate cortex, the thalamus, the hippocampus and the basal ganglia, all of which are associated with various forms of control (as well as specific frequency bands, as described in sections 1.4 to 1.6). A blindfolded subject with synesthesia, who involuntarily perceived colors when presented with words and letters, showed activation of primary visual areas, relative to blocks in which only high and low tones were attended to, when words were presented (by earphone) or when she had to generate words starting with a certain letter [2]. In a PET study, directing attention to right versus left hemisphere stimuli resulted in contralateral activation in somatosensory and visual cortex depending on whether stimulation, which was bilateral, was tactile or visual [140]. Again, the areas specialized in the processing of the information being controlled are influenced by the control. When movements are imagined, similar effects on motor cortex activity are found as when actual movements are performed [206]. These effects involved so-called beta-band activity, which will be discussed in section 1.6.

A hypothetical principle about how functional units distributed over the brain interact has been proposed in a number of different but largely analagous wordings. The principle is described here as working-with-memory (WwM [159]), but also exists in other forms, e.g. as the global workspace hypothesis [46]. WwM was originally proposed as a hypothesis concerning confabulations: statements that involve unintentional distortions of memory. Confabulations occur following frontal-lobe damage, and appear to follow from a deficit in the strategic retrieval of existing memories, not from damage to the memories themselves. In one study, the hypothesis was tested using cued memory retrieval involving personal and historical cue words, to which amnesic patients, some of whom had frontal lobe damage, had to respond by retrieving a specific, detailed autobiographical (episodic) memory or a historic event (semantic memory) related to the respective cues [159]. Confabulations were restricted to the frontal-lobe damaged group, and involved both distortions of content and of chronology, but more of content, suggesting that the deficit goes further than simply ordering a correctly retrieved set of memories in time. Confabulations were also found for both episodic and semantic memory. Such results are consistent with the WwM hypothesis: that there exists a memory system on the one hand, and a working-with-memory system on the other. The memory system is conceived to be modular. A modular system consists of independent, stereotyped information processing entities, which automatically process information in a given way, unrelated to one another or to current goals. From a processing instead of a structural standpoint, a "modular system" could also be described as "primary process" or "automatic processing" as described earlier. Modular memory retrieval and encoding would be reflexive and cue-driven. WwM refers to the harnessing of the memory system to fulfill goals. At encoding, WwM organizes the to-be-remembered information; at retrieval, WwM initiates the conditions for relevant memories to be retrieved; and when retrieved memories are used, WwM evaluates their use in achieving task goals.

Note that, although in the clinical setting "memory" generally was measured in the context of declarative tests, the WwM hypothesis can be applied broadly, including memory for task sets. Subjects with damage to the prefrontal cortex have indeed been shown to have deficits related to task switching, as tested with the alternating runs task [7]. Ambiguous visual stimuli were presented, consisting of words in shapes. The words "left" and "right" and arrows pointing left and right were task-relevant stimuli, while "XXX" non-words and rectangles provided neutral stimulus dimensions. Patients showed greater switch costs in reaction time than controls at both short and long preparation intervals. Further effects were related to damage sites. Patients with damage to the right but not left prefrontal cortex showed a large switch cost in errors for short but not long preparation intervals, and for incongruent relative to congruent stimuli. Greater damage to the inferior frontal gyrus, in the group of right-hemisphere patients, correlated with greater residual switch costs, and smaller decreases of switch cost with preparation time. The left-frontal group showed the highest switch costs at short preparation intervals, but did not commit more errors. This group also had difficulty with incongruent relative to congruent stimuli, but the effect did not interact with other task conditions. So, in agreement with generalization of the confabulation-based

WwM hypothesis, the prefrontal cortex also appears to play an important part in task switching. Further results on what underlying role the prefrontal cortex could play in brain function are given below.

The essential feature of the WwM hypothesis is a specific kind of division of labor: memory content and automatic memory processes are separated from goal-directed memory activation. Evidence for the suggested role of prefrontal cortex in this division has been provided by a study using dynamic causal modelling, which provides estimates of regression parameters, quantifying the dependence of one region's activity on another, that change due to experimental conditions [148]. In this study, stimulus categories were used - houses, faces and chairs - with distinguishable patterns of activation over occipitotemporal cortex. When subjects perceived such stimuli, connectivity from early visual areas to the characteristic category regions of presented stimuli was increased. When subjects visualized such stimuli, the activity in the characterstic regions of the imagined stimulus became dependent on prefrontal regions. Aspecific connectivity between parietal cortex and the precuneus and occipitotemporal regions also increased during imaging, but did not show the category-specificity of prefrontal cortex. In agreement with the imaging studies of functional specialization discussed above, the same areas were active in different contexts - perception, category-specific control, and aspecific visualization control. If the idea of a division between representation and organization is strictly followed, then without anything to work with, a WwM structure would be "blind". An indication that this is the case is given by the imaging studies above, which showed increased activity in motor and sensory areas when memories of their modality were required in a task, in the absence of external events. That specialized, especially sensory, areas are not only somehow involved in but also essential to all cognition involving their function is a stronger claim. In fact, a dissociation between visual perception and visual imagery has been found, in a patient with focal lesions in extrastriate cortex [16]. The subject (madame D.) could, for instance, draw clear pictures of imagined objects when so requested, but could not subsequently recognize those drawing. It was concluded that early visual areas are not in fact necessary in mental imagery. This may imply that the WwM model is too simplistic, but not necessarily; the required nuance may lie in the nature of functions attributed to specific regions (further, of course, subtle details in the damage location may be important; recall that any region contains many columns, covering different cortical layers). Consider a patient who has lost his eyes; the eyes were necessary for perception, but it would not be surprising for this patient to have completely unaffected mental imagery. So, just because a region of the nervous system is needed for perception, does not imply that it is needed for higher cognition. The strict WwM hypothesis is that, if perception involves a certain region's function, and that function is also required in a working memory task or is the target of controlled processing, then the function will be implemented by the same region in the new context. When the function is very broadly defined - e.g. "visual processing" - dissociations must be expected, that might be avoided for more precisely defined functions, ideally in terms of local neural computation. Nevertheless, the case of Madame D. illustrates that hypotheses based on a WwM model can never be less vague than the functions ascribed to brain regions. Disregarding such practicalities for a moment, it could still be argued from principle that, if the function of a neuron, cortical column or larger grouping is defined by its connectivity with respect to itself and the rest of the brain, then each such unit's function is unique by definition, and accessing that function implies activating that unit.

From the WwM perspective, an important question when considering brain activity at a given location is how it relates to brain activity elsewhere, especially activity in specialized regions with perhaps better known properties. This provides an attractive divide-and-conquer approach to understanding the brain. The task switching experiments to be discussed in subsequent sections were designed and interpreted in this framework. When changing goals and switching tasks, new neural states must be computed that determine how subsequent input will be mapped. Tasks can be chosen so that the distribution of regions involved in prior and new tasks can be roughly predicted. The question is how the specialized functions of these regions can be voluntarily recombined so that the required behavior emerges. That is, the question involves mapping of input to brain, from stimulation or memory, not only onto some output vector of the brain, but onto the way the brain itself processes information. Simply the ability of subjects to switch between tasks, or attempt to fulfill different goals, implies that what the brain does cannot be conceived solely as the selection of a behavioral output based on sensory input. It must also compute what to change about its own state; it's "output" can be directed inwards. To understand task switching, it must be understood 1) how the functional units of the brain (at some level of description) can be flexibly organized to determine transient, goal-directed global input - output relationships, and 2) what neural events trigger changes in this organization. As reviewed below, prefrontal cortex seems likely to play an important part in such processes.

1.3.2 Prefrontal cortex

The prefrontal cortex (PFC) is the most anterior part of the brain, and is strongly related to goals and the communication of information over time [63], and as described above, to WwM [159]. The main division of the region is into the orbital, medial and lateral regions. The orbital and medial regions (including the cingulate gyrus) are related to emotion and motivation, the lateral (including the supplementary motor area (SMA)) with the temporal organization of processing and behavior [63], lesions to each region resulting in predictable symptoms. Orbital lesions, as suffered by the famous Phineas Gage [85], result in impulsiveness, distractibility and disinhibited instinctive behavior. Medial region damage leads to apathy, in the extreme case to akinetic mutism [43]. Lateral lesions lead to planning disorders [138]. Lateral patients have difficulty in performing sequences, especially novel or complex ones, of behavior. Such problems seem to fit within a WwM perspective, as basic functions of perception and action do not seem to be damaged, only their relation to goal-directed behavior, or the selection of goals themselves. PFC has reciprocal connections with the brainstem, thalamus, basal ganglia, limbic system, hippocampus and parietal cortex, but not directly to primary sensory or motor areas. This connectivity appears to bring together highly processed sensory information and its motivational significance, and is therefore in a position essential to goal-directed behavior, or control. Imaging studies have shown frontal activation in response to increased working memory demands, e.g. task switching as opposed to task repetition (discussed in section 1.3.3), color versus letter naming in the Stroop task [50] and 2-back versus 0-back conditions of n-back tasks [50].

Frontal cortex shows a spatially distributed hierarchy, from primary motor cortex containing phyletic motor memory (i.e. building blocks of movement generation common to the species), to premotor cortex representing acts and programs, defined not by specific movements but by goals and trajectories, to the PFC which no longer specifies specific movements but broader plans of action [64] [63]. Various regional distinctions have been drawn within PFC, e.g. based on the domain of information [73], but recent data appears to favor a gradient in temporal tuning, suggestively similar to that shown in sequence-sensitive Hopfield networks (see 1.1.4). PFC cells have been found with receptive fields extending both "back" and "forward" in time; such neurons encode stimuli no longer or not yet present, during delay periods after external stimulation is removed or prior to the arrival of an expected stimulus, as well as behavioral responses before they are given [63]. Cells with such retrospective and prospective memory capabilities do not seem to have separate distributions over PFC [191]. Frontal slow negative potentials in the electroencephalogram (EEG) also indicate a role for PFC in prospective memory, as described in section 1.3.4. In Hopfield networks, temporal tuning is antagonistic to pattern-specificity [6], and something similar appears to be the case in PFC. The same cells may integrate quite different stimuli. For instance, a study was performed in which one of two tones was followed, after a 10 s delay, by a choice between two colors. The tone determined which color had to be chosen (high tone - red, low tone - green). Cells were found that encoded both of the associated tone - color stimuli; e.g., a cell that showed an increase in firing rate when a high tone was presented might also be sensitive to presentation of the red tone. Most cells that responded selectively to one or the other tone also responded selectively to the associated color. A point to be made in interpreting such results is that a cell's activity is described in terms of external events as opposed to the cell's local environment. It does not seem completely clear that it is the color a cross-modal cell is responding to, even though there is a statistical relation; possibly the color reactivates the memory of the tone, and this is what the PFC cell responds to.

Within lateral prefrontal cortex, differences were found between dorsal and ventral regions that appear to follow the temporal tuning gradient [91]. Monkeys were trained to perform the following task, during registration of single-unit potentials from neurons in their dorsal prefrontal cortex. Two cues were presented together, each with a white square to its left or right, separated by a delay of about one second. One cue indicated with which arm the response was to be made, while the other indicated whether a left or right target was to be touched. The order of arm and target cues was fixed within blocks. It may be worth describing here some details of the in vivo method. The firing rate of neurons, calculated for 10 ms bins locked to trial events and using different trials as observations, were related via the fit of general linear models (ANOVA and regression models) to various experimental conditions. For instance, a significant increase might be found for a neuron's activity when an arm-cue is presented relative to when a target-cue is presented, or a difference might be found between activity for a "left" relative to "right" cue, regardless of whether the cue specified the arm to be used or the target location. Using classifications based on statistical cut-offs, neurons could be assigned (not necessarily exclusive) labels such as "position-specific", and the proportion of such neurons in different regions could be compared. After presentation of the first cue, more neurons were found that responded to specific combinations of cue direction (left or right) and cue type (arm or target) than to cue direction regardless of cue type in dorsal than in ventral regions. Also, in the dorsal relative to the ventral region, more neurons had activity that could be explained (in the statistical sense) by cue type. After the second cue, ventral neurons showed similar position-specific activity in response to the cue; that is, they appeared to encode whether the square was on the left or right side, regardless of what kind of instruction the cue was giving. In contrast, many (that is, around one in five; all results concerning regional comparisons involved proportions of this order) dorsal neurons encoded combinations of the first and second cue, for instance responding selectively to right - right combinations. The timing of neuronal responses was also compared between dorsal and ventral regions. For the first cue, activity related to the position of the cueing square arose at 110 and 190 ms post-cue in ventral and dorsal region respectively. Within the dorsal region, activity related to cue type started at 250 ms, while the proportion of cells showing such selectivity was not large enough in ventral regions for onset to be determined. For the second cue, responses associated with either selectivity to the second cue alone or to cue combinations arose at around 125 ms in ventral and 205 ms in dorsal regions. Thus, as a group, ventral neurons responded around 75 ms more quickly to external events than dorsal neurons. A control task was used to determine whether visual attributes of (combinations of) the central cues might confound the results; this was not found to be the case. It was concluded that ventral neurons primarily served to detect only spatial features of the most recent cue, while dorsal neurons also retrieved information about what the cue instructed and encoded cue combinations. Thus, the dorsal neurons tended to integrate information over a broader temporal span. The temporal span determines possible functions, e.g., with only a narrow temporal receptive field cue - stimulus couplings could not be encoded.

A similar functional gradient in lateral prefrontal cortex has been found using fMRI, with tasks in which the information conveyed by cues, contextual signals and stimuli was varied [119]. Two tasks were used, both of which used series of 12 stimuli, each preceded by an episodic instruction cue. One task was a motor task, in which left and right responses were mapped to squares of different colors. One and two forced-response episodes were distinguished, in which, respectively, such stimuli were presented so that only left or right handed responses had to be made, or both. Eight colors were used, half of which (green, red and white) had a consistent, half of which (cyan, yellow and blue) had a varied color - response mapping, depending on the cue. The consistent and varied colors were always separated, so that blocks either involved stimuli that did or did not require the episodic information, given by the series' cue, for correct responses. Within the varied mappings, a further distinction was made between the one and two forced-response conditions. There were two variants of the one forced-response conditions, in which the color yellow or blue was used as a distractor (no response) in the left and right response conditions, respectively, and the remaining colors were mapped to the response. In contrast, there was only one color - response mapping in the two forced-response condition, cyan always being the distractor and yellow and blue being mapped to the left and right buttons, respectively. The two forced-response condition was presented twice. These conditions were translated into information theoretic terms. The cues in the consistent and varied color - response mappings were described as conveying 0 or non-zero bits of episodic information, respectively. In the non-zero conditions, the one and two forced-response conditions involved 2 bits and 1 bit of information respectively, based on the number of alternative mappings (four versus two). The informational interpretation seems to be best understood as an indication of the uncertainty that would have remained in the absence of the cue. For stimuli in the consistent mapping group, the response was independent of the cue. So, given the stimulus (and, implicitly, well-learned task knowledge), the required response is known. Now consider the varied-mapping group. Depending on the cue, colors could be either a distractor or mapped to a left-button response. The mapping in a given one forced-response series only occurs in 25 % of the varied-mapping blocks. So, the expected uncertainty, or surprise, involved in the actual response selection in that condition was 2 bits. In the two forced-response condition, which was presented in two of the four varied-mapping conditions, both times with the same color - response mapping, the entropy was half this. That is, without knowing the cue, responses in agreement with the two forced-response condition's color - response mapping would be less surprising, considering the color - response associations over the blocks involving the varied-response colors. Note that the double presentation of the two-forced response block is essential to this part of the information-theoretic interpretation of contrasts between conditions.

The other task was termed the task experiment. Now, stimuli were colored letters. Subjects had to respond to the letter, depending on the task set signalled by the color; the task-set defining color was termed the contextual signal. Conditions were defined similarly as in the motor task. Consistent and varied colors now determined the task, as opposed to the response. Instead of one and two forced-response conditions, now there either one or two tasks that were signalled in a block. Conditions were now distinguished based on the information conveyed by cues, as above, and by the contextual signals. The results supported a cascade model of PFC organization. Both reaction time and activation in fMRI data varied linearly with the different kinds of information. Rostral (more anterior) regions showed an effect only of episode information; caudal (more posterior) regions of episode and context information; and premotor regions of episode, context and stimulus information. Effective connectivity results were also in accordance with a cascade from rostral through caudal to premotor regions. Path coefficients from rostral to caudal to premotor regions increased as episodic information increased. Path coefficients from caudal to premotor regions increased with contextual information. Increasing stimulus information was not associated with any top-down increases in path coefficients. The results were described as follows: rostral regions associate contextual signals with task sets, and this association is represented in caudal regions; the task sets themselves are represented in premotor regions. It should be noted that the interpretation in terms of information, while elegant, is an abstraction based on comparisons of quite different task conditions, and even on the specific protocol of block presentations; further, it has been noted that the three distinguished kinds of information sources may involve differences in temporal gradient, as described above [64]. The series cues required a broader temporal tuning than the contextual cues, and contextual information, even if physically presented together with imperative stimulus, has to be carried over time to be combined with information provided by the imperative stimulus. Nevertheless, the results reveal something of prefrontal organization, as well as providing further evidence for the role of prefrontal cortex in goal-directed behavior.

A somewhat different mid-dorsolateral - mid-ventrolateral functional division was found in a PET study that compared a spatial span and a spatial 2-back task, equated on their level of difficulty [176]. In the spatial span task, a five-element spatial sequence had to be remembered and reproduced. In the 2-back, or spatial manipulation task, on every trial one circle in a display would turn white, and subjects had to indicate which circle had turned white two trials ago. Both tasks showed, relative to a visuomotor control task, right-hemisphere parietal and premotor activation (i.e. increase in cerebral blood flow) as well as right-hemisphere prefrontal activation. Mid-ventrolateral PFC was active in both the spatial span and spatial manipulation tasks, but mid-dorsolateral PFC was active only in the spatial manipulation task. The data were taken as evidence for a two-stage model of spatial working memory [181], in which the maintenance and manipulation of information are functions of ventrolateral and dorsolateral regions of the PFC, respectively. In terms of temporal tuning, both functions would seem similar, the difference involving over how many events cells integrate as opposed to over how long a time.

In conclusion, cells in the prefrontal cortex encode information integrated from various sources, which may be separated in time. A gradient of functional specialization appears to follow a broadening receptive field, especially in time. An associated loss of content-specificity - e.g. the same PFC cell's activity might represent a tone, or it might represent a color [62] - would agree with the content-blindness expected by a WwM system. However, if prefrontal activity reflected purely organizational functions, it might not seem that any stimulus representations would be expected at all. Some comments concerning the methods of in vivo studies may be relevant to evaluating their significance for a WwM framework. Selectivity is searched for using statistical relations, usually with external events - does a neuron have a greater response to a specific stimulus or movement than it does to others? From a receptive-field point of view, this makes sense, but from a network point of view, perhaps the neurons with aspecific responses to specific stimuli are at least as interesting. In one study for example, around 200 of 325 sampled neurons did not show stimulus-specificity, but did respond to task-relevant events (cue and stimulus onsets) [62]. It was noted that many common aspects exist defining the events, and the aspecific neurons may have been encoding these; but it may also be possible that such neurons are organizational, leaving all content to whatever modules are active. In that case, the events with which statistical relations should be looked for would be defined in terms of patterns of network activity. It is also unsure whether a neuron specific to a certain stimulus in a certain experiment would not also respond to many other stimuli. In that case, its informational content over many task situations would be low. Each prefrontal neuron might respond to, for instance, 50 percent of all possible stimuli and still, in a task in which any two stimuli were used, stimulus-specific neurons would be found.

The computational principles of prefrontal function remain elusive, but in any case prefrontal activity must be considered as part of a network [63]. Obviously, PFC relies on posterior and subcortical areas for input and on motor areas for output. But for PFC to be so essential to goal-directed behavior, part of its output must also be aimed at changing the way it and its input areas process information. Various suggestions on what these changes might be, at a somewhat abstract level, have been given, but seem similar to the functions of controlled processing, for instance as made explicit by CAP2 [205]. In that model, the control system modulated the activity of automatic processes in the data matrix. Prefrontal function, similarly, is generally proposed to bias the relative activity of posterior functions or representations [45]. For instance, visual neglect has been simulated in a model of visual processing, built up from abstract pools of neurons, subjected to common inhibition to achieve competition. The model contained three modules, for feature extraction, spatial location and object recognition. The model was trained to recognize a number of objects. Top-down control was implemented by biasing either an object's or a location's pool. Lesions in the position module could generate location- and object-based neglect (i.e., either objects in one visual hemisphere were degraded, or one side of all objects was degraded). Whatever the computational nature of its control, prefrontal corticocortical connections to parietal cortex seem likely to be especially relevant to task switching. Cells in parietal cortex shows a very similar range of behavior as PFC cells, including delay activity [36]. Lesions to parietal cortex result in deficits of attention: subjects show problems in selecting and processing information from primary sensory areas. The canonical example is spatial neglect, in which patients are unaware of the left hemisphere of objects, their world and themselves. Such patients are able to plan and attempt to achieve goals, but may fail to implement the necessary attentional state to achieve them. The role of parietal cortex in a delayed response task was assessed in an fMRI study involving the cueing of responses [229]. Trials contained a visual cue, a delay of 1 to 21 seconds, and an auditory trigger signal indicating whether or not a response had to be made. Cues indicated both the correct finger and with 75 % validity whether the response would actually have to be given. Sustained delay period activity was found in parietal cortex, but equally following both go and no-go cues. This activity was thus independent of movement probability, and was related to motor intention, as opposed to the motor preparation that would occur to a greater extent following go than no-go cues (such activity was found in precentral cortex). The parietal cortex was suggested to "cover a range of potential responses defined by task settings," in contrast to focussing on "a probable movement defined by the task contingencies." The data and interpretations appear to suggest a difference between simply knowing what response is relevant, and using that knowledge to prepare. Such a distinction is similar to the concepts involved in the failure to engage hypothesis [47] described in section 1.2; in that case, intention involved knowing the task set, but this was discoupled from "engaging" the intention, or actually using it to prepare. Both prefrontal and parietal cortex will be seen below to be involved in task switching.

1.3.3 fMRI studies of task switching

Task switching studies using fMRI differ on a number of dimensions, some of which have been compared experimentally [200]. Studies may allow task-specific preparation or not, and they may involve different kinds of switching, e.g. of relevant modality, stimulus dimension or response rules. In a study in which subjects switched between stimulus dimensions (color and motion), with no opportunity to prepare, both dimension-related and aspecific switching activity was found [132]. Subjects saw a display of moving, colored dots, which changed direction and color once per second. One stimulus dimension was relevant per trial, and subjects responded when one of two target stimuli (of a possible six) in that dimension occurred. The response consisted of both a button press (using the right thumb for both responses) and for one target a switch of relevant stimulus dimension. Effects of sustaining attention (or maintaining a task set) were found by comparing the BOLD responses following the hold targets for motion and color. Remaining with motion resulted in a response at, bilaterally, superior / inferior parietal lobe, precentral gyrus (attributed to the frontal eye fields) and middle / inferior temporal gyrus (attributed to the MT+, or motion, area). Remaining with colorwas followed by activation of right medial superior frontal gyrus and right (and left, at a lower threshold) fusiform gyrus, which is near to known color-sensitive areas (e.g. V4/V8). Regions activated while changing task set (termed transiently shifting attention) were determined by taking the conjunction of areas with a switch - hold effect for both motion and color. The precuneus, left intraparietal sulcus, left precentral gyrus and bilateral calcarine sulcus (primary visual cortex) showed this conjunction. The parietal and precentral activity were suggested to provide an abrupt attention-shifting signal, while the visual cortex activity was speculated to reflect some form of refresh of the visual system. A possibly related effect, involving occipital theta-band activity, was found in the experiment described in section 2.2. Notably, prefrontal switch-related activity was not found; this is in contrast to other studies, as were the behavioral results which showed no switch costs.

Subjects were provided with a preparatory period in a study that manipulated knowledge of task pairs [215]. Letter - digit pairs were presented, and color signalled the correct task (a consonant - vowel or even - odd judgment). The first and second trial were separated by a 6 s preparation period. In foreknowledge conditions, subjects did not know what the first task of a pair would be, but did know whether the second task would be the same or the other task. In no-foreknowledge conditions, subjects had to wait for stimulus presentation to determine the relevant task. Endogenous task adjustment was possible only for the switch & foreknowledge condition, while exogenous adjustment was most necessary for the switch & no-foreknowledge condition. Switching and foreknowledge increased and decreased reaction time, respectively, but no interaction was found. Right lateral prefrontal cortex, left superior posterior parietal cortex and right temporal cortex showed increased activity in the preparatory period when foreknowledge was available (at lower thresholds, the activation was bilateral). Without foreknowledge, activity was higher in motor and motor / parietal cortex, the thalamus and caudate nucleus. The right prefrontal and left parietal regions were further studied, to see whether preparatory activation increased further for switch relative to hold trials. This was the case only for the prefrontal region. Higher prefrontal activation also predicted faster reaction times. Effects related to exogenous adjustment, occurring after presentation of the second stimulus, were also found. In the foreknowledge condition, activity was higher in hold than switch trials, in the posterior cingulate cortex and right occipital cortex. In the no-foreknowledge condition, switch trials showed higher activation, in superior prefrontal cortex, left posterior parietal cortex, posterior cingulate cortex, and occipital cortex. In the no-foreknowledge condition, when subjects had to perform an exogenous switch, prefrontal activation predicted slow responses, in switch trials only. The parietal region showed no such effect of reaction time. It was noted that different areas of prefrontal cortex were involved in endogenous and exogenous switching, in agreement with the idea of endogenous and exogenous contributions to switch costs [197]. However, despite differences between endogenous and exogenous reconfiguration, it remains possible that they have a common ”final route” onto task-related changes in information processing.

Prefrontal cortex activity was found in a study in which switching or holding the response - stimulus mapping (involving the characters + and -, and left and right response keys) was signalled by stimulus color [53]. Trials were spaced 15 s apart. No task-specific preparation was possible, because subjects only knew whether they had to switch task at stimulus presentation. Switch costs were found on both reaction time and accuracy. Notably, switch costs in reaction time were around 175 ms, even after 15 s of available ’decay time’, suggesting either robust stimulus - response associations or the absence of reconfiguration opportunities. A number of regions were activated following switch relative to hold trials: bilateral lateral prefrontal cortex, bilateral premotor cortex, bilateral anterior insula, left intraparietal sulcus, the SMA / pre-SMA, the cuneus / precuneus, the posterior cingulate and bilateral thalamus. So, some overlap with the color - motion switching study above was found, for parietal areas, but now prefrontal areas were also involved. All of these areas also showed activation in hold trials, relative to fixation. This was taken to imply that task switching is not achieved by special executive areas, but by changes in activation in common, task-related areas. However, increased metabolism in the same regions may still be due to different subsets of cells or cortical layers, which may qualify such results concerning overlapping regions of activity. Further, the experiment was set up so subjects could not prepare, so possible switch-specific anticipatory processes were not involved.

The reverse extreme in terms of available task-specific preparation was provided in a study using Rogers and Monsell’s alternating runs paradigm with long (8 s) stimulus onset asynchronies [111]. Stimulus-locked BOLD responses for switch trials, over those for hold trials, would then reflect only exogenous switching [197]. Switch costs were 137 ms. Region of interests were defined by activation evoked by stimuli on hold trials. All of the resulting nine regions showed greater activation for switch trials, although only three of these regions showed significant effects: right inferior parietal lobe, left precuneus and left precentral gyrus, similarly to the color-motion switching and stimulus - response remapping studies above. Using the same regions of interest, greater activity preceding switch trials was found for a BOLD-evoking ’event’ 4 s post-stimulus. Whole-brain subtractions were also performed, showing switch-related activation in the left superior parietal lobe for the stimulus-locked activation. No effects were found for the preparatory-period time point. The results were shown not to be due to reaction-time differences. Analyses using reaction time as a covariate did not show significant results, either for reaction time or interactions of reaction time with switching. However, effects on reaction time may be weak because of ceiling effects due to the long stimulus onset asynchrony, or preparation time; shorter periods may provide a more even mix of preparatory states (section 1.2.4). The effect of reaction time can also be studied in a different way than as a linear and quadratic covariate, as in the following study.

In this study, a double dissociation was found between the regions involved in transient and sustained types of cognitive control [27]. Transient control refers to processes necessary to switch between tasks on a trial-to-trial basis within a mixed-task block, such as updating goals. Sustained control refers to more tonic processes in mixed-task as contrasted with single-task blocks, such as sensitivity to the cues that will signal a change of task and coordinating representations of the various task sets in working memory. Areas in the left hemisphere, including prefrontal and parietal cortex, showed increased activation for switch trials relative to non-switch trials in mixed-task blocks. Areas including the prefrontal cortex in the right hemisphere showed increases for sustained-control related activity. The relationship between behavior and brain activity was studied by including response speed in the analysis by comparing fast and slow sets of trials, motivated by the failure to engage hypothesis [47]. Prefrontal activity was increased prior to stimulus presentation for fast trials and post-stimulus for slow trials, similarly so for switch and non-switch trials. Also, left parietal cortex showed higher activation for switch than for non-switch trials, but only for fast trials.

In a study involving fMRI and transcranial magnetic stimulation (TMS), two types of switching were compared [200]. Switches involved exerting control over sensory or motor conflict, or ambiguity, in visual switching and response switching tasks respectively. The task involved sequences of 9 to 11 trials, preceded by a cue. The cue signalled either that subjects had to shift task or continue with the previous sequences task. In the visual switching task, trial stimuli consisted of two forms, one red, one green, and one a triangle and one a square. The task involved detecting and responding to rare targets in the relevant form, which could be defined by the current task rule, involving either color or shape, counterbalanced over subjects. For instance, subjects might have to respond to targets only when presented in red forms, and then switch color. In the response-switching task, only one stimulus was presented, a triangle or square. Switch cues signalled a reversal of the mapping of left and right responses to the forms. Responses were followed by a 70 ms feedback signal after 100 ms, and the next stimulus was presented after another 800 ms. In the visual switching task, a switch cost of 86 ms was found on the first trial. Switch cues were followed by increased activation in the cingulate sulcus and the SMA / pre-SMA. Decreases were found in the anterior paracingulate sulcus, the ventral subcallosal cingulate and very anterior medial frontal cortex. In the response-switching task, four left medial frontal regions showed higher activation following switch than hold cues: pre-SMA, rostral and causal cingulate zones and an anterior medial region. Hold trials showed higher activation at very anterior sites and in subcallosal cingulate cortex. A 100 ms switch cost was found on the first trial in a sequence in the response switching task. In subsequent experiments, TMS was applied after the cue, finishing before the first trial stimulus, or after the first trial stimulus was presented. TMS was applied either over the pre-SMA, dorsal premotor cortex or a more posterior control site. For the cue-period TMS applied over the pre-SMA, a disruption of performance was found only for the response switching task when a switch was necessary. Dorsal premotor TMS disrupted performance only when applied following the trial stimulus (only the response switching task was tested with this TMS site). The control region had no measurable disruptive effect. Thus, although the pre-SMA was activated for switch cues in both tasks, it only appeared to be essential for switching in the response switching task.

So, preparing to switch a task appears to involve activity in regions including prefrontal cortex [216]. It would seem reasonable to conclude that some kind of goal-directed (re-)organization occurs preceding switch trials. Further information on the time course of switch-related activity is provided by EEG and MEG studies reviewed below.

1.3.4 EEG / MEG studies of task switching

The experiments described in this thesis concern electroencephalogram (EEG) signals. The EEG reflects the summed effect on scalp potentials of post-synaptic potentials of many pyramidal cells lying in parallel, perpendicular to the scalp [136]. For effects to summate and survive to be measureable at the scalp, the post-synaptic potentials must be synchronous. The magnetoencephalogram (MEG) is a similar technique, but measures magnetic instead of electrical fields; this technique is sensitive to horizontally aligned cells. So, both the EEG and the MEG use scalp recordings to measure the summed effects of large numbers of cells. Due to the noisy transmission from cortex to scalp, and due to the effects of summating from in principle the whole brain, spatial resolution is low in these techniques. Temporal resolution is high, as the source of the signals is the actual membrane potential and effects are transmitted instantaneously. It turns out that such recordings capture robust patterns of brain activity. For instance, following a visual stimulus, a characteristic temporal pattern is evoked involving a sequence of peaks and troughs, positive and negative relative to a pre-stimulus baseline. On single trials, the pattern is not in general visible over noise, but is calculated by averaging over many signals time-locked to similar events. This event-locked average is called the evoked response potential (ERP). ERP's consist of, possibly overlapping, components: patterns within the ERP that can be distinguished by their spatial or temporal distribution, and responsiveness to experimental manipulations. Thus, for instance, a manipulation may have an effect on one early, frontally distributed component, but not on another, frontocentrally distributed component that appears later after the event.

ERPs can be locked to different kinds of stimuli (e.g. visual versus auditory), and effects of stimulus properties can be compared; but they can also be locked to (ideally) physically identical events, which evoke e.g. different control processes. Typically, some kind of cue is then the locking event, and the manipulation involves what information the cue provides on how upcoming stimuli must be processed, that is, what a subject can do to prepare. Various kinds of slow negative potentials can be locked to such cues.

Slow negative potentials develop between an event that triggers preparation and a second event that triggers a (not necessarily overt) response. These events can be evoked by either internal (memory) or external stimuli. When the second event is an overt response, e.g. when subjects generate voluntary movements (in which case the first event is internal), the component is called the readiness potential or movement-preceding negativity [33]. Its topology is central, and depends on response side and effector; further, larger amplitudes predict faster responses. When the events are a warning stimulus (or cue) and a subsequent imperative stimulus (to which a response must be given), the component is called a contingent negative variation (CNV) or stimulus-preceding negativity [33]. That such a negativity is truly not related to overt responding was shown in the knowledge of results task, in which subjects received feedback (on the timing of their response) around 2 seconds after responding [33]. A stimulus-preceding negativity arose backwards-locked to the feedback stimulus. During long (3 - 4 s) intervals between warning- and response-stimuli, the two types of component both occur, first an early (up to around 400 ms post-cue) fronto-centrally distributed component, then a later (around 500 ms onwards), or terminal, CNV [33] [131] [74]. The generators of the early component have been localized in the SMA and the anterior cingulate gyrus [74]; the involvement of such areas seems to suggest that the early CNV reflects goal-related activity. The later component increases as the cue stimulus provides more bits of information, e.g., movement parameters such as direction, force, and effector [131]. It also increases when subjects are instructed to exert more effort when cued to do so (in which case they can earn a reward for responding quickly) [57]. Following effort cues, a frontal-positive / occipital-negative peak arose at 200 ms (the P2 / N2), followed by a large parietal positivity from 300 to 600 ms (the P3b), followed by an increased fronto-central slow negative potential (the late CNV). In a study in which subjects compared either abstract stimuli or familiar faces, a CNV arose 500 - 900 ms between two stimuli to be compared, that was greater for face stimuli [156]. In an MEG study of the magnetic analogue of the CNV, the side at which auditory stimuli would be presented was cued, and the late CNV originated from auditory cortex (the superior temporal gyrus) [74]. In general, slow potentials do not seem to be a unitary phenomenon, but a reflection of many kinds of neural activity. The common factor appears to be communication over time. So, when subjects must prepare for a task, since task-cue information must be conveyed to the time of stimulus presentation, slow negative potentials would be expected to arise (see below).

The readiness potential is strongest over the motor area contralateral to the response that is being prepared. The contralateral - ipsilateral difference, averaged over response hands, is called the lateralized readiness potential (LRP) [131] [37]. A pre-stimulus LRP occurs when specific muscle movements can be prepared [131]. In a study in which movement parameters (force and direction (extension versus flexion)) were cued, additionally to left versus right hand, while the CNV increased as more movement components were provided, the pre-stimulus LRP only showed an increase relative to only-hand cues when full movements were specified [131]. Post-stimulus, the LRP provides two measures, related to the large LRP peak observed at the time of response. The two measures are the intervals between stimulus and onset of the response-LRP (the S-LRP interval), and between that LRP-onset and the overt movement (the LRP-R interval) [130]. The intervals reflect processes before and after response selection. Valid versus invalid priming of hand and direction (flexion versus extension) results in shorter S-LRP but not LRP-R intervals [130], so that subjects appear to exert preparatory control over pre-response selection processes as opposed to those involved in response generation.

The P3 or P300 is a post-stimulus peak that has been shown to consist of two components, the frontal P3a and parietal P3b. The P3a occurs shortly after cues, and has been shown to be sensitive to novelty, or unexpectedness (e.g. dog barks in a series of tones), and attentional requirements (e.g. difficulty of stimulus discrimination or the presence of distractors) [102] [39]. The P3a has been interpreted to reflect orienting, or preparing to process concrete task-related information [102] [39]. The P3b is found over parietal sites, and may persist for up to around 600 ms after stimuli. The P3b is larger when stimuli are relevant (”target” stimuli) and infrequent, that is, when they must be processed up to some response and the brain is selectively anticipating them [102] [39].

A number of studies have used the ERP, in particular the CNV and LRP, to study brain activity related to task switching. Wylie et al. (2003) used sequences of three trials with the same task set, providing switch, nested and pre-switch trials for the first, second and third trial in each sequence. Tasks were cued by the stimulus color, as well as by the AAABBB... sequence. The data showed effects on sustained positivities occurring late in the trials, that is, preceding the upcoming stimulus. It was found that the ERP level preceding switch, nested and pre-switch trials was, at parietal sites, most positive for pre-switch trials, while at frontal sites nested trials showed the greatest positivity. These sustained positivities were interpreted to reflect sustained activity. Based on this interpretation, it was argued that it would be unexpected, from an assumption of frontal areas playing a controlling role in preparing for switch trials, that frontal sites did not show the greatest sustained positivity on pre-switch trials. However, as described above, negative shifts such as the CNV may reflect anticipatory processing, so that the interpretation of a relatively positive

ERP level as more sustained activity may not be correct.

Other studies have reported frontal effects related to changing task set. Lorist et al. [137] found frontal and parietal negative shifts prior to switch and hold trials, respectively, also using an alternating runs paradigm. Karayanidis et al. [108] found switch-related effects in an alternating runs paradigm (Rogers and Monsell, 1995): a response-locked parietal positivity and a stimulus-locked midline negativity for switch relative to hold trials. The positivity and negativity were attributed to endogenous (anticipatory) and exogenous (stimulus-triggered) reconfiguration processes, respectively. The point was made that these pre- and post-stimulus switch - hold differences were dissimilar, while in the failure to engage framework, reconfiguration occurs either pre- or post-stimulus, as opposed to one part of preparation occurring pre- and another post-stimulus as suggested by Rogers and Monsell. While different pre- and post-stimulus ERP components are not predicted by a hypothesis based on intention activation failures, they do not seem to be necessarily incompatible. As an example, let anticipatory switching be triggered from memory, e.g. by visualization of the upcoming stimulus, which is then followed by an effective (for reaction time and accuracy) change in the communication pathways between stimuli and responses via the nervous system (i.e., task set). The same change in pathways might be triggered by stimulus onset, if not already achieved pre-stimulus. What differences are subsequently found would depend on the measurability of the various events - the endogenous triggering, e.g. visualization, the perhaps different triggering effect of stimulus-onset, and the eventual state of the (perhaps complex and recurrent) chains of communication implementing the task set. If for instance only the endogenous triggering event were measurable in a given study, switch - hold effects would be found only pre-stimulus, while, if, in contrast, only the encoding of the final stimulus - response relations affected the dependent variables used, pre- and post-stimulus switch - hold effects would be identical. The method to test the hypothesis of occasional occurrences of (failures of) anticipatory switching used in this study is the comparison of a variety of measures of activity during putatively switched and not switched subsets of trials. In comparison with the non-switched switch trials as well as with hold trials, switched (i.e., having established the correct task set prior to stimulus presentation) switch trials should contain some kind of unique preparatory activity, reflecting anticipatory switching that only occurs preceding switched switch trials. Barcelo [14] found an anticipatory frontal effect, on the P3a, related to shifting task, following a shift cue in the Madrid card sorting test

In a task switching experiment using either informative or non-informative cues, Hsieh and Liu [92] studied the stimulus- and response-locked LRP and the P300. Switch - hold differences were found on reaction time and stimulus-locked LRP onset, but not P300 latency. This suggested that task switching affects processes occurring between stimulus identification (of which the timing was indicated by P300 latency) and the completion of response selection (as indicated by the onset of the stimulus-locked LRP). Cueing the task decreased the reaction time, the time to stimulus-locked LRP onset and also P300 latency, suggesting that task cueing influenced the speed of stimulus identification. In support of the apparently different cognitive stages on which task switching and task cueing have effects, there was no switching by cueing interaction on P300 latency or stimulus-locked LRP onset. It was suggested that these additive effects support the idea that switch costs are due to automatic carry-over effects that are not affected by advance reconfiguration. If advance knowledge of the upcoming task would provide an opportunity to intentionally overcome carry-over effects, switch - hold effects should interact with task-cueing effects. While this did not hold for P300 latency and stimulus-locked LRP onset, it was the case for reaction time and the response-locked LRP interval. Thus, both additive and interacting effects were found of advance preparation and task switching so that, following the additive factors reasoning, a process involved in task switching may be influenced by advance preparation. These data would place the locus of this process quite close to response execution. The data could be interpreted as suggesting that the way preparation interacts with previous task interference involves overcoming a difficulty in actually giving a response, after that response has already been selected to be given, that has become associated with a different stimulus. Such a "deficit" in performance could have an ecological advantage if it results from a double-check mechanism, making sure the response is really suitable for the current stimulus, even though it is not the currently dominant response.

The above sections provide some support for and substance to the following general hypothesis: first, goal-directed preparatory processes exist that are specifically related to switching task set or goal; and second, these processes involve the prefrontal cortex working-with-memory. However, the experiments to be discussed in this text concern a dimension of brain activity not yet discussed: rhythm.

1.3.5 Rhythmic brain activity

Recall that cellular bistability, or self-sustaining oscillation, is a robust phenomenon that arises from simple neuronal interactions (section 1.1.4). It was presented as one way in which information can be communicated over time, but, as will be described in following sections, many different functions and states appear to involve oscillatory brain activity. This section provides a basic explanation of the measures used in studying rhythmic activity.

A rhythmic pattern is any pattern - over time or space or another dimension - that repeats itself. When the pattern repeats itself over time, the pattern can also be called a periodic signal. Periodic signals, as other signals, can be shifted, stretched and scaled, so that a family of functions can be defined that differ only on such operations on a basic signal, for instance a sine wave. In periodic signals these operations are given as parameters, respectively phase, frequency and amplitude. So, if it is assumed that a periodic signal is, for instance, sinusoidal, it can be completely described by the three parameters. A less restrictive assumption is that a periodic signal is a weighted sum of sines, which leads to the frequency-domain description of a signal, with for a set of frequencies an amplitude and phase.

If a signal's parameters change over time, the signal is called non-stationary, and its parameters are called instantaneous. Describing a signal in terms of time-varying parameter functions is called time-frequency analysis. Such analyses can be achieved in different ways (e.g. event-related desychronzation, temporal spectral evolution, or wavelet analysis), but all come down to trying to find an estimation of amplitude and phase parameters at different time points for different frequencies.

Event-related potentials are waveforms that are locked in time, or phase locked, to an event. Such waveforms are termed evoked responses [228]: when the brain undergoes stimulation, it reponds with a waveform that is added to background noise, from the point of view of averaging the time course of event-locked EEG signals. However, considering the EEG as an ongoing signal, event-locked effects on its parameters, e.g. the amplitude of oscillations of a certain frequency, could also occur. Such effects on EEG signals would not be described as a waveform added onto background noise, but as a modulation of continuous waveforms. Such modulations, in which a parameter (especially amplitude) is locked to an event, are termed induced responses [228]. A signal of which a parameter is event-locked does not have to phase-locked itself. For instance, perhaps from 300 to 800 ms post-stimulus the amplitude of 5 Hz oscillations increases: this is an induced effect. This does not imply that the oscillations have the same phase relative to the time of stimulus presentation. When the amplitude increases, the signal may be peaking, or at a peak, of at a trough; that aspect of the signal is left free by the induced change. Averaging such a signal to create an ERP could average out the oscillations, leaving no sign of the induced effect. By estimating the amplitude time course per trial and then averaging that parameter's time course, the arbitrary phase of the oscillation can be ignored, and the induced effect revealed.

Time-frequency analyses were applied to EEG data in the experiments discussed in this thesis. The resulting description includes matrices containing amplitude spectra at successive time points. Such data can be further analyzed similarly to event-related potentials, resulting in an average amplitude associated with each signal at each time point for each frequency. Figure 1.1 shows an example of such a time-frequency amplitude "ERP". The figure shows instantaneous amplitude following a warning cue and an imperative stimulus (for more details, see section 2.3. Relative to the pre-cue baseline, amplitude increases soon after the cue at relatively low frequencies of 5 - 7 Hz, and frontal decreases at a later time, but still pre-stimulus, around 10 Hz. Under what circumstances such activity is found, and with what brain activity they are associated, will be discussed in following sections.

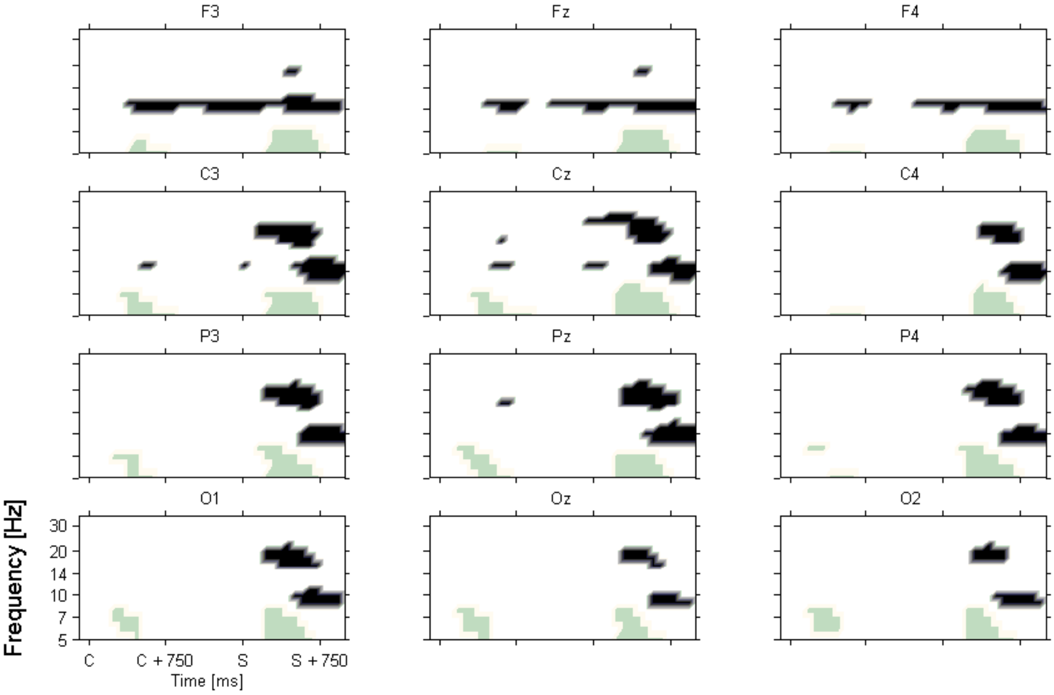


Figure 1.1: An empirical example of event-related instantaneous amplitude. The time period covers a cue (C) - stimulus (S) interval of 1500 ms. The vertical axis shows frequency. At each time - frequency point, the proportion change from the pre-cue baseline was calculated for the associated frequency band. The largest increases and decreases are plotted in gray and black, respectively. E.g., the low gray clouds seen at most electrodes reflect an increase in 5 - 7 Hz amplitude soon after cue and stimulus presentation.

Another parameter of interest to the current text is phase locking. A signal's phase is usually meaningless on its own, as the phase is only given relative to an arbitrary zero, defined as a technical artefact by the positioning of some basis function in the estimation of parameters. However, this artefact is consistent for all signals, so a shift in phase between signals is meaningful. To measure whether this phase difference is consistent over events, phase vectors can be summed and averaged. The phase-locking value (PLV) [124] used in the experiments is based on the summed phase vector; further details are given in section 2.2. PLV values are estimated for every signal pair, frequency and time point (relative to the time-locking event), and summation occurs over trials in the same experimental or quasi-experimental condition.

The following sections review literature on brain activity in the frequency bands of interest to the experiments.

1.4 The theta band: large-scale relational encoding

1.4.1 Introduction

The theta band is the 4 - 8 Hz range of frequencies. Theta-band activity in the brain is of interest in a variety of neuroscientific settings. EEG / MEG studies have found associations of theta-band amplitude with the performance of working memory tasks [20] and long-term memory encoding and retrieval, e.g. [116]. Intracranial recordings have linked cortical theta-band oscillations to behavioral and mental states, e.g. [192]. In particular, hippocampal theta-band activity has had a strong impact on neuroscientific theory [24]. In-vitro studies have shown that long-term potentiation is sensitive to theta-band oscillations [145]. These results will be reviewed below.

1.4.2 Scalp recordings: short- and long-term memory

Theta-band amplitude and coherence measured using EEG / MEG recordings are sensitive to a wide variety of experimental conditions and behaviors. Two broad lines of research involving the theta-band may be distinguished: those focussed on long-term memory and those focussed on working memory.

Increases in theta-band amplitude have been shown to be related to long-term memory encoding and retrieval [116] (the alpha band has also been shown to be relevant to memory processes; see 1.5). In this line of research, conditions are defined based on what subjects remember of stimuli and their presentation. This is called the remember / know paradigm [232] which distinguishes two kinds of recognition: the presentation (including the stimulus) may be recalled as an episode ("remember"), or the stimulus may be familiar but the presentation-event not recollected ("know"). Note that this is an example of behavior being used to define conditions. Experiments have shown effects of memory on theta-band amplitude during both encoding and retrieval. In a recent retrieval-focussed study, [227] presented words in different colors and distinguished three subsequent recognition conditions: of both the word and its associated color, of the word but not of its color, and failure to recognize the word. In the theta-band, frontal amplitude and widespread coherence at the time of encoding increased as the level of recognition increased, from misses to word-only to word and color. The amplitude effects of recognition versus miss were found over a period of 1500 ms post-stimulus. Word and color showed higher amplitude than word-only relatively early in the interval, at around 500 ms. A similar temporal pattern was found for theta-band coherence, except now no significant word-only versus miss effects were found. In [117], the time course of theta-band amplitude was studied at retrieval. Subjects had experienced a series of stimulus presentations and were unexpectedly asked in a probe set whether they recalled the stimulus presentation ("remember"), were only aware that the stimulus was familiar ("know"), or thought that the stimulus had not been presented previously ("new"). Following stimulus presentation, theta-band amplitude peaked (over the whole scalp, around 175 ms post-stimulus) and then dropped. The increase at the peak was greatest for remembered stimuli, but at around 300 ms post-stimulus amplitude was higher for known stimuli, as amplitude had dropped more strongly for the remembered stimuli.

The second line of research shows that theta-band amplitude is higher when subjects hold and use information in working memory. In [69], theta-band amplitude at midline frontal electrodes was shown to be higher in blocks of the more difficult condition in a working memory task. The easy condition of the task involved a target letter + position, and subjects had to indicate whether probe stimuli matched the target on either identity or location. In the difficult condition, the target was defined as the stimulus three trials back. The frontal midline theta rhythm was estimated to arise from a dipole in the area of the anterior cingulate cortex. In a more recent study, MEG and EEG measures were combined to estimate two sources explaining frontal midline theta [8]. The signal that was explained by the sources was constructed by averaging the MEG time-locked to the peak of theta waves in the EEG at Fz. The sources were located in prefrontal cortex and the anterior cingulate gyrus. The two sources showed alternating activity, which was interpreted as evidence that frontal midline theta bursts are due to interaction between prefrontal cortex and the anterior cingulate gyrus. In an MEG study [100], it was shown that increasing the size of the memory set in a Sternberg task increased frontal theta-band amplitude during the retention interval and during the comparison of the probe stimulus to the memory set. In a delayed-response task, prefrontal - posterior theta-band EEG coherence was higher in the delay period than during the preceding period of stimulus presentation [203]. Subjects performing the Wisconsin Card Sorting test show increased EEG theta-band amplitude in the 2 sec after stimulus presentation, relative to a baseline in which stimuli were presented but subjects were not required to respond [75]. In this test, a set of reference cards are presented together with a target card. The subject has to match the target with one of the reference cards based on an initially unknown matching criterion: this could be the color, number or shape of the symbols on the card. The increase in theta-band amplitude was estimated to be due to frontal and temporal sources. In a study of visuo-spatial working memory in which subjects had to remember the position of a target during a delay, [18] found a sustained decrease in EEG frontal theta-band amplitude when the target was removed and had to be remembered relative to when the target remained on-screen. The authors hypothesized that this was related to improving signal-to-noise ratio in hippocampo-cortical loops (see below).

Some extensions to the working memory line of research are studies of language, the error-related negativity (ERN) and intelligence. In a language comprehension study, [17] showed region-specific effects on phasic theta amplitude, between 200 - 500 ms after word onset. Phasic amplitude increased at left and right anterior electrodes following syntactic and gender agreement violations, respectively. In a study in which sentences were presented word-by-word, [19] showed a theta-band specific linear increase in amplitude as words were added to the sentence. The electrodes showing this effect were central and parietal-temporal, bilaterally. Two possible interpretations were presented for the amplitude increases. One is that it reflected the formation of an increasingly specified episodic memory trace; the other is that it reflected increased working memory load. Single words were followed at around 350 ms by a phasic increase in theta-band amplitude. The ERN has been proposed to reflect theta-band bursts phase-locked to responses [139]. The ERN is a frontal midline ERP peak that occurs following speeded responses that subjects realize are incorrect as they are made. From 100 ms pre- to 600 ms post-response, theta-band amplitude was higher for incorrect than correct responses. Regardless of the extent to which the ERN component is due to phase-locked theta bursts, the study showed that theta amplitude is associated with consciously incorrect responses and so possibly also the associated affective evaluation [139]. In a study comparing the induced brain activity of subjects with high- and low-intelligence, differences in the time courses of theta-amplitude were found a in dual task [97]. Subjects performed a 1-back comparison task while counting the number of squares presented. The high-intelligence subjects showed a pattern of early increase (0 - 500 ms post-stimulus) in theta-band amplitude, over the whole scalp, followed by a decrease, relative to the pre-stimulus baseline. The low-intelligence group showed increases in amplitude for up to 2000 ms post-stimulus. This was interpreted in terms of earlier completion of the task, and so earlier reduction in mental effort as indexed by the theta-band time course [169], in the high-intelligence group.

1.4.3 Intracranial measures: cognitive gating, delay-period activity and hippocampal theta

[192] used intracranial EEG with epileptic patients while they performed a Sternberg task. Trials contained an orienting cue, 1 - 4 memory-set stimuli (consonants), a delay, a probe stimulus and a response. The patients differed in some details of the task and in overall trial duration, but all patients showed an elevation of theta-band amplitude from cue to response. This was termed cognitive gating of the theta oscillation. It was of special interest that the amplitude increase was also present for the delay interval during which no external stimuli were presented. Only some regions of cortex were sampled by the electrodes and electrode grids, and these regions were different for the different patients. It seemed that cortical gating was widely present, with instances found at frontal, temporal, parietal and occipital sites. Also using recordings in epileptic patients, [238] found effects on the theta-band amplitude of LFP's in the anterior cingulate gyrus. A peak around 500 - 800 ms post-stimulus was found following rare auditory tones in oddball task and following the presentation of memorized words in a word memory task. The amplitude in this period was higher following rare than frequent tones and memorized than new words.

In a study using monkeys, [231] the transcortical field potential was studied during trials containing a warning stimulus followed after a 3 s delay by a stimulus to which the monkeys had to respond within 0.5 s. Brain areas in prefrontal cortex showed an increase in theta-band amplitude during the delay period. The activity was suggested to be a homologue of human midline theta rhythms. Local field potentials (LFP's) and single-unit activity (SUA) were measured in extrastriate visual cortex of monkeys during a delayed matching to sample task by [128]. The sample stimulus was presented at variable contrasts. At the low contrasts, monkeys did not perform above chance, whereas at higher contrasts their accuracy was significantly higher (about 90 % correct). During the delay period, the time course of theta-band amplitude showed clear differences following low- and high-contrast sample stimuli. High-contrast cues were followed by a peak in amplitude whereas the amplitude following low-contrast cues remained low. The peak in amplitude decreased prior to the probe stimulus. SUA was shown to have a preferential phase relative to LFP theta-oscillations (around 220 degrees). Using statistics on SUA taking phase into account, the authors showed that more than half of the V4 neurons were involved in delay-period activity associated with one of the sample stimuli. Furthermore, selective modulation of neurons by their preferred stimulus over non-preferred stimuli was greater during their preferred phase period. Finally, it was noted that increases in theta-band oscillations were not associated with increases in the overall firing rate of around 15 Hz. This was contrasted with results from prefrontal and inferior temporal neurons which did show increases in firing rate during working memory delay periods.

Theta-band activity in the hippocampus has been related to different kinds of overt behavior [233], to sensorimotor integration [25] and to cognitive mapping [173]. The hippocampus is a cortical circuit in the medial temporal lobe. Information from sensory and frontal cortex is passed from region to region within the hippocampus via excitatory synapses and eventually returned to sensory and frontal cortex. Superficial and deep layers of the entorhinal cortex provide input to and output from the hippocampal circuit, respectively. The entorhinal cortex, in turn, has reciprocal connections with frontal and peri- and postrhinal cortex, the latter two having reciprocal connections with uni- and multimodal sensory cortices. The question then, is what transformation the hippocampus performs on the extensive pattern of neural activity it has access to. There are now three lines of research to consider, which concern memory, movement and mapping.

In a well-known case, patient H. M. underwent bilateral removal of the hippocampus and was subsquently unable to encode new information into long-term memory, but did not suffer retrograde amnesia [207]. In a study using rats, experimental lesions of the hippocampus showed that the hippocampus is involved in detecting associative mismatches, but not novelty [89]. This study used the orienting response to show that, due to hippocampal lesions, rats that had habituated to tone - light pairings responded to novel visual stimuli following a tone but not to a remapping of tone to visual stimulus. fMRI studies have confirmed that the hippocampus is involved in the encoding of relational information. In [151], subjects were scanned during encoding and retrieval blocks in a paired-associate task. Medial temporal increases in hemodynamic response were found for encoding blocks relative to fixation blocks and, within encoding blocks, for novel word pairs relative to repeated word pairs. In the right hippocampus, this novelty-specific effect was higher for the subjects with better memory performance. At retrieval, the hippocampal hemodynamic response to a cue was higher for succesful than for unsuccesful retrieval of the cued associate (this was significant for the right hippocampus, a trend for the left). The study emphasized the common regions involved in both encoding and retrieval, referring to computational work [146] that shows how a single network can both A) detect novelty and subsquently encode the novel information as a new pattern in memory (pattern separation) and B) recognize a pattern and restore a wider pattern of activity related to previous experience (pattern completion). In a face - name association task, the hippocampus was, as in [151], activated more for novel than repeated pairings [218]. Specifically anterior hippocampal involvement in a somewhat different kind of relational encoding was reported in [44]. In this study, subjects had to perform a rote rehearsal and an elaboration task, cued per trial. In rote rehearsal, a presented triplet of words was rehearsed in a given order. In the elaboration task, subjects reordered the presented three words in terms of desirability. Elaboration of the triplet, but not rote rehearsal, was shown to result in greater than expected frequencies of the recognition of all three words in a triplet. The frequency-expectation was based on the cubed hit rate. The result implied that relatinal encoding within the triplet occurred during elaboration. Elaboration trials showed higher activation in the anterior hippocampus, while rote rehearsal showed higher activation in the entorhinal and perirhinal cortices. For elaboration but not rote rehearsal trials, higher activation in the anterior hippocampus predicted better subsequent memory performance. Activity in the entorhinal and perirhinal cortices predicted decreased memory performance for elaboration trials and was not related to memory for rote rehearsal trials. The results further strengthen the role of the hippocampus, specifically the anterior hippocampus, in relational encoding, and suggest a possible role of entorhinal and perirhinal cortex in working memory. A previous study had also found hippocampal activity (mostly strongly right) during a delay period that could have been related to working memory [193]. In this study, subjects had to hold a target face in working memory to compare it with a probe face after a 7 s delay. This condition was compared with encoding and retrieval blocks, with the same temporal structure as the working memory blocks but only one stimulus presentation, either before or after the "delay". The time course of the delay-period activity in the right hippocampus showed sustained activity during the delay, following an initial peak. It was noted in both studies that a hippocampal role in working memory is hard to distinguish from coincidental encoding during working memory. For instance,

the sustained activity in the hippocampus in [193] may serve to encode the association between the faces, not maintain the first stimulus' representation. However, the lack of a posterior-hippocampal memory effect for rote rehearsal trials in [44] suggests that activity in this area does not determine the quality of encoding. It was also noted that working memory is not dependent on hippocampal intactness [65]. Despite this, redundancy in the brain may allow subjects with hippocampal damage to be able to compensate for the loss of a possible contribution to working memory function. In general, however, encoding, in particular relational encoding, is strongly related to hippocampal activity.

Theta-band activity is involved in the synaptic processes that implement memory encoding in the hippocampus. In a study using rats [145], electrical pulses were delivered to the perforant path, which led to a population excitatory postsynaptic potential (pEPSP) in the dentate gyrus (these are both regions in the hippocampal circuit). The rats performed a delayed non-matching to position task which required them to hold a visual stimulus in working memory. This resulted in a phenomenon termed the reset theta [71]. The reset theta is an effect on the ongoing hippocampal theta rhythm, in which a peak and trough occur phase-locked to stimulus onset. The effect has been shown to occur when the stimulus is involved in a working memory task involving comparison of the current stimulus to the previous stimulus, but not when the stimulus can be evaluated by itself [71]. The reset theta was used to time high-frequency stimulation (HFS) to the perforant path, so that stimulation arrived at either the peak or trough, as recorded from the dentate gyrus. Sessions contained three series: first only test pulses were given, then HFS, then a post-HFS series of test pulses. HFS administered at peaks resulted in potentiation of the pEPSP spike that was absent (for slope) or at least significantly smaller (for amplitude) when HFS was given at troughs. The authors hypothesized that the reset theta serves to optimize memory encoding of stimuli, but note that further study is needed to determine whether other theta peaks than the reset theta also provide enhanced potentiation. However, at least for the reset theta, long-term potentiation in the hippocampus is dependent on theta-band activity. Since both the hippocampus and changes in synaptic weights seem likely to be involved in memory encoding, this dependence of long-term potentiation on theta activity may underlie the results of the memory line of research in scalp-recorded theta-band activity. The specificity of the reset theta to a working memory condition, specifically, comparisons over time [71], may point either to a relation between working memory and memory encoding, or to a role in implementing working memory itself.

In early intracortical studies in the rat, hippocampal theta oscillations were observed to occur during large-scale voluntary behavior [239] and during exploratory behavior like sniffing, but not automated behaviors such as eating or grooming [233]. Such action-related oscillations were termed type 1, while type 2 theta oscillations occurred during immobility under stress [120]. However, not all effects on hippocampal theta-band activity could be related to specific behavioral states. During lever presses - a large-scale voluntary movement - theta activity is weak [239]. In [246], rats were trained to press two levers in sequence, one to start a trial and then one of two choice-levers in response to a stimulus. The initial lever press was associated with an increase in amplitude in the 800 ms around the movement. In contrast, the amplitude decreased around the choice-press, starting 400 ms before the press and reaching a minimum 400 ms after. In a second task in the same study, rats were trained to run to and press two levers in sequence, and received a reward for the second press. Theta amplitude decreases around both lever presses, but to a greater extent for the second, rewarded lever press. It was concluded that behavior alone cannot predict effects on hippocampal theta amplitude, but that the behavioral context is essential. The sensorimotor integration hypothesis [25] was considered to be a suitable framework for explaining the results. This hypothesis differentiates the inputs and outputs of type 1 and 2 hippocampal theta and assumes separate subsystems for their generation. Type 2 theta is argued to be generated by sensory inputs to the hippocampus and to influence covert aspects of voluntary motor behavior. Such covert aspects are preparation for a movement, the intensity with which a future movement should be initiated or the need for a change in an ongoing movement. Type 1 theta results from inputs from motor systems involved in voluntary behavior and determines the speed of movement initiation and intensity changes in ongoing actions. Type 1 theta is further assumed always to be accompanied by type 2 theta, while type 2 theta can occur by itself. The main point of the sensorimotor hypothesis is that, during voluntary movements, signals from the type 1 system are continually integrated with inputs from the type 2 sensory processing system. The final output to motor systems could thus provide feedback to the motor systems on their consequences on the environment.

A final kind of result is involved with the existance of place-cells in the hippocampus. For these cells, the location of an animal in its environment determines their firing rate [171]. This gave rise to the cognitive mapping theory: that the hippocampus is the neural substrate for space relative to the organism [172]. [24] describes how this discovery played a role in a shift from a behavioristic to a cognitive paradigm for interpreting brain activity. Place-cell activity is also related to theta oscillations. As an animal moves through the receptive field of a place cell, that cell's discharges occur at specific phases of the hippocampal theta rhythm due to the voluntary movement [173]. At each cycle of theta, the phase of the discharges precesses.

So the hippocampus and hippocampal theta-band activity have been ascribed two broad kinds of role: first, memory encoding and retrieval, in particular relational and spatial encoding, and second, sensorimotor integration and possibly working memory. It was explicitly noted by [25] that the hippocampus may have multiple functions, of which sensorimotor integration would be only one example. Another possibility is that of confounds in the kind of setting and task used in the different fields of study. For instance, in behavioral research, animals have to be trained, so that memory retrieval is in some way involved whenever they perform trained behaviors. Or, in memory studies, it may be that the recall of a memory always triggers a signal to motor systems in case an adjustment in actions is necessary. A third possibility is that the different functions can be reduced to a single neural role from which, under different circumstances, the various specific functions can arise. For instance, sensorimotor integration could be seen as an example of pattern completion over time, the pattern in this case including activity in the motor system. Due to operant conditioning in combination with the environmental context, each pattern could continuously evoke changes in the sensory input, resulting in a change in the motor part of the new pattern that gets completed, and so on. In cognitive mapping, the place-cell activity may serve to update a sensory representation of the environment - which could also be described as pattern completion - changing relative to the animal as it moves. This would then be an example of motor-to-sensory feedback, a kind of reversal of the sensory-to-motor feedback relationship described by the sensorimotor hypothesis. While there is as yet no clear, precise answer to the question of what transformation the hippocampus performs on cortical patterns, it seems possible that it involves the translation of relations between, e.g., sequentially presented items or sensory feedback for motor control, into phase relations in the theta band.

1.4.4 Short- and long-term relational encoding

The research of theta-band activity seems to follow two lines. In one line, the studies show theta-band activity during the maintenance and tranformations of current patterns of cortical activity (e.g. [128] [18] [25]). In the other, theta-band activity is shown to be involved in the encoding and retrieval of such patterns to and from long-term memory (e.g. [116] [227] [145]). In the long-term memory studies, relational encoding, between objects as opposed to features, in the hippocampus seems likely to underlie the various results. In the working memory studies, relational encoding of a somewhat different type (time scale) and origin may also be the essential role of theta activity. As described in 1.1.4, relations between ongoing neural activity and an event in the past may involve oscillations and phase coding. Relations between dimensions of stimuli may also involve the formation of cell assemblies defined by their rhythmic activity. The data reviewed here suggest that at least some such phase-coding of relationships is reflected in the theta band. The integration of sensory and motor activity [25] extends the requirement for some form of short-term relational encoding to relations between motor and sensory activity. As reviewed in 1.3.2, it is the prefrontal cortex that seems to plays an important role in setting up and changing short-term relations between distributed patterns of cortical activity. While there is not yet direct evidence for a prefrontal role in theta-band phase coding of motor and sensory activity, prefrontal and distributed theta-band activity are at least indirectly linked through their common involvement in working memory.

It seems, then, that theta-band activity may provide the relational encoding of cortical representations, and that this activity has two sources: first, hippocampal activity retrieving patterns from long-term memory, e.g. [151], and possibly setting up the conditions for optimal encoding [145] and second, prefrontal regions and anterior cingulate cortex (and possibly also the hippocampus) involved in working memory, e.g. [231]. This leads to the expectation that conflicts may arise between these two sources of phase-coding: perhaps long-term memory will exert a patterning force due to pattern recognition and completion, while working memory is stabilizing a different, more recent pattern of phase-coding. Such conflict may be the physical basis for some of the behavioral effects that resulted in the ideas of automatic and controlled processing and the supervisory attentional system [167]. If a similar end-product, in terms of influence on cortical activity, exists for prefrontal and hippocampal structures, data concerning one kind of activity may help understand the other.

If sensory and motor activity are indeed both part of the pattern completion / phase-coding reach of theta-band activity, then the relation of stimuli to responses could be flexibly encoded by phase relations. Since task sets are defined as sets of mappings of responses to stimuli [157], task switching seems a promising experimental setting to study the theta band.

1.5 The alpha band

1.5.1 Introduction

The alpha frequency band runs from 8 to 12 Hz. Oscillations in this band can have amplitudes large enough to be clearly seen in raw EEG traces, and were observed in the first EEG recordings. Interpretations of the alpha band initially centred around the basic idea that alpha-band oscillations reflect an absence of mental activity, or neural information processing. More recent findings and studies of thalamocortical interactions have suggested that alpha-band oscillations reflect specific kinds of inhibitory processes. Note that activity in this frequency band thus has a very different behavior in relation to experimental manipulations and hypothetical neural function than the theta-band activity discussed in 1.4.

1.5.2 Idling

Alpha band oscillations were for a long time taken to reflect an absence of mental activity [152] or, in later terms, a state of neural tissue in which it processes no information [187]. The idea of the presence of brain activity reflecting the absence of mental activity goes back to very early EEG studies. As described by Millett [152], the EEG was developed by Hans Berger (1873 - 1941) in the first decades of the twentieth century. Berger developed an interest in the physical form of mental events, that was triggered by the experience of a near-fatal accident. During a military exercise, he was thrown from his horse in front of a horse-drawn artillery gun. Berger escaped injury, but he later received a telegram from his father, sent at the urging of his sister who had felt that something terrible had happened to him. Such telepathic occurences were not obviously in contradiction with the dominant scientific idea of that time: the conservation of energy [152]. Lehmann [129] had applied the conservation of energy idea to mental events by postulating the existence of psychic energy ("P-energy") as just another form of energy. Chemical energy, released by metabolism in the brain, could be converted into heat, electricity and P-energy, of which the P-energy was necessary for mental states. Thus, a subtraction logic could be devised: the difference between chemical energy and the sum of heat and electrical energy would be the amount of P-energy available for perception, feeling, emotions and conscious thought. Grounded in such ideas, the essential problem of Berger's psychophysiology was how to study the transformations of energy sources in the brain into P-energy. Berger's work on attempting to measure the non-P-energy of brain function seems to have to be understood from an additive energy model: as more total energy becomes available to the brain, more can be converted to P-energy; and given a certain amount of cerebral energy, a decrease of heat or electricity must be associated with an increase in P-energy, to preserve the conservation of energy. Berger performed both thermometric and electrical studies, his breakthrough occuring in 1924. In that year, Berger was stimulating the cortex of a patient named Zedel, when he switched the electrodes from a stimulator to a galvanometer used for electrocardiograms. The galvanometer recorded electrical oscillations from Zedel's cortex. In 1927, after some years of technical improvements, Berger was able to consistently produce EEG tracings measured from the scalp. This was before the approach of calculating ERP's, before digital storage and manipulation of signals were available at all. Nevertheless, two characteristics of the brain's electrical activty were visible: the 10 Hz, large-amplitude alpha and the 20 Hz, smaller beta waveforms, the latter of which were thought to reflect metabolic processes. Bursts of the alpha waveform appeared during mental rest, and disappeared - as a substrate for P-energy? - during mental activity and sensory stimulation.

Berger's framework for interpretation seems to suffer specifically from coming before information theory, lacking access to an idea that something non-physical (although still not specifically mental, or conscious) - information - can exist both in parallel with and systematically related to physical processes. Still, his interpretation of alpha-band activity as a negative indicator of mental activity remained dominant for a long period, in a somewhat different form. Neuronal spikes have become generally conceived of as events involving both physical processes and information processing, entwined together [230]. However, the negative relation between specifically alpha band oscillations and mental activity remained, only this became interpreted to mean that "idling" neuronal areas, i.e. areas that are not currently processing information, fire synchronously in the alpha band frequency range [187]. Berger's findings were taken as evidence for the idling hypothesis, as well as new data. One of the basic findings was that of 7 - 14 Hz sleep spindles, caused by thalamocortical interactions [222] discussed below. Alpha band effects were also found in awake subjects, extending early findings.

The time course of alpha band activity has been shown to be related to experimental conditions and behavioral events; such effects have further been shown to be, in some cases at least, localized. In two cued-task experiments, the pre- and post-stimulus alpha-band power were compared and the time course of power in the upper (10 - 12 Hz) and lower (8 - 10 Hz) alpha band was studied [113]. In both experiments a warning tone was followed by a one, two or three second pre-stimulus interval. In the first experiment, the task was to silently read a word or a number. For these data, conclusions were based on the computation of event-related desynchronization (ERD) instead of the observation of alpha waveforms in the raw EEG. An ERD time course can be seen as an ERP based on decreases in instantaneous amplitude (in practice, the directly associated measure of power is used, but for consistency the term amplitude will be used throughout to describe amplitude-related parameters) relative to a baseline, positive values being given by reductions in amplitude [187]. Negative ERD values would reflect event-related synchronization (ERS). ERD values can be computed by band-pass filtering a signal, rectifying it, and averaging epochs time locked to repeated events of the same kind. In these data, ERD was greater post- than pre-stimulus, and increased post-stimulus with longer pre-stimulus intervals. The lower alpha band showed a roughly one second period of ERD following warning signals, which then dropped until stimulus presentation. An exception to this appears to occur at frontal sites, where the ERD persisted. The upper alpha band ERD did not respond to warning signals, and decreased pre-stimulus, increasing at posterior sites post-stimulus. The warning signals in this experiment were taken to increase alertness, or non-specific attention, but not expectancy, or the selection of specific processing pathways. The second experiment used conditions with blocked or randomized trial types to distinguish such general and specific forms or preparation. The task was to judge words as animals versus tools, and numbers as even versus odd. In blocked conditions subjects could prepare for the specific task, while in random conditions whether a word or number judgement was upcoming was unknown. For the blocked relative to the random condition, the upper alpha band showed a lower ERD, both pre- and post-stimulus, and the greatest increase in ERD at stimulus presentation. The latter result was interpreted as a reflection of a more relaxed state in the blocked condition. The upper alpha band showed greater differences over scalp locations (measured as a posterior - anterior difference) and the average ERD was greater in the lower alpha band. The results were interpreted to suggest that ERD in the upper alpha band reflects specific computational processes, due to its more specific scalp distribution and response to stimulus presentation, while ERD in the lower alpha band, showing a more generalized and stronger ERD, reflects overall alertness. These interpretations were used in a later study on memory performance and ERD (described below), but do not seem to rest on strong evidence. For instance, could some kind of general but phasic alertness not peak post-stimulus, invalidating the assumption that activity arising post-stimulus must be assigned to specific processing? Nevertheless, these systematic effects on alpha band ERD provided a basis for further research. Whether the presented stimulus is (recognized as) an object or not has also been shown to influence alpha-band amplitude [234]. Using the MEG, the amplitude of an alpha rhythm originating from the parietal-occipital sulcus was measured following presentation of line drawing of objects, and of non-objects created by randomly rotating areas of the drawings. Subjects were instructed to indicate whether they perceived a coherent and meaningful object or not. Alpha desynchronization was greater following presentation of an object than a non-object. Missed objects showed an intermediate level of alpha activity. These differences were found in the period 300 - 1000 ms post-stimulus. When subjects did not have to respond, differences in a lpha activity between objects and non-objects were lost. The results were interpreted in terms of disengaging the parieto-occipital sulcus from low level visual cortices, in which case it was described as resting as opposed to selecting a target for further processing.

A more explicitly functional role than a reflection of idling was assigned to alpha-band activity in a study that compared tasks requiring the observation of external stimuli (sensory intake tasks, e.g. searching for Mooney faces, pictures of faces which are reduced to black and white areas, making them hard to recognize) or internally directed attention (sensory rejection tasks, e.g. mental rotation of a geometric figure). In both conditions, tasks were such that cortex was not expected to be idling, regardless of the intake - rejection distinction. Performing tasks that required sensory information to be processed decreased right-hemisphere parieto-occipital alpha-band activity, relative to tasks involving only internal representations [194]. Alpha band activity is also related to memory performance [115]. A "difference based on later memory performance", or Dm, effect, was found for high- and low-performing subjects in an incidental memory task. Subjects first performed a task in which they made semantic judgements on words, and were then confronted with an unexpected memory task in which they they had to recall as many of the words presented in the judgement task. Finally, subjects were presented with a cued-recall task in which the six categories from which the presented words were taken were provided (e.g. birds, vehicles, weapons). Upper and lower alpha band ERD was measured during semantic judgement trials, and compared between trials for which the presented word would be remembered or forgotten at memory testing. Trials consisted of a warning signal, followed after a delay of around one second by a word, followed after 1500 ms by a signal indicating that the response could be given. The subjects were divided into a good- and a bad-memory group based on a median split of the free-recall scores. Alpha-band ERD was greater for bad performers, most strongly at parieto-occipital sites. A post-stimulus difference between frontal-central upper and lower alpha ERD occured, that was described as stronger ERD in the lower alpha band. However, inspection of the figures shows that it is ERS in the upper alpha band, relative to baseline, that causes the difference, which may be relevant in terms of later results and hypotheses on the alpha band described below. Good and bad performers both showed a memory-dependent effect, but in different frequency bands. Good performers showed a peak in lower alpha ERD 200 - 600 ms post-stimulus for remembered words, while bad performers showed a more gradual increase in upper alpha ERD for remembered than non-remembered words. Based on the earlier study concerned with lower and upper alpha activity, lower and upper alpha activity was interpreted to reflect general alertness and specific processing (semantic encoding), respectively. Good performers were assumed to more easily encode the stimuli while being more alert during stimulus presentation, and given these interpretations and assumptions, the ERD could be explained. As argued above, the grounds for this interpretation did not seem to be strong, and no specific mechanisms underlying the various effects or an explanation for the strong ERS relative to the baseline in the upper alpha band was provided.

Motor activity evokes alpha-band event-related desynchronization over cortical areas associated with the moved limb [188] (in the context of motor activity, the alpha frequency range is termed mu). Foot, hand and tongue movements result in ERD topologies that could be related to the underlying sensorimotor homunculi [185] [186]. For instance, hand movements are associated with mu ERD at electrodes C3 ad C4, while Cz responds to foot movements. A related phenomen called focal ERD / surround ERS has been demonstrated, which refers to ERS occurring at areas around a desynchronized region [186]. In a study comparing self-paced ballistic movements, sustained contractions, and the release of a contraction of the wrist, mu-band activity was shown to decrease at central and parietal sites from around a second prior to movement to a minimum around half a second to one second after movement onset [1]. Around contraction releases, the reduction in alpha amplitude was weaker than around ballistic movements and sustained contractions. Motor imagery has been shown to result in similar patterns of desynchronization as actual movement, both showing lateralization depending on real or imagined movement of the left versus right hand [147]. Desychronization was, however, weaker for imagined movements. Anticipatory hand-switching results in increased alpha-band coherence [208]. Subjects either performed 30 s of flexion - extension movement with their right hand, or switched to left-hand movements after 15 s following a verbal cue. Subjects knew whether a switch would occur. In the first 15 s, subjects showed higher mu-band coherence in switch blocks, bilaterally but mostly within the hemispheres (importantly for later discussion, no effects in the beta band were found). No differences in power were found. Results using directed transfer functions showed higher directed coherence from frontal to more posterior areas (motor and parietal) in the right hemisphere (i.e. the hemisphere of the hand to be switched to), and these results were interpreted to reflect a frontal-to-central flow of information. The left-hemisphere directed transfer results were not reported. The results were taken to reflect a communicative function of between-signal alpha-band coherence, as opposed to the idling "null-function" of within-signal alpha band activity.

Results on alpha-band activity during the presentation of probe stimuli do not seem to be fully explainable by the idling hypothesis. A Sternberg study in which lower and upper alpha-band ERD was measured showed differences in alpha band responses to memory set presentation and probe stimuli [121]. Auditory stimuli consisting of four vowels were presented, after which a target vowel was presented. Subjects had to determine whether the target was in the probe set. During the memory set presentation, mostly from 1 - 3 sec into the presentation, the lower and upper alpha bands showed synchronization, the lower and upper bands showing predominantly occipito-parietal and broad distributions, respectively. Following the probe, ERD occurred in both bands. In the lower band, the ERD had an occipito-parietal distribution and was significant from 500 to 3000 ms after the probe. The upper band ERD had a parietal, central and occipital distribution and was significant at two time points, around 1 s and 2 s following the probe. However, the ERS during probe presentation is difficult to explain in terms of idling - are neural areas doing less while probes are being perceived and memorized than during a baseline resting period? A similar finding of ERS during a pre-stimulus period of activity was found in a delayed response task [18]. Subjects were shown a target location which either remained visible or disappeared during a delay, of one or four seconds, preceding a required response (touching the target location). During the four second delay, both lower and upper alpha band amplitude over posterior electrodes rose above baseline. Again, an interpretation purely in terms of idling does not seem able to explain these results. Why should areas be expected to systematically process less than during baseline? As described below, alpha-band activity appears to reflect not so much the reduction of cortical information processing, but what makes such a reduction possible in the face of constant afferent input.

1.5.3 Inhibition

More recent EEG studies [58] [61] [245] have found further results that do not fit with an interpretation of alpha band activity as an index of idling. These studies suggest that it reflects active inhibition. In an intermodal attention study [58], subjects were cued to direct their attention to either the visual or the auditory modality. Alpha-band effects were found in the one second delay between the cue (the word BEEP or FLASH) and the compound visual - auditory stimulus. Stimulus targets were defined by a mismatch between two component stimuli in the cued modality. Mismatches concerned the tone frequency of binaurally presented toned or the position of bilaterally presented circles. Starting around 500 ms post-cue up to stimulus presentation, alpha-band amplitude began to diverge for the two cue types over parieto-occipital sites. Following cues indicating an auditory task, alpha-band amplitude increased in this interval, while it decreased when the visual task was cued. Similar effects were found using an auditory instead of a visual cue [61]. Auditory cues were single or double clicks, succeeded after 1200 ms by, randomly, a unimodal or compound audio-visual stimulus. Subjects had to detect targets in the cued modality. Again, around 500 ms post-cue, parieto-occipital alpha-band amplitude diverged, increasing when the auditory task was cued and decreasing when the visual task was cues. Spatial-cueing effects on alpha-band amplitude have been found within the visual modality using a go - no go task [245]. Cues indicated whether stimuli would appear, following a 1000 ms delay, in the left or right hemisphere. Stimuli consisted of rotated T's in one of four rotations or dots moving in one of four directions, one of each stimulus type being the target for a block. Stimuli were presented in either the upper or lower visual field in different blocks. Following the cue, amplitude dropped to a minimum after around 400 ms, and subsequently increased to a maximum before and around stimulus presentation. Pre-stimulus, the electrodes over occipital cortex ipsilateral to the cued side showed a greater increase in amplitude than those over contralateral cortex. Amplitude increases were highest over parietal-occipital areas. The topology of amplitude increases was also dependent on whether stimuli would be presented in the upper or lower visual field, with more medial - dorsal distribution for the upper visual field. The focality of the amplitude increases and the attention-dependent shifts in location suggested that the alpha-band activity reflects active inhibitory process as opposed to a passive idling state.

Using experimental manipulations designed to have subjects direct their attention to external stimuli or internally, further arguments were given for the hypothesis that alpha-band activity reflects inhibition of task-relevant areas, as opposed to idling or intake-rejection [40]. Subjects were given either easy or more demanding questions to answer about upcoming sequences of sensory stimuli (e.g., no question, the number of stimuli presented, the number of different stimuli presented). Visual, tactile and auditory stimuli were used. After the blocks in which these sequences were presented (called the externally directed attention condition), subjects performed the same tasks but now with imagined stimuli (called the internally directed attention condition). Alpha-band activity was lower during sequence presentations than during sequence imagining, while following more demanding questions alpha band activity increased, either significantly or as a trend for all modalities. No interaction between the task demand and internal - external factors was found. The findings were taken to argue against the idling and intake-rejection hypotheses, due to the either reversed or indifferent predictions, respectively, concerning effect of task demands. The inhibition hypothesis was argued to provide a parsimonious explanation, as it would predict the inhibition of task-irrelevant areas regardless of whether such inhibition is necessary due to the protection of internal processing or higher task demands. Referring back to the difficulties in explaining results in terms of the idling hypothesis described above, inhibition of task-irrelevant neural areas, or processes, may provide a better, although unspecific, kind of explanation. As probes are presented or a response-goal must be both delayed and maintained, the inhibition of potentially interfering effects may be necessary. It may, as suggested by the results above, be the case that whether such interference comes from external stimuli or memory processes is irrelevant. It does seem possible that the effects of stimulus presentation will require the greatest inhibition. Ecologically, it would make sense to remain sensitive to at least some classes of potentially dangerous or advantageous events in the outside world. This somewhat gray relation between sensory events and internal processes, as well as the link between inhibition of the effects of such events and processes and alpha band activity, can be mapped quite directly onto the consequences of thalamocortical connectivity.

1.5.4 Alpha rhythms, augmenting responses and the thalamus

Cortical alpha-band activity is strongly linked to thalamocortical interactions [162]. All input to the neocortex from sense organs, as well as low level brain areas such as the cerebellum and mamillary bodies, is relayed via the dorsal thalamus (hereafter referred to as the thalamus). The thalamus sends excitatory output to all regions of the cortex (layers IV and VI), as well as to the striatum and amygdaloid complex, from so-called relay cells, and receives cortical feedback from layers V and VI. Input is also received from the brain stem and the thalamic reticular nucleus. Interactions between the inhibitory cells in the reticular nucleus and the thalamic cells that relay peripheral information are the basis of thalamocortical alpha rhythms, due to a recurrent inhibition pattern (see paragraph 1.1.4) discussed in more detail below. The thalamus consists of nuclei of cells that relay a specific type of information - e.g. visual, thermal, auditory etc, resulting in maps of sensory space (e.g. the position on the retina) on the thalamus. The nuclei contain two kinds of relay cells, first- and higher-order, which receive input from the characteristic peripheral input type and from the cortex, respectively. The input to first-order relays is termed driving afferent input, and is communicated via the thalamus in parallel, that is, without direct interactions, with the information being transmitted in other nuclei. Higher-order relays provide a means of interaction between cortical areas, as one cortical area may project to another's relaying thalamic nucleus. The effect of such corticothalamic connections is modulatory: it cannot change what driving afferents will be relayed by a certain nucleus, but can change how they are relayed.

The modulation of the behavior of relay cells concerns their firing mode: tonic firing, synchronous bursting and asynchronous bursting [162]. Given a constant excitatory input, relay cells with a membrane potential that is more depolarized than around -65 mV respond with the production of single spikes, at a low frequency (around 10 Hz, but these single spikes are not the source of the alpha rhythm measurable in the EEG). More hyperpolarized relay cells temporarily open so-called transient-type calcium channels; this results in a low threshold Ca^{2+} conductance. When these channels are open, excitatory potentials are increased, as the channels do not close immediately as the opening hyperpolarization is lost (the response lag of these channels to membrane voltage lies around 100 ms). This mechanism underlies the post-inhibitor rebound described below, and results in a transient high-frequency burst of spikes. Such bursting can occur synchronously over multiple nuclei, under which circumstances peripheral information is not being relayed (as nucleic output then communicates the event of synchrony as opposed to events that are transmitted by driving afferents). Asynchronous bursting also occurs, however, and in this case bursting has been argued to still convey information about driving afferents, but different information than transmitted by single spikes. The difference is based on linearity relations between stimulus intensity (or afferent input) and the response in spikes per second. In tonic mode, spikes increase somewhat linearly with increased intensity, while in burst mode, showing more all or none than gradual responses, the intensity - response relation is flatter. In other words, the response is more sensitive to the intensity in tonic firing mode. If excitatory input causes a burst, the event of an increase in intensity in the relayed, e.g. sensory, variable may be more strongly communicated than by the singles spikes in tonic firing mode. This would be at the cost of more subtle coding of intensity. The burst mode of firing is associated with thalamic alpha rhythms, especially synchronous rhythms which would result in alpha-band waves of cortical excitation at scales that would be measurable in the EEG. Burst firing and thalamic alpha rhythms are related via the augmenting response described below.

When thalamic and cortical neurons are stimulated in the alpha frequency range, their response increases, in terms of depolarization and spiking, from around the first to the fifth stimulus [223] [21]. This augmenting response involves a secondary depolarization that appears at the second stimulation, with a relatively late onset in the order of 10 ms. The augmenting response is thus a form of short-term plasticity that depends on an increased tendency to depolarize at a certain point in time following a previous neuronal event. Thalamic stimuluation leads to stronger augmenting responses in the cortex than stimulation of the cortex directly, due to spike bursts generated within the thalamus. A mechanism for generating augmenting responses is the post-inhibitory rebound [21]. Such rebounds occur after (recurrent) inhibition which leads to hyperpolarization, which leads to the deinactivation of low-threshold Ca^{2+} currents, which leads to a greater response to subsequent excitatory inputs as described above. So, if the inhibition is time locked to the arrival of the next stimulation, e.g. due to recurrence between thalamic relay and reticular cells, augmentation can occur. Computational modelling has been done on augmenting responses in thalamocortical networks [21]. Both the thalamus and cortex layers in the model contained excitatory (thalamocortical cells in the thalamus and excitatory cortical cells) and inhibitory neurons (thalamic reticular cells and inhibitory interneurons). Only AMPA and GABA receptors were included in the model, as related experimental data had been acquired under an NMDA-blocking anesthesia. The simplest thalamocortical model contained one of each of the four neuron types listed above, with recurrent inhibition within the thalamus and the cortex, and with the excitatory cells projecting onto all other cells. Thalamic stimulation that arrived after recurrent inhibition from reticular cells resulted in an augmented burst of spikes in thalamocortical neurons. This burst subsequently evoked EPSP's in the cortical layer. More complex models showed that further interactions could occur between thalamic augmenting responses and cortical activity. One result, that may be especially important to understanding cognitive control, was that cortico-thalamocortical feedback could induce augmenting responses in other cortical areas than the area initially targetted by the stimulated thalamus cells.

Connections within the thalamic reticular nucleus may be essential for the ability to direct attention. In a computational thalamocortical model built up from modules which contained the basic relay - reticular, excitatory - inhibitory connection, inhibitory intrareticular interactions were shown to be able to reproduce the focal ERD / surround ERS finding [225]. In this model, a cholinergic neuromodulatory input (which is the type provided by the brain stem) was included that excited relay and inhibited reticular cells. When this input was low, cells achieved sufficient hyperpolarization for rebound spikes and thus bursting alpha activity to occur. When the modulating input was applied to only one of two mutually inhibitory reticular nucleus cells in a two-module model, the modulated module lost its alpha activity while the other module showed an increase in alpha activity. The mean hyperpolarized state associated with alpha activity was suggested to result in the withholding of sensory information. In this model this state was taken to underlie a resting state, but is also compatible with an interpretation in terms of internal versus external attention.

So, the thalamus generates alpha-band activity that, just as in the EEG results described above, is not restricted to any one simple function. Sensory rejection seems likely to be one function, but corticocortical interactions via the thalamus can also occur, with unknown but potentially important computational results. Further and perhaps relatedly, it does not seem that thalamic alpha-band activity necessarily reflects the lack of information transmission. It may serve as a ”wake-up call” [211], transmitting a strong interruption to ongoing cortical processing. This may be part of corticortical interactions, for instance if the result of some cortical computation is the overruling of whatever another area is doing.

1.5.5 The alpha band and task switching

The EEG results and the anatomical and physiological properties of thalamocortical interactions suggest hypothetical roles of alpha-band activity in task switching. Recall that backwards inhibition of task sets occurs, as shown by a difficulty in returning to a task previously switched away from [142]. This inhibition was described as an automatic processes, but the initial activation of such a process (i.e. setting up the triggering conditions) could nevertheless be the result of cognitive control aimed at achieving a target task set. The use of tasks involving different sensory modalities provides an opportunity to study the role of inhibition in a task switching context. If two tasks differ on their stimulus sets, then switching between them may be achieved by inhibiting the undesired set of stimuli, and thereby effectively the stimulus - response mapping [200]. For instance, let task A map a square and a circle to the right and left index finger, respectively. Then let task B map a high and a low tone to the right and left index finger, respectively, and let all stimuli be compound: a visual and auditory stimulus are presented together, so that only the internal state of the subject can determine which of the two tasks will be performed. In this case, when subjects switch from the visual to the auditory task, the relay of visual information might be inhibited, which would, as described above, be associated with an increase in cortical alpha-band activity prior to and during stimulus presentation. Such behavior would basically replicate the general findings on anticipatory occipito-parietal inhibition: subjects are simply cued to perform their next task, which involves certain inhibition demands. Preparing for hold trials would not be expected to be essentially different, perhaps showing somewhat smaller amplitudes because of the decay of previous-task interference to be inhibited. Consideration of backwards inhibition would seem to lead to the expectation of high parieto-occipital alpha amplitude when switching to the visual task, relative to when repeating the visual task.

In a similar way, alpha-band activity may turn out to reflect other limitations of preparation when switching between and repeating task sets. One way to view switch costs is as a failure to inhibit interference from the previously active task set. If subjects use inhibition to control their behavior, inhibition of the visual modality should be stronger preceding auditory than visual trials.

However, if this control is limited preceding switch trials, leading to switch costs, anticipatory, inhibitory alpha-band activity might not be able to occur prior to auditory switch trials. It would then be expected to be strongest while preparing to repeat an auditory trial.

Finally, cortico-thalamocortical connections open the possibility that changes in thalamocortical activity may not be involved directly with the relay of sensory information but with changes in cortical processing. If such changes plays a role in preparation in a task switching task, they would be expected to occur prior to stimulus presentation, as opposed to being part of an adjusted state determining how driving stimulus information is transmitted, which would have to persist at least up to stimulus presentation.

Similarly to shifts between input modalities, certain task combinations may allow switching to be achieved by shifts in output modalities. By using response sets which contain only movements all made by either the left or the right hand, measures of response-hand related lateralization of, e.g., mu-band ERD could be used to follow preparatory processes involved in switching between and repeating tasks. This kind of amplitude lateralization would also be expected for the beta band, and will be discussed further in section 1.6.

Finally, the anatomical distinction between driving first-order afferents and modulating, corticothalamic higher-order afferents to the thalamus may be part of the reason why switch costs are confined to the first trial following a switch, that is, why they disappear after a single trial performed using a new task set. One of the two clear differences between preparing for an upcoming trial and actually responding to a stimulus is that only in the latter case is there driving peripheral input from an external stimulus. The second difference is the analagous occurrence of an actual motor response after stimulus presentation. This difference will be discussed in the following paragraph in relation to beta-band activity.

1.6 The beta band

The beta band covers the frequencies from 15 to 26 Hz, and has a similar response to behavior and task demands as the motor-related alpha, or mu band activity. It has also been interpretated similarly, as an idling rhythm [187], although more recent studies suggest a more specific role [30]. Some differences between mu and beta band activity do exist, in terms of time course, location and the effects of manipulations, as will be described below.

1.6.1 Beta band activity during, after and preceding movement

Beta band activity decreases around responses over contralateral motor cortex, starting around 1.5 seconds prior to the onset of voluntary movements, recovering around one second post-movement, and subsequently overcompensating, with a peak at around two seconds post-movement [165] [220] [1]. This overcompensation is termed the beta rebound, and may be of special interest to a certain type of task switching, as described below. in the beta band, the rebound is more temporally localized, peaking and recovering more quickly, than in the mu band [165]; it also has a more anterior maximum [164]. Similarly to data showing alpha-band increases relative to baseline, the beta-band rebound suggests that such oscillations reflect a blocking of processing, as opposed to only its absence. As seen below, in vivo recordings show striatal increases in beta band activity during a movement task relative to rest, in contradiction to an interpretation of the beta band in terms of passive idling. Intracortical recordings from epilepsy patients show somewhat different effects of mu and beta activity in primary sensory and motor areas and the supplementary motor area (SMA) proper, preceding voluntary movements [174]. The SMA, being a more anterior prefrontal area than primary motor cortex, would be expected to be involved in organizing the brain in situations in which broad receptive fields in terms of time and content are needed. The SMA is sometimes termed the SMA proper to distinguish it from the pre-SMA; of these two, only the SMA proper has known corticocortical connectivity with primary motor and sensory cortices [175]. In primary areas, contralateral waveforms showed earlier pre-movement ERD than ipsilateral waveforms (around 1.5 versus 0.8 s), for both mu and beta bands but most clearly in the beta band. The mu and beta bands showed the strongest ERD in sensory and motor cortex, respectively. The difference between ipsilateral and contralateral ERD onset was not seen in the SMA proper, which showed a beta-band ERD starting 4 s pre-movement.

Using electrocorticogram data from epilepsy patients, movement-related coherence in the mu and beta band range was found between primary sensorimotor areas and the SMA [175]. In this study, partial coherence was used to avoid spurious coherence due to a common reference; a partializing electrode was used that showed no movement-related potentials. Subjects performed wrist or finger extensions, at 7 second intervals, and EMG onset was used to locate trials. Movement-related ERD and post-movement ERS, with a broad spread over frequencies centred around the beta band, was found in the primary motor and sensory areas and the SMA. The onset of ERD was earlier in the SMA (-1.8 s) than the primary regions (around -1.25 s). Mu-band coherence between the primary areas and the SMA proper was found, peaking at movement onset. Significant coherence, with a maximum in the beta band, was found between the pre-SMA and the primary sensory and motor cortices. The phase lag between coherent signals was near zero in more than half of the analyzed signal combinations.

1.6.2 Subcortical involvement in motor cortex beta activity

The cerebellar thalamus and the basal ganglia have been found to be related to cortical beta-band activity. In one study, a deep brain stimulation electrode was implanted in the cerebellar thalamus of patients with disorders of movement control (tremor and myocolunus), allowing scalp and thalamus measurements [177]. The cerebellar thalamus projects to primary motor cortex; see section 1.5.4 for a further description of thalamocortical interactions. The cerebellum itself receives input from climbing fibres and mossy fibres. Climbing fibres come from the inferior olive in the brain stem, which receives input from the cerebellum itself, spinal cord, brain stem and motor cortex. Mossy fibres project from the cerebellum itself, vestibular cells, the spinal cord, reticular formation, and bsaliar pontine nucleui, which receive inputs from the neocortex. Lesions to the cerebellum cause motor corrections (that is, goal-directed adjustments based on the current motor state [133]) to be badly performed, leading to suggestions that the structure is necessary to transform a negative feedback signal into a corrective movement; this transformation, from a desired consequence to a motor action, is called an inverse model, as opposed to a forward model that would predict the consequences of a motor action [244]. In the implantation study, subjects performed self-paced wrist movements. Slow pre-movement potentials, starting two seconds before movement onset, were observed both on the scalp and in the thalamus. Scalp and thalamic alpha and beta band ERD were also found, with roughly 2.5 s pre-movement onsets except for a later thalamic alpha onset at 1.2 s prior to movement. Finally, a band of thalamus - scalp coherence was found around 20 Hz, that diminished around 0.5 s before movement onset. Thus, similar thalamocortical interactions may exist for the beta band and motor behavior as for the alpha band and perception.

Another study used electrodes surgically implanted in the subthalamic nuceus of patients with Parkinson's disease [242]. The subthalamic nucleus is part of the basal ganglia, a complex of structures that receives input from sources including sensory, motor and association cortices, the hippocampus, the limbic system, the thalamus and the cerebellum; and that outputs onto the thalamus, especially nuclei projecting to frontal cortex (section 1.3.2), lateral habenular nucleus and superior colliculus [242]. A possible role that has been suggested for the basal ganglia, based on its anatomical connectivity, is the learning of goal-directed disinhibition of transthalamic interactions [243]. In general agreement this idea, in Parkinson's disease, the basal ganglia degenerate and a rigidity has to be overcome to make voluntary movements. In the implantation study, patients performed a cued go - nogo task, in which a cue presented two seconds prior to the trigger stimulus was either informative as to the required movement (left or right responses) or not. For the informative (100 % valid) condition, beta-band ERS was seen just after (within 200 ms) cue presentation, followed by ERD up to around 0.5 s post-cue. In non-informative (50 % valid) blocks, only the post-cue ERD occurred. Thus, the basal ganglia contain cue-related beta-band activity. In an in vivo study of normal (non-Parkinsonian) monkeys, beta band activity in the local field potentials at sites in the caudate nucleus and putamen increased, relative to rest, during performance of an oculomotor task in which animals had to fixate on dots in a grid [41]. During rest, beta-band activity at different locations was highly synchronous. Task performance resulted in reduced beta-band amplitude and synchrony around saccades, starting around 100 ms before movement onset and ending around 100 ms after the saccade was completed. Thus, although over whole task blocks, beta activity was high relative to rest, the time course follows the idling prediction. Desynchronization (now literally, not as an interpretation of EEG amplitude) between regions was not global; sites could become desynchronized from a group of other sites, which did not show saccade-related desynchronization. This study noted a technical issue that may have prevented such findings in earlier studies. Local field potentials measure the relatively slow post-synaptic effects of many spikes, from perhaps distant neurons, as opposed to individual spikes. Spike data may be less suited to detecting relatively global rhythmic activity. The beta-band activity was hypothesized to serve as a selective filter: only strong inputs to specific striatal modules could lead to their activity being distinguished from the global synchrony. The task-related increasing in amplitude would serve to make such break-throughs harder to achieve, and so facilitate a selective state, in this task, focussing on one specific point.

1.6.3 Cortex - muscle coherence

Axons from pyramidal cells in primary motor cortex descend to the the ventral horn of the spinal cord, from which spinal motoneurons project onto skeletal muscle fibres [34]. Despite the complex circuitry of the spinal cord itself, direct relations have been found between cortical (EEG) and muscle (electromygram, EMG) activity. As desribed below, beta band activity has been found in electrical activity measured from muscles as it has been found in cortical signals, and beta-band coherence occurs between the cortical and muscle signals [202] [30].

In one study, subjects performed isometric contractions of finger, toe and foot muscles, and EEG - EMG coherence was studied [80]. As well as coherence, a time-dependent measure called phase synchronization was used, which measures the deviation of a set of phases' distribution from uniformity. Beta-band coherence between the EMG and contralateral primary motor cortex was found, as well as periodic bursts (which were themselves in the beta range) of beta-band phase synchronization time-locked to the onset of motor-unit potentials. Phase lags were found that were consistent with conduction times from motor cortex to the muscles (e.g. 15 ms for finger and 41 ms for toe muscles). It has been further shown that cortex - muscle coherence depends on the specific characteristics of movement demands [110]. The coherence was measured between MEG signals over left sensorimotor cortex and EMG's from the right arm, while subjects pressed together two levers in a precision grip task. Subjects had to pattern the force they exerted between finger and thumb, guided by visual feedback: first they held the lever at 1.3 N for 3 s; then they linearly increased the force, over 2 s, to 1.6 N, where that force was held for a further 3 s. Four conditions were created based on the stiffness versus compliance of the levers. More compliant levers had to be moved a longer distance to achieve the required force. Three levels of compliance were used, and an isometric condition in which the lever did not move at all. Over the whole task period, MEG and EMG power showed both mu and beta peaks, while MEG-EMG coherence showed a beta peak. Time-frequency analyses showed modulations of beta amplitude, which was highest during the hold periods of the task; this was not found in the mu band. Significant MEG - EMG coherence was found only during the hold periods, and, except for the isomatric condition, was higher during the second period. The hold-period coherence increased with compliance. The same increase for the second hold period was found when grip force was increased in a jump, as opposed to over a ramp. The results show that beta-band activity and cortex - motoneuron communication are related to not allowing movement, as opposed to the absence of force production; and further that parameters of the system not to be moved influence the level of cortex - muscle coherence. A similar hold-specificity of beta-band EEG - EMG coherence was found in monkeys [13]. The monkeys were taught to perform a precision grip task, in which they held the position of levers between finger and thumb for around one second. Beta-band oscillations in local field potentials occurred once the hold position was reached, as well as beta-band coherence between cortical signals. Cortex - muscle coherence was also found in the beta band, again during the hold portion of trials. The oscillatory activity was suggested to reflect a computationally robust neuronal state, suited to maintaining a motor state.

1.6.4 Beta band activity during motor imagery

The imagination of movement also affects beta-band activity [165]. Motor imagery, or action simulation, appears to rely on the same processes and structures as expressed in motor performance [98], see section 1.3.1. A 'resonance-like' [165] oscillation was affected by movements and imaging in an MEG study using sensory stimulation [206]. The median nerve of subjects' right arm was stimulated at 1 Hz, resulting in a somatosensory evoked field over the contralateral primary somatosensory cortex. Over primary motor cortex, during rest conditions, the stimulation caused a transient increase in beta-band activity, peaking at around 500 ms. This post-stimulus rebound was reduced by movements but also by the imagination of movements. This beta rebound was also suppressed during the observation of actions, in an MEG study in which subjects manipulated a small object or observed someone else, with their arm lying close to the subjects, manipulating the object [84]. Mu and beta band activity have been shown to respond somewhat differently to motor imagery, using the EEG [147]. Subjects either opened and closed the hand ipsilateral to a stimulus, or imagined doing so. During movements, mu and beta ERD were observed bilaterally, but most strongly contralateral to the movement. ERD was more focal in the mu band, over postcentral sites (CP3, CP4) close to somatosensory cortex. The same pattern, although with smaller ERDs relative to rest, was found for imagery. Left - right differences in the mu band were as strong for imagery as actual movements. Such results, together with data showing pre-movement ERD as described above, involve beta-band activity in the WwM framework of section 1.3.1.

1.6.5 Motor-related rhythmic activity and task switching

Motor-related beta-band activity may be relevant to task switching in a number of ways. First, such activity may be involved with destroying part of a previous task set. Task switching is associated with motor-related effects: the diminishment of response repetition benefits [197] and the prolongation of the LRP-R interval [92]. As, further, switch costs are caused by obsolete stimulus - response associations, cognitive control aimed at reducing switch costs may change the conditions for giving responses. That is, task-set reconfiguration may not involve (only) the route from stimulus to response, but the feedback involved in controlled responding: is the response achieving the correct goal? Such a change, since task sets have stability [3], requires energy to break through the old attractor. Mu- and beta-band ERS appear to be worth studying as hypothetical sources of this energy. The imagery results already show that motor-related ERS is under intentional control. So, if the brain cancels response-related states by modulating motor-related ERS, this should be observable during task switching, especially during intentional switches (i.e. response remapping) [200].

Second, the reverse pattern could occur: preparation for a new task could involve motor-related ERD. If this is the case, it would suggest that the control involved in task switching is more interested in setting up the new task than tearing down the previous one. These first two processes could also take place in sequence, ERD following ERS as the path is cleared for the new task set.

Third, if tasks differ on response effector, switching tasks becomes equal to changing the bias between the effectors. If either the right or the left hand is used, a switch to the right-hand task could be achieved by putting the left hand into a hold state, which would be visible in beta-band EMG-EEG coherence.

Finally, the beta ERS following responses may be part of the reason why switch costs are mostly confined to a single trial. At a muscular level, beta band activity is associated with a holding pattern; perhaps something similar is the case cortically, so that once a response is given, the preceding task set is stabilized. If this is the case, faster responses should be seen following higher beta ERS for hold trials, but the reverse should be the case for switch trials.

1.7 Questions and how to ask them

Many questions remain unanswered in the research discussed in the preceding sections. It does not seem to be the case that any field of study has yet provided complete, detailed theories about central questions - e.g. where switch costs come from and how they can be overcome or diminished, how the prefrontal cortex, among many other involved regions, exactly interacts with the rest of the brain so that goal-directed behavior emerges, or why oscillations of different frequencies would or would not be expected to arise in relation to various behavioral outcomes, such as switching the conditions for responses. Further, it is a question in itself what kind of questions should be asked, what kind of answers would be sufficient. Would it be enough to know under what exact circumstances - in terms of stimulation, behavior or experimental manipulation - a specific brain region requires more energy? That its neurons fire at higher frequencies? In a certain spatio-temporal pattern? But the relation between neuronal activity and large-scale events is only an observed correlation - stimuli and responses don't just plug into the firing rate of neuron X. To understand neuronal activity, a step closer to the local, deterministic world of that activity must be taken, but then stimulus and response events must be rewritten in terms of neural communication. Such descriptions and decompositions of those external events are needed so that they can be identified with what the brain does with stimuli, that is, how they cause responses. But how likely is it that such a neurally-linked description would be achieved using only the observation of behavioral data? Even if something like controlled processing or preparing to switch or attention could be defined in detail as a robust constellation of behavior patterns, is this an explanation or only a description of behavior?

It seems that one needs to understand behavior in neural terms to understand the brain, but one needs to understand the brain to understand behavior in neural terms. The resulting catch-22 could be broken because the problem doesn't have to be solved at once. Tentative progress in understanding or even just describing behavior provides hypotheses on the underlying brain function, or maybe just how to study it; and as something more is understood about the brain, inferences on how it produces behavior can be generated. The experiments in the following sections form a microcosm of this interaction. On the one hand, behavioral results on task switching are used to recognize distinct groups of trials, or behavioral conditions. Then the brain activity associated with these conditions is analyzed, and so perhaps something about the function of such brain activity will be suggested. On the other hand, due to the association of brain activity with kinds of information processing, neuroimaging data may constrain behavioral interpretations of distinguished conditions.

The behavioral conditions and types of activity in the experiments concern preparatory states. Preparation is basically defined behaviorally as whatever improves subsequent performance, and so cannot also be used to explain such improvements without some more informative elaboration. The main type of preparation involves that of an upcoming task, especially in the context of task switching, as discussed in section 1.2. If preparing for a switch task involves different processes than preparing for a hold task, such differences should be visible in some measure of brain activity. If preparatory switching is a fallible process, then a difference between fast and slow switch trial should be found, reflecting that process, that is absent for hold trials. Task-set preparation may involve activating (recalling or reducing the noise in) the memory of a task set, which may involve widespread activity involving the prefrontal cortex (section 1.3.2). So, preparation for a visual versus an auditory task may be associated with differences at occipital regions, for example. A now-irrelevant task set or its residual interference may need to be inhibited, which under some circumstances may involve motor inhibition (section 1.6). Other experiments (sections 2.5 and 2.6) involve the preparation of responses, elaborating effects found in the task switching studies, especially on measures of motor-related lateralized activity. One of these experiments involves the preparation of sequences of responses, or motor programs; this kind of preparation will be discussed in that section, 2.5.

To summarize the preceding sections: in a very general sense, subjects performing a task are in some kind of stable state involving how information is processed. The kind of (behaviorally defined) state that task switching research has focussed on is the task set: which stimuli are mapped to which responses. The stability results, almost by definition, in a difficulty in changing switching tasks, but subjects are able to do so. They also appear to be able to do so, at least to some extent, before a task-related stimulus is presented. This appears to involve controlled, goal-directed behavior, as the behavior may even be independent from stimuli. E.g. the stimulus ”prepare task A” may require either switching or maintenance, depending on the context. However, the role of control in task switching is controversial. Perhaps the behavioral patterns found in task switching studies result from automatic processes interacting with different contexts. While subjects do clearly intentionally switch tasks, such behavior does not necessarily imply an underlying switching mechanism or control thereover. Studying brain activity during preparatory periods may help better understand what happens when subjects prepare for switch trials as opposed to hold trials. Such an attempt was made using both time-frequency analyses and consideration of reaction time distributions, as described in the next section.

Chapter 2

Experiments

2.1 Switching between hand - modality combinations

This section is based on an article by Thomas E. Gladwin, Job P. Lindsen and R. de Jong, accepted by Biological Psychology in 2005.

2.1.1 Abstract

The task-switching paradigm provides an opportunity to study whether oscillatory relations in neuronal activity are involved in switching between and maintaining task sets. The EEG of subjects performing an alternating runs [197] task-switching task was analyzed using event related potentials, the lateralized readiness potential, instantaneous amplitude and the phase-locking value [124]. The two tasks differed in the relevant modality (visual versus auditory) and the hand with which responses were to be given. The mixture model [47] was used to assign pre-stimulus switch probabilities to switch trials based on reaction time; these probabilities were used to create a fast - slow distinction between trials on both switch and hold trials. Results showed both time- and time-frequency-domain effects, during the intervals preceding stimuli, of switching versus maintenance, response speed of the upcoming stimulus, and response hand. Of potential importance for task switching theory were interactions between reaction time by switch - hold trial type that were found for a frontal slow negative potential and the lateralized readiness potential during the response - stimulus interval, indicating that effective preparation for switch trials involves different anticipatory activity than for hold trials. Theta-band oscillatory activity during the pre-stimulus period was found to be higher when subsequent reaction times were shorter, but this response speed effect did not interact with trial type. The response hand of the upcoming task was associated with lateralization of pre-stimulus mu- and beta-band amplitude and, specifically for switch trials, beta band phase-locking.

2.1.2 Introduction

Voluntary actions are characterized by a combination of flexibility and persistence [76]: responses to similar stimuli may change, as new intentions are formed, and responses to changing stimuli may remain constant, as goals are maintained over time and situations. The state of the brain that determines its response to different stimuli is described by the task set [157], defined as the mapping of stimuli to responses. Under changing circumstances, either switching between different task sets or holding a task set may be required. Patients with prefrontal damage show a lack of control of flexibility in response to environmental demands [15] [153]. Such patients are able to set up stimulus-response mappings, but may fail to keep the task set active when confronted with distractions, or persevere in a task set when a switch is required, as in the Wisconsin Card Sorting Test [77]. The task-switching paradigm provides an opportunity to study the control of task sets.

The task-switching paradigm involves the presentation of sequences of trials that require either changing or maintaining task sets. The mean reaction time of trials for which subjects have to change task set is higher than that of trials requiring the same task set as the previous trial [3] [197] [149]. These switch costs can be reduced by increasing the length of the preparation interval, but they are still present at long intervals [157]. The persistent switch costs at long preparation intervals are called residual switch costs. Some form of interference due to a previously realized task set, such as task set inertia, a persisting bias of the previous task set [3], or the automatic retrieval of previously used specific stimulus - response associations [247], is one way of explaining switch costs. The decay of the effect of previous task sets over time could explain the reduction of switch costs by increased preparation interval. Even if preparation for switch and hold trials involves the same mechanisms for preparation, the effect of decaying interference on these mechanisms could lead to an interaction of trial type and preparation interval on reaction time [70]. Another hypothesis explaining switch costs is that a time-consuming task set reconfiguration process is necessary to switch task sets, and that this process can be only partially completed prior to stimulus presentation [197]. Decreased switch costs for longer preparation intervals would then reflect the completion of the initial, endogenous part of the reconfiguration process. Arguments for an anticipatory contribution to switch costs were provided by the findings that switch costs could be restricted to the first trial after a switch [197] and that when inter-trial interval (i.e., decay time) and cue - stimulus interval (preparation time) were disentangled, an increase in cue-stimulus interval was still found to reduce switch costs [149]. Even though by definition some kind of change in stimulus - response mapping must be initiated to allow a switch to occur, whether a switch-specific reconfiguration process must be assumed to underlie this switch would be hard to infer from data on switch costs [70]. Further, the retrieval of task-set goals, as opposed to subsequent reconfiguration, may play an important part in anticipatory processing [118] [144].

The distributions of reaction times supply further information on residual switch costs than only the means. In the mixture model of task switching, the distribution of the reaction times of long-interval switch trials is described as a mixture of two other reaction time distributions [47]. One is the short-interval switch distribution, with contains the longest reaction times: the influence of the previous task set is greatest in this condition, whether this is best described by strong inertia or the lack of time to initiate reconfiguration. The other is the long-interval hold condition, which contains generally fast responses. In this condition, the previous task set was already correct. A mixture of these two conditions' distributions can be used to model the condition containing residual switch costs, in the simplest case using a single parameter that specifies the proportion of trials from the fast, "no switch necessary" distribution. The residual switch cost is then due to the subset of trials from the slow distribution in which a switch is necessary but not made pre-stimulus. That is, in the mixture model, a subset of reaction times when subjects have to switch has the same, fast distribution of reaction times when switching is unnecessary.

The mixture model has been shown to provide good fits to data [49] [47] [48] [166]. One explanation of the characteristic pattern of reaction time distributions is the failure to engage hypothesis [47], which states that subjects intend to switch on most trials, but sometimes fail to engage the intention during the pre-stimulus interval, that is, to reconfigure their task set prior to stimulus presentation. In that case, their state at stimulus presentation is no better than when they were given only a short interval between trials. If they do successfully switch, on the other hand, they are as fast as when no switch was necessary at all at stimulus presentation, that is, as fast as hold trials under the same further conditions. Other explanations are of course possible: for instance, some form of proactive interference could be hypothesized to only occur on a certain proportion of trials. The mixture model does, nevertheless, open the possibility that despite persistent switch costs, full task-set reconfiguration may still be possible, pre-stimulus, on a subset of trials. Taking physiological data into account may help clarify the underlying causes of switch costs, and provide starting points to reduce the concepts of switching and holding tasks to specific physical and computational processes.

Psychophysiological studies of task switching have measured various aspects of the brain's behavior during cognitive control and task switching. fMRI studies have found prefrontal and parietal areas with increased activity during preparation for a switch [215] [28] [50]. The event-related potential (ERP) has also been shown to be sensitive to brain activity associated with switching task sets. The ERP components that were of most interest to the present study were the contingent negative variation and lateralized readiness potential.

If preparation for a task switch involves an anticipatory switching process, and if this process can either occur or not as the failure to engage hypothesis suggests, then a reaction time by switch versus hold interaction would be expected to occur on slow negative potentials, as such potentials (i.e. the late contingent negative variation (CNV) [131] [156] [198], readiness potential [42] and the stimulus-preceding negativity (SPN [32]) appear to reflect processes that occur between a cue that indicates some form of cognitive action that must be performed in the future, and the point at which the action is expected to occur. Such future actions may involve either stimulus processing or motor responses [32], and may be complex, e.g. the selection and maintenance of a cued part of a stimulus to be compared with another stimulus to be presented later [156]. A frontocentral increase in the CNV has also been found to increase with effort [57]. The term CNV will be used in the present paper to refer to such slow, pre-stimulus negative potentials. The lateralized readiness potential (LRP) [37] [131] may also measure preparation of task sets, when the sets differ on which hand must be used to respond with. The LRP is a measure of the lateralization of the slow negative potential preceding a response, the contralateral motor cortex showing increased negativity. A pre-stimulus LRP occurs when specific muscle movements can be prepared [131]. So, if task sets differ on response hand, so that a set of left- or right-hand finger movements could be prepared, the LRP may reflect differences in switching between and holding those task sets. If switching between tasks involves switching between hands, the fast switches may show a greater pre-stimulus shift in LRP than slow switches. That is, the lateralization for the response on the previous trial would have a different sign from that on the next trial, and preparation may involve a shift in lateralization towards the correct sign. If hold trials show a reversed fast - slow LRP pattern, such a preparatory LRP effect on reaction time would seem to be due to post-response variability of left- versus right-hand bias. However, if no such fast - slow differences are found during preparation for hold trials, then the presence of an LRP effect for switch trials would seem to reflect variability due to a switch-specific preparatory process that occurs only, or to a greater extent, preceding stimuli followed by fast responses.

A number of studies have used the ERP to study brain activity related to task switching. Wylie et al. [248] used sequences of three trials with the same task set, providing switch, nested and pre-switch trials for the first, second and third trial in each sequence. Tasks were cued by the stimulus color, as well as by the AAABBB sequence. The data showed effects on sustained positivities occurring late in the trials, that is, preceding the upcoming stimulus. It was found that the ERP level preceding switch, nested and pre-switch trials was, at parietal sites, most positive for pre-switch trials, while at frontal sites nested trials showed the greatest positivity. These sustained positivities were interpreted to reflect sustained activity. Based on this interpretation, it was argued that it would be unexpected, from an assumption of frontal areas playing a controlling role in preparing for switch trials, that frontal sites did not show the greatest sustained positivity on pre-switch trials. However, as described above, negative shifts such as the CNV may reflect anticipatory processing, so that the interpretation of a relatively positive ERP level as more sustained activity may not be valid. Other studies have reported frontal effects related to changing task set. Lorist et al. [137] found frontal and parietal negative shifts prior to switch and hold trials, respectively, also using an alternating runs paradigm, and Barcelo [14] found an anticipatory frontal effect, on the P3a, related to shifting task, following a shift cue in the Madrid card sorting test. In a task switching experiment using either informative or non-informative cues, Hsieh and Liu [92] measured the stimulus- and response-locked LRP and the P300. Switch - hold differences were found on reaction time and stimulus-locked LRP onset, but not P300 latency. This suggested that task switching affects processes occurring between stimulus identification (of which the timing was indicated by P300 latency) and the completion of response selection (as indicated by the onset of the stimulus-locked LRP). Cueing the task decreased the reaction time, the time to stimulus-locked LRP onset and also P300 latency, suggesting that task cueing influenced the speed of stimulus identification. In support of the apparently different cognitive stages on which task switching and task cueing have effects, there was no switching by cueing interaction on P300 latency or stimulus-locked LRP onset. It was suggested that these additive effects support the idea that switch costs are due to automatic carry-over effects that are not affected by advance reconfiguration. If advance knowledge of the upcoming task would provide an opportunity to intentionally overcome carry-over effects, switch - hold effects should interact with task-cueing effects. While this did not hold for P300 latency and stimulus-locked LRP onset, it was the case for reaction time and the response-locked LRP interval. Thus, both additive and interacting effects were found of advance preparation and task switching so that, following the additive factors reasoning, a process involved in task switching may be influenced by advance preparation. These data would place the locus of this process quite close to response execution. The data could be interpreted as suggesting that the way preparation interacts with previous task interference involves overcoming a difficulty in giving a response that has become associated with a different stimulus. This may be related to the finding of Rogers and Monsell [197] that the response repetition benefit was lost on switch trials. Karayanidis et al. [108] found switch-related effects in an alternating runs paradigm [197]: a response-locked parietal positivity and a stimulus-locked midline negativity for switch relative to hold trials. The positivity and negativity were attributed to endogenous (anticipatory) and exogenous (stimulus-triggered) reconfiguration processes, respectively. The point was made that these pre- and post-stimulus switch - hold differences were dissimilar, while in the failure to engage framework, reconfiguration occurs either pre- or post-stimulus, as opposed to one part of preparation occurring pre- and another post-stimulus as suggested by Rogers and Monsell. While different pre- and post-stimulus ERP components are not predicted by a hypothesis based on intention activation failures, they do not seem to be necessarily incompatible. As an example, let anticipatory switching be triggered from memory, e.g. by visualization of the upcoming stimulus, which is then followed by an effective (for reaction time and accuracy) change in the communication pathways between stimuli and responses via the nervous system (i.e., task set). The same change in pathways might be triggered by stimulus onset, if not already achieved pre-stimulus. What differences are subsequently found would depend on the measurability of the various events - the endogenous triggering, e.g. visualization, the perhaps different triggering effect of stimulus-onset, and the eventual state of the (perhaps complex and recurrent) chains of communication implementing the task set. If for instance only the endogenous triggering event were measurable in a given study, switch - hold effects would be found only pre-stimulus, while, if, in contrast, only the encoding of the final stimulus - response relations affected the dependent variables used, pre- and post-stimulus switch - hold effects would be identical. The method to test the hypothesis of occasional occurrences of (failures of) anticipatory switching used in this study is the comparison of a variety of measures of activity during putatively switched and not switched subsets of trials. In comparison with the non-switched switch trials as well as with hold trials, switched (i.e., having established the correct task set prior to stimulus presentation) switch trials should contain some kind of unique preparatory activity, reflecting anticipatory switching that only occurs preceding switched switch trials.

These switched and not switched subsets were determined using reaction times. Fast and slow groups of trials were created based on the mixture model so that the pre-stimulus periods of these groups, created for both switch and hold trials, could be compared on ERP and other, oscillatory EEG measures, as has been done for fMRI by Braver et al. [28]. Preparatory task-switching was expected to occur preceding fast switch trials but not slow switch trials or either fast or slow hold trials. The fast and slow groups were defined in terms of the mixture model and failure to engage hypothesis, as described in detail in the methods section. The basic idea of this approach is that each switch trial belongs to either the (endogenously) switched or the not switched subset. While it is in principle unknown to which subset a specific trial belongs, it can be reasoned that the faster the reaction time on a trial, the more likely it is to belong to the switched subset, as opposed to being an outlier of the unprepared subset. Using the mixture model, Bayes' theorem and estimations for the switched and non-switched reaction time distributions, the odds that a specific switch trial belongs to the switched and non-switched can be calculated based on that trials reaction time. These odds could then be used to define groups of fast and slow trials which could be interpreted as having high probabilities of belonging to the switched versus the not switched group. Differences in physiological measures could then be determined between these groups. If effective preparation for switch trials involves different anticipatory processes than for hold trials, a fast - slow by switch - hold interaction should be found during the response - stimulus interval on one or more psychophysiological measures.

Note that within each subset of fast and slow trials, there is still variance and this may be due to other forms of preparation than a specifically switching-related process such as endogenous task-set reconfiguration or some form of goal replacement. These other forms of preparation, in the general sense of any pre-stimulus changes in the state of the brain that bias it to perform a certain task with heightened efficiency, were also of interest.

Oscillatory EEG characteristics [228] were also measured in the present study. Rhythmic behavior can easily arise in neuronal systems: for example, populations of coupled excitatory and inhibitory neurons can respond to afferent activation with synchronized oscillations [237] [10] [226], and oscillations can also be caused by intracellular dynamics (e.g. chattering cells [79] or wave propagation [169]. Rhythmic behavior may play a role in assembly coding [196]. Assembly coding, the distribution of information over specialized neuronal populations, has been argued to be an important coding strategy for the brain [212] [196]. The phase of oscillations of neuronal activity can be seen as a way to create space for spatially and temporally overlapping patterns of activity. Letting the activity of members of assemblies oscillate in phase with each other and out of phase with members of other assemblies provides a mechanism to achieve this. Experimental evidence for such a role for phase locking has been found by Engel et al. [56]. The relevance of assembly coding for task switching is that a task set can be seen as a set of assemblies of stimulus and response representations which must be simultaneously active and yet separated into the correct pairs. A number of frequency bands are of potential interest in studying preparation in a task switching context: the theta, alpha and beta frequency bands. Each band may reveal part of the neuronal changes that occur during preparation for different tasks.

The 5 - 7 Hz, or theta frequency band, has been associated with working memory [192], memory encoding [115] and retrieval [116] and sensorimotor integration [25]. Areas related to functions that are involved in distributed processing have been shown to have increased theta-band activity, e.g.

for language areas following syntactic violations citebastiaansen2002. In a recent study using an alternating runs task, it was found that switching to a visual task was associated with a transient increase in occipital theta-band amplitude during the response - stimulus interval [72]. The present study involved task sets which mapped right and left hand responses to visual and auditory stimuli respectively. These task sets involve separable neuronal areas (the left and right motor, the visual and the auditory cortices), so that switching between tasks might show shifts in patterns of theta amplitude depending on which task is relevant.

The alpha (8 - 12 Hz) frequency band (called mu when related to motor-cortex activity) has been considered to be an idling rhythm [187], because it is reduced occipitally during visual stimulation [23] and at motor regions during movements [184]. Alpha-band oscillations have been proposed to play a more specific role within the coordination of neuronal activity as a localized inhibitory mechanism [40]. Cooper et al. suggest the interpretation that "increased alpha power may index the active inhibition of non-task relevant cortical areas." The anticipatory suppression of distractors in the visual modality has been shown to be associated with increases in parietal and occipital alpha-band oscillations [61] [245] [58]. Such a mechanism may then play a role in the control of irrelevant task sets during task switching. Evidence for the existence of inhibition at the level of task sets has been found in behavioral studies by Mayr and Keele [142]. For the task used in the present study, task sets differed on modality, so that the irrelevant sensory cortex could be repressed to choose, by elimination, the correct task set. Similarly, the hand to be used for responses had to be switched, so that alpha-band waves might influence competition between hands and in that way specify the relevant task set. Such an effect could be studied in the present task, when preparing for left and right hand responses in the context of switching and holding task sets.

Each task set in the present experiment contained two responses that were restricted to one hand. So, the response on switch trials was always made with the other hand than that used for the previous trial, while hold trials required a response with the same hand. This allowed the LRP formula to be applied to amplitude time courses, to provide a measure of motor-related amplitude asymmetry (MRAA) defined as L-R(prepare for left-hand task) - L-R(prepare for right-hand task). Here L-R(condition) refers to the difference in amplitude between the left and right motor regions for the specified condition. A positive MRAA during the pre-stimulus period, calculated for a given frequency band, would for instance occur if the amplitude over the motor region to be used for the upcoming response showed a decrease relative to the opposite motor region.

Beta band (14 - 30 Hz) oscillations decrease over the contralateral motor cortex when a movement is made [189]. This effect was interpreted similarly to the idling of alpha waves described above. Recently, beta waves have been argued to be related, not to idling, but to an active maintenance of stable positions [30]. If foreknowledge is available about the hand to be responded with, these ideas lead to the same prediction. If preparatory processes are allowed to determine that hand's motor cortex's activity, its beta amplitude, as well as mu amplitude, is expected to decrease relative to the irrelevant motor cortex. Alternatively, holding the irrelevant hand in check, and so leaving only the unrestrained hand able to respond, would increase the beta power over the irrelevant cortex relative to the relevant cortex. In both cases, lateralization of beta amplitude would be expected to measure motor preparation, similarly to the MRAA described above.

A further frequency band that has been related to psychological states and processes [228] is the gamma band (30 - 70 Hz). This band will not be discussed here because frequencies above the beta band were not analyzed in this study, due to the possible artefactual influence of muscular activity.

In summary, a number of questions concerning ERP's and oscillatory EEG activity were of interest in this explorative study. Perhaps most importantly for hypotheses concerning task switching, it was studied whether effective preparation, as determined by subsequent reaction time, was different for switch and hold trials. Trial type by reaction time interactions were looked for on various measures. A fast - slow difference in the CNV or LRP occurring only or more strongly for switch trials would suggest anticipatory behavior related specifically to switching between task sets. Theta-band activity might show differences in memory retrieval, for instance if switching to a new task requires the re-triggering the task memory to a greater extent than when preparing for a hold trial. Inhibitory processes involved in successful anticipatory switching would be expected to be related to alpha-band activity. An effective anticipatory switch might involve stronger pre-stimulus inhibition of previous-task areas than that occurs preceding slow switch trials. If pre-stimulus switching involves motor processes, lateralization of oscillatory beta band activity would be expected to occur during response-stimulus intervals (due to the restriction of each task's response set to either the right or the left hand). Some more general questions concerning oscillatory EEG activity were also of interest. First, could increases of theta activity be found that were related to task-relevant cortical areas? Second, could increases of alpha activity be found that were related to task-irrelevant areas? Third, what motor-related asymmetries could be found over motor cortices in the mu and beta frequency bands? Fourth, were there task-related changes in phase-locking between stimulus- and response-related areas?

2.1.3 Methods

Subjects

17 right-handed, young (age 18-25) females with normal or corrected to normal eyesight were tested. Subjects were paid for participation and were informed of the experimental goals and procedures.

Task

The task was a variation of Rogers and Monsell's [197] alternating runs paradigm. In this paradigm two tasks A and B are performed in an AABBAABB... sequence. On each trial a letter (an X or an O) and a 1200 or 400 Hz tone were presented simultaneously. Subjects responded to the letters with the index and middle finger of one hand, and to the tones with the fingers of the other hand. Which hand was initially assigned to which task was counterbalanced over subjects. All subjects switched task - hand assignments twice during the experiment, after the first and third set of blocks (see below). A 2 by 2 matrix was continuously present on the screen and the letters were presented in a clock-wise sequence in the four cells of the matrix. Each cell of the matrix was associated with one of the two tasks. The assignment was randomized, but consistent per subject and was always such that the AABB... sequence was followed during the clockwise rotation of the relevant cell. Subjects were trained on the day prior to the experiment, and performed a short refresher session prior to the EEG measurements.

Besides the mixed-task blocks in which the sequence is AABBAABB ('switch-blocks') subjects also performed 'pure-task' blocks. The pure-task blocks resemble the mixed-tasks blocks in terms of presentation of the stimuli, but in these blocks the subject only has to perform one of the tasks. These blocks were not of interest in the EEG analysis presented here.

The experiment consisted of 4 sets of 6 blocks, each block consisting of 100 trials. Each set contained 4 mixed-task blocks and one pure block for each task. The assignment of the hands to the tasks was switched twice during the experiment: after the first and the third group of six blocks. This was done to be able to calculate the LRP and MRAA per subject, per task, without each subject having hand confounded with modality. Three response-stimulus intervals (RSI's) were used in this experiment: 150, 750 and 1500 milliseconds. These RSI's were randomly distributed over the trials, but because only the long intervals would be analyzed in the EEG trials preceded by long intervals were presented more often. Because only the shortest and longest intervals were relevant for the distributional reaction time analysis described below, the middle RSI was set to the lowest probability. The odds of occurrence of the short, medium and long RSI's were 2:1:3.

Procedure

Subjects were seated in a comfortable chair in front of a table on which their forearms could rest. The distance between the subject and the computer screen was approximately 60 cm. Subjects were instructed to keep as still as possible during the execution of the task.

The day before the actual experiment a practice session was held to reduce learning effects during the experiment. During this practice session subjects performed sets of blocks as described above until they reached an accuracy of at least 90 % and reported that they were familiar with the task. A short warm-up session was held before the actual experiment. Halfway through the experiment subjects were allowed to take a break to reduce the effects of fatigue.

Measurements

The EEG was recorded using a 125-electrode cap (Electro-cap International Inc., Eaton, Ohio, USA). REFA-128 amplifiers (TMS International) were used. Two earlobe electrodes were used as reference electrodes and a chest electrode was used for the common signal. EOG was measured using four electrodes (HEOGL+, HEOGR+, VEOGL+ and VEOGL-). The data were sampled at 500 Hz using the data acquisition program Onyx (version 1.02, Silicon Biomedical Instruments BV, The Netherlands). The data were filtered online, with a time constant of 10 s and a low-pass stop frequency of 250 Hz. Impedance was kept below 5 kOhm for all electrodes during the experiment. A five-button response box was used for response collection.

Reaction time analysis

The mixture model model describes the cumulative distribution function (CDF) of the reaction time of long-RSI switch trials (F[switch, long RSI]) as a weighted sum of the CDF's of "switched" and "not switched" switch trials (initially termed "prepared" and "unprepared" [47]); that is, the population of response times in this category is modeled as a mixture of two other populations:

$F[mixed](t) = \alpha * F[switched](t) + (1 - \alpha) * F[notswitched](t)$

The CDF maps reaction time to cumulative distribution, given two basis distributions F[switched] and F[not switched]. "Switched" refers here to having the correct stimulus-response mappings prior to stimulus presentation, that is, full pre-stimulus task-set reconfiguration. Note that the switched and not-switched conditions still contain any other preparatory source of reaction time variance apart from the switch of task sets. The model formalizes the statement that the condition in which residual switch costs are found contains two subpopulations of trials: those when the subject has already switched task sets at stimulus presentation and those when he or she has not. This condition is therefore termed the mixture distribution. The α parameter stands for the proportion of switched trials. The switched and not-switched CDF's are estimated from long-RSI hold trials and short-RSI switch trials, respectively. It is possible, as suggested by the hypothesis of an endogenous and an exogenous reconfiguration, that even switch trials which were preceded by a switch are not just as fast as the fastest subset of hold trials. An extension of the model including this possibility shifts the estimated switched distribution by δ ms:

$F[switched](t) = F[long - RSI, hold](t - \delta)$

The α and δ parameters can be estimated from reaction time data using the multinomial maximum likelihood method [249] [47].

Once the α and δ parameters are known, and if the model fit is satisfactory, Bayes' theorem can be used to assign odds to trials on the basis of their reaction times. Bayes' theorem provides the following equation:

$P(switched|t) = P(t|switched) * P(switched)/[P(t|switched) * P(switched) + P(t|notswitched) * P(notswitched)]$

where P(switched — t) stands for the chance that the subject was prepared given a reaction time of t and P(t — switched) for the chance of the reaction time given the switched state. The a priori chances P(switched) and P(not switched) are α and $(1 - \alpha)$ and P(t — switched) and P(t — not switched) can be estimated using the long-RSI hold and short-RSI switch cumulative density functions.

Ideally, this procedure would provide two extreme subsets of long-RSI switch trials, with the probability of successful preparation of the switch being either very high or very low. In practice, given the limited total number of trials and the need to retain a sufficient number of trials in each category for psychophysiological analyses, a compromise had to be made. The decision to assign trials to prepared and unprepared groups was therefore taken in two steps. First, the fastest third of the trials were assigned to the switch-prepared group and the slowest third of the trials were assigned to the switch-unprepared group, regardless of probabilities. Second, if the preparation probability of any remaining trials was above 0.9 or below 0.1, those trials were assigned to the prepared or the unprepared group, respectively.

To study switch- or hold-specific parts of preparatory activity, a similar fast-slow split was made for the hold trials. Since the mixture model does not specify subsets of hold trials, the same proportion of trials were assigned to fast and slow hold categories. That is, for each subject, if the fastest x % of the switch trials were assigned to the fast switch category, then the fastest x % of the hold trials were also assigned to the fast hold category. This leads to fast and slow categories that are similar in a relative sense: e.g., fast switch trials may be slower than fast hold trials, but both categories contain trials from the same part of the reaction time distributions they are drawn from.

Preprocessing of the EEG-data

Only the trials with a RSI of 1500 ms were analyzed. EEG-data were low-pass filtered (cut-off 124.5 Hz, pass 93.375 Hz) and downsampled to 250 Hz (in the interests of disk space and the time required to run programs). Brain Vision Analyzer (version 1.03, Brain Products GMBH, München, Germany) was used for preprocessing. The average of the two ear electrodes was used as the new reference for the data. Segments containing artifacts were removed based on visual inspection. Blinks were removed using the ocular correction algorithm of Gratton, Coles and Donchin (1983).

Cluster analysis

A simple semi-data-driven cluster analysis was used to define the regions for the frequency domain analysis. Correlations were calculated between all combinations of electrodes. This was done per condition per subject. A number of anchor electrodes were selected around which a cluster was to be formed. For each anchor the optimal cluster of electrodes was calculated by seeking the correlation cut-off for cluster membership that maximized the mean ratio of the correlation between EEG signals with the anchor within the group and to the mean ratio outside the group. The segments of EEG signals that were to be analyzed (the response-stimulus period, with one second before response and 2.5 seconds afterward stimulus) were used to calculate correlations. Consistency of ROI membership was calculated as a value between 0 and 1, indicating the fraction of cases an electrode was appointed to a certain cluster (0 = never, 1 = for all subjects for every condition). Electrodes were assigned to the cluster with which they were the most consistent, provided that their consistency was above 0.5; that is, that they were at least more likely to be included than they were not to be included in the cluster. The cluster analysis was performed with the following 11 anchor electrodes: Fz, F3, F4, C3, C4, Pz, P3, P4, Oz, T3 and T4. Anchors were chosen to provide a reasonable coverage of the scalp and to roughly correspond with underlying brain regions - frontal, parietal and occipital cortex, and left and right motor cortex. The spatial resolution seemed to be sufficient to capture the topography of the expected effects (i.e. occipital and parietal regions for effects of modality, or left and right motor regions for effects of hand preparation), and greatly reduced the number of statistical tests to be performed relative to using individual electrodes. The use of the data-driven component in determining clusters was hoped to reduce the pooling of dissimilar signals. The amplitude signals were averaged over the electrodes in the region. In the case of phase-locking between regions, the average was taken over all the inter-region electrode pairs.

Transformation to the frequency domain

Considering a signal as a sum of oscillating component signals with varying phase and amplitude, wavelet analysis can be used to determine the time course of amplitude and phase of the component signals. Wavelet analysis is based on the convolution of signals with wavelets: oscillatory functions which have finite energy and are therefore localized in time. Wavelets have a mean and standard deviation in time and frequency, specifying their location and the uncertainty of their localization. In this study, the complex Morlet wavelet was used, which is based on the product of Gaussian curve with a real cosine and an imaginary sine. The Morley wavelet has a Gaussian distribution both in the time domain (standard deviation σ_t) and in the frequency domain (standard deviation $\sigma_f = 1/(2pi\sigma_t)$, around the center time and frequency of the wavelet. By convolving a signal with the wavelet, the time course of the amplitude of the signal around the frequency mean of the wavelet (the instantaneous amplitude IA) can be found. Formally:

$IA(t, f) = |w(t, f) * s(t)|$

where w(t, f) is a normalized, complex form of the Morlet wavelet:

$w(t, f) = (1/sqrt(\sigma_f * sqrt(pi))) * exp(-0.5 * (t/\sigma_t)^2 * exp(i * 2\pi * f * t),$

where f is the frequency around which the signal is to be analyzed. The complex form can be interpreted as a mathematical way to separate the cosine- and sine-based wavelets, as $exp(2i\pi ft) = cos(2\pi ft) + isin(2\pi ft)$. The respective convolutions measure the similarity of the signal to a cosine and a sine; using these measures as Cartesian coordinates defines a vector of which the length abstracts amplitude from phase. The convolutions are performed for each frequency around which the signal is to be analyzed. The vectors over time of amplitude for each trial were averaged per time point relative to the time of the response of the previous trial. This provided the typical amplitude time courses during the response - stimulus interval. Note that amplitude and power are directly related, power being 0.5 times the square of the amplitude.

The angle of the cosine and sine similarity vectors provides the phase of the signal, with 0 rad being the phase of the cosine component of the wavelet. Phases can be used to calculate phase locking between two signals, that is, the consistency of their phase difference. Synchrony is a special case, with a phase difference of zero, but a finding of any consistent phase difference suggests a non-random relationship between the involved signals at the analyzed frequency band. The phase-locking value (PLV [124]) is a measure for phase locking between two signals that will be used in this study. It is calculated as the length of the mean phase-difference vector over N trials as follows:

$PLV(t) = (1/N) * |SUM(n = 1..N) exp(i * (\phi 1(t, n) - \phi 2(t, n))|$

The phase-difference vector, $exp(i * (\phi 1(t, n) - \phi 2(t, n))$, is a complex number with length 1 and an angle equal to the phase difference between two signals, at a given time - frequency point. The more this phase difference remains constant over trials, the longer the sum of the vectors over trials will be as they will extend the summed vector in one direction, maximally away from zero, instead of making it crooked. If the phase-difference is random over trials, the vectors to be summed will cancel each other's directions and the length will tend to zero. The PLV is calculated for all time - frequency points of interest, for all combinations of signals.

In the present study, a wavelet-based analysis approach (as described in section 2.1.3) was used in which a set of wavelets were chosen, together with an associated set of uncertainties. The wavelets were chosen so that the frequency range of interest (theta to beta frequency bands) was sampled with a 1 to 2 Hz resolution, and with temporal variance small enough to detect changes in oscillatory characteristics that arise over a period of at least 100 - 200 ms. The chosen frequencies were 5 to 25 Hz, in steps of 1 Hz from 5 to 15 Hz and of 2 Hz from 15 to 25 Hz. The σ_f's were equal to the step size. The frequencies 30, 40 and 70 Hz were also analyzed, with σ_f's of 4, 5 and 5 Hz. These frequencies were analyzed to determine the possible influence of EMG artefacts.

Statistical procedures

The false discovery rate procedure (FDR) [22] [68] was used to correct for the chance capitalization involved in multiple tests. The false-discovery rate (FDR) procedure controls the proportion of false positives among the tests for which the null hypotheses is rejected, in contrast to Bonferroni correction, which controls the chance of any false positive among all tests. The procedure works for any statistical test that generates a p-value and consists of the following steps:

1. Let q be the desired FDR between 0 and 1. This is the expected proportion of false discoveries.

2. Order the P values form smallest to largest: $P(1) <= P(2) <= ... <= P(V)$, where V is the total of simultaneous performed tests.

3. Compare each P(i) sequentially with $(q * i)/V$, starting with the largest P value. Let k be the largest i for which $P(i) <= (q * i)/V$.

4. The threshold for all test statistics is P(k). Reject all null-hypotheses H(i), i = 1,2,..,k.

The value of the q-parameter was set to 0.05 in this study. This means that of all the rejected null hypotheses, no more than 5 percent is expected to be a false positive. The FDR procedure is far less conservative than Bonferroni correction, which controls the chance of any false positives at all.

The logarithm of instantaneous amplitudes was taken to normalize their distribution and so that differences between conditions reflected relative changes in amplitude. The PLV was normalized by taking the artanh transform of the square root of the PLV values.

For the time-frequency domain measures, a number of contrasts were tested, using the FDR procedure separately per contrast. Conditions belonging to a category to be compared were pooled. For instance, in the comparison "visual versus auditory, given switch and prepared", the left- and right-hand response trials were pooled, and unprepared and hold trials were excluded. This example compares the data found when successfully switching to a visual, versus an auditory task set.

Lateralization

The LRP is derived from EEG (usually measured at C3 and C4) by means of the double subtraction described in the introduction. For the LRP, the double subtraction is subsequently multiplied by 0.5. This allows the LRP to be interpreted as the mean effect on the contralateral, relative to the ipsilateral, motor area, averaged over the left and right hand. Having instantaneous amplitudes for several frequency bands available for the C3- and C4-regions, analogous LRP-type measures can be derived using IA instead of raw EEG [107]. These motor-related amplitude asymmetries (MRAA) were calculated using the log-normalized IA, as the double difference (IA, C3 - IA, C4, left-hand) - (IA, C3 - IA, C4, right-hand). The hand used for determining conditions was considered to be the hand to be used for the upcoming task.

2.1.4 Results

The data of six subjects were lost: five to technical problems and one due to the use of medication. This left 14 subjects for behavioral analysis and 11 subjects for EEG analyses.

Behavioral data

Mean reaction time and accuracy results are shown in figure 2.1 (data for the pure-task conditions are shown for sake of completeness and will not be analyzed). Switch costs decreased as the RSI increased, suggesting that subjects were on average benefiting from opportunities for advance preparation. The accuracy and reaction times were analyzed using repeated measures MANOVA with factors task (visual vs. auditory), trial type (switch vs. hold) and RSI. Accuracy showed a significant effect of trial type (F(1, 9) = 12.9, p = .005). For reaction time, the analysis yielded significant main effects of trial type (F(1, 10) = 53.9, p = .000) and RSI (F (2, 9) = 30.8, p = .000), and significant interactions of trial type by RSI (F(2, 9) = 38.1, p = .000) and task by RSI (F(2, 9) = 9.5, p = .006).

Vincentized cumulative density functions of reaction times are shown in figure 2.2, for hold, long-RSI, switch, short-RSI, and switch, long-RSI trials. Note that the switch, long-RSI distributions have a smaller mean but a substantially larger variance than switch, short-RSI distributions. This unusual feature, together with the fact that the fast parts of the switch, long-RSI distributions approach that of the hold, long-RSI distributions whereas their slow parts approach that of the switch, short-RSI distributions, suggests that the condition in which residual switch costs are found may consist of a mixture of two subsets of trials: one with a fast, "no switch necessary at stimulus presentation" distribution, one with a slow, "not switched at stimulus presentation" distribution.

The fit of the switch, long-RSI distribution as produced by the mixture model is also shown in figure 2.2. The overall impression of a reasonable fit was confirmed by goodness-of-fit tests focused

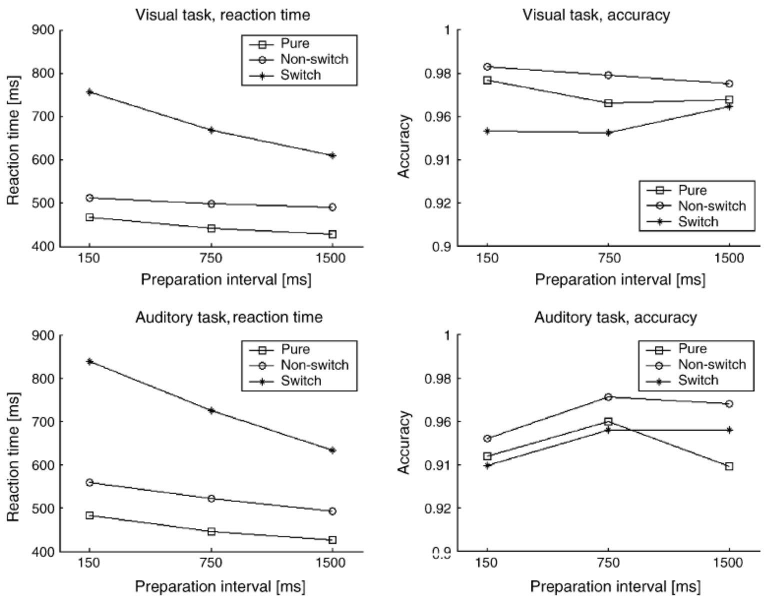


Figure 2.1: Reaction time (left column) and accuracy (right column) data for the visual task (top row) and auditory task (bottom row). The preparation interval refers to the time between the response on the previous trial and onset of the subsequent trial's stimulus. The different lines show the data for pure (single task) blocks and the switch and non-switch trials within mixed blocks.

on the fast part of the distributions as in de Jong [47]. For the visual task, the fit was G2(11) = 12.85, p ¿ .1, with mean estimated $\alpha = 0.61$ (SE= 0.05) and mean estimated δ = -1.6 ms (SE= 6.7). For the auditory task, the fit was G2 (11) = 12.47, p ¿ 0.1, with mean estimated $\alpha = 0.69$ (SE= 0.05) and mean estimated delta = 9 ms (SE= 8.2). Thus, the present results are in accordance with previous suggestions that occasional failures to effectively engage in advance preparation may, at least under some circumstances, be the predominant cause of residual switch costs [47].

As the mixture model produced adequate fits to the data, it was possible to associate individual reaction times on switch, long-RSI trials with estimated probabilities of pre-stimulus switching, using the Bayesian procedure described above. The mean estimated probabilities of successful preparation were 0.92 and 0.97 for the fast subgroups of trials in the visual and auditory tasks, respectively; the associated mean reaction times were 405 ms (SE= 9) and 400 ms (SE= 8). The probabilities for the slow subgroups were 0.21 and 0.24 for the visual and auditory task, respectively, with corresponding mean reaction times of 967 ms (SE= 46) and 1009 ms (SE=54). Though the mean probabilities for the slow subgroups are somewhat higher than we might have wished for, the very substantial difference in mean probability between the fast and slow subgroups should provide a solid basis for subsequent analyses.

As described above, hold, long-RSI trials were also subcategorized into fast and slow groups. The associated mean reaction times were 365 ms (SE = 8 ms) for the fast visual group, 679 ms (SE = 27 ms) for the slow visual group, 353 ms (SE = 9 ms) for the fast auditory group, and 749 ms (SE = 44 ms) for the slow auditory group.

As noted by a reviewer, the reaction time of trials may have been partly caused by the switches in hand mapping that occurred twice during the experiment. This would confound the preparatory

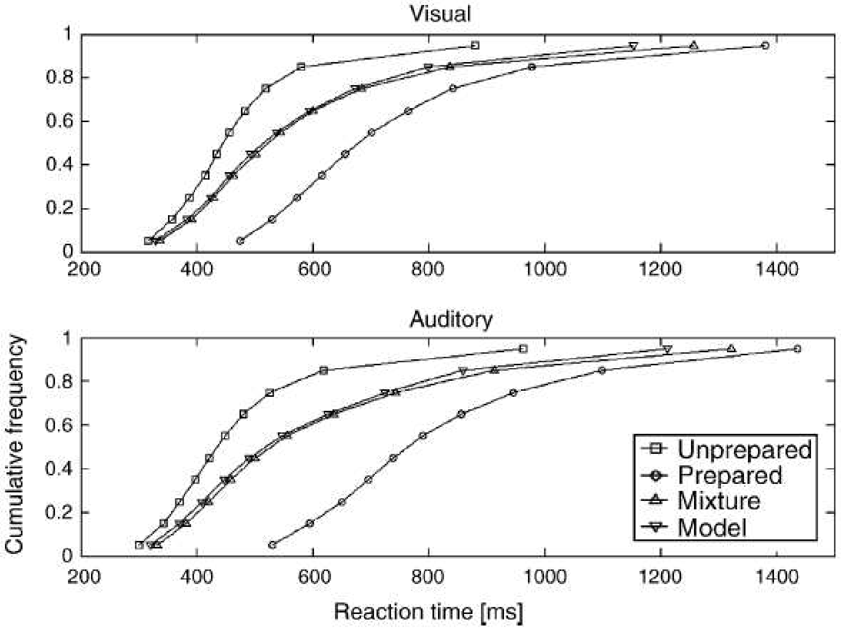


Figure 2.2: Cumulative distribution functions for the reaction times of the visual (top) and auditory (bottom) tasks. The different lines show the data for the conditions used to estimate the prepared and unprepared conditions (long response - stimulus interval, non-switch trials, and short response - stimulus interval, switch trials, respectively), the mixed condition (long response - stimulus interval, switch trials), and the modeled distribution of the mixed condition.

interpretation of the fast and slow subsets. However, reaction times did not show a learning effect following the switches of hand-mapping. This was tested by comparing the average number of trials since a change in mapping for the fastest and slowest thirty trials, separately for switch and hold trials. No significant effect was found, suggesting that it was not the case that the slower trials occurred sooner after a mapping switch.

EEG time-domain measures

Pre-stimulus: CNV and LRP

For the CNV the 100 ms preceding the previous response was used as the baseline. For this and some subsequent analyses, it should be noted that, due to the alternating-runs paradigm used in this study, this baseline is confounded by the previous trial-type (i.e., hold trials are always preceded by switch trials, and vice versa). Therefore, some care must be taken in interpreting the results (see below). Figure 2.3 shows the grand-average CNV's for fast and slow switch and hold trials. The differences between fast and slow trials seem maximal at frontal and central areas, and seem to be generally larger for switch trials. The differences between CNV's were tested, using the mean values over the second half of the RSI, with repeated measures MANOVA. Besides the factors trial type (switch / hold), speed (fast/slow), and modality (visual/auditory), the five midline channels Fpz, Fz, Cz, Pz and Oz were included as a factor in the analysis. The significant main effects at the 0.05 level were channel ($F(4, 7) = 23.6$, $p < .0005$) and speed ($F(1,10) = 10.0$, $p < 0.01$).

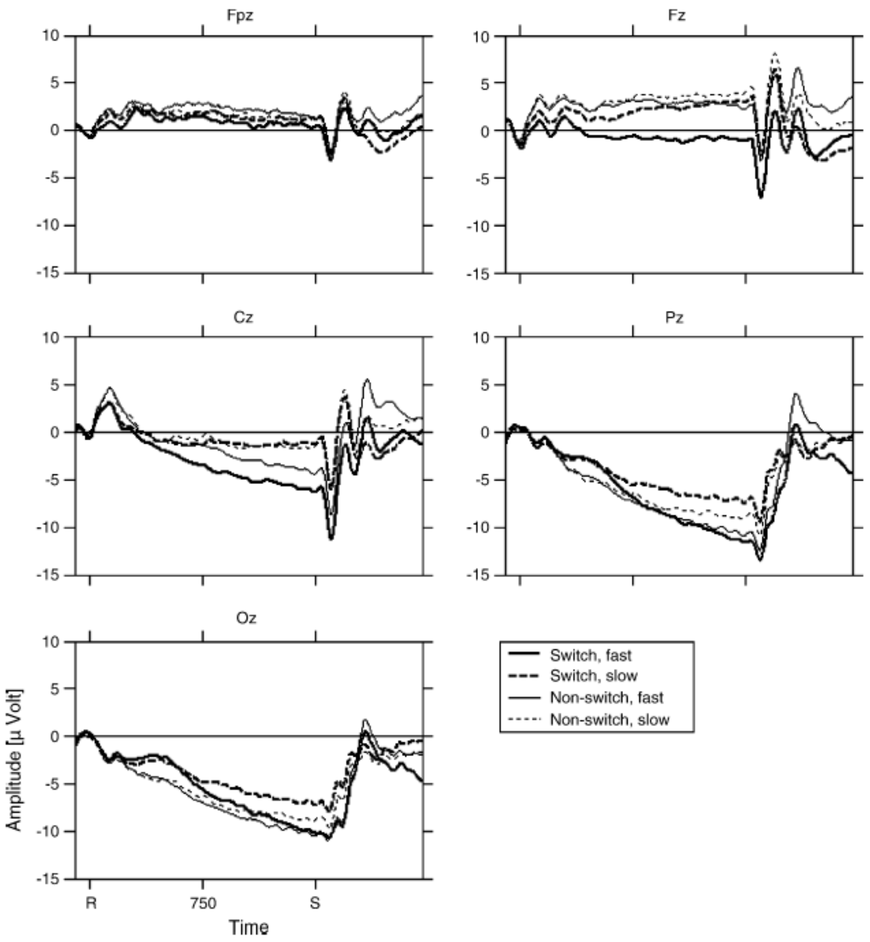


Figure 2.3: The ERP, locked to and baselined (from -100 to 0 ms) at the response of the previous task, for switch and non-switch trials, separated for trials which will have fast and slow responses.

The interaction between trial type and speed was significant (F(1,10) = 8.8, $p < 0.02$), as was the interaction of channel and trial type (F(4, 7) = 5.0, $p < .05$). No effects involving modality approached significance. The trial type by speed interaction was studied further. It was significant only for electrodes Fz (F(1, 10) = 9.0, p = .013), Cz (10.2, .01), Pz (5.2, .046). At Fz and Pz, the fast - slow difference was only significant for the switch condition, while it was significant for both switch and hold at Cz.

Figure 2.4 shows the grand-average lateralized readiness potentials (LRP) of the fast and slow switch and hold trials. The LRPs were computed based on the identity (left hand / right hand) of the previous response, so the LRP associated with the upcoming response changes sign for switch but not for hold trials. Recall the formula LRP = L-R(previous response left-handed) - L-R(previous response right-handed), where L-R(X) refers to the difference between the C3 and C4 electrodes in condition X. The LRP will always be positive for the previous response. For hold trials, the next response, following the response-stimulus interval, will again show a positive LRP, as the same hand is used again. So, at that time, the L-R(left) - L-R(right) form is preserved during the current response, even though the "left" and "right" qualifiers are based on the previous response.

For switch trials, however, the LRP at response becomes negative, as when the previous response was right (or left), the next response must be left (or right). The formula written in terms of the second response thus reads L-R(current response right-handed) - L-R(current response left-handed) for switch trials, and so the LRP is reversed for the switch responses.

The LRP for both fast and slow hold trials can be seen to gradually decay during the RSI towards a relatively low but significant level of lateralization in the direction of the upcoming response hand. The LRP for switch trials exhibits a similar time course during the RSI, with the LRP for slow switch trials remaining lateralized in the direction of the previous instead of the upcoming response hand, and the LRP for fast trials exhibiting a somewhat stronger decay but falling short of reaching a significant level of lateralization in the direction of the upcoming response hand by the end of the RSI. The differences between mean LRP amplitude during the second half of the RSI (750 ms interval before stimulus onset) were tested using repeated measures MANOVA, with trial type, response speed, and task modality as factors. The analysis yielded a significant interaction of trial type and response speed ($F(1,10) = 11.62$, $p < 0.01$). The interaction was due to the effect only occurring prior to switch trials ($t(10) = 2.8$, $p < .05$).

A further aspect of the waveforms in figure 2.4 can be noted. Within 150 ms after stimulus onset, all waveforms exhibit a steep increase of lateralization towards the upcoming response hand. For fast trials, this increase could be thought to be associated with response execution, as such an acceleration of LRP amplitude is commonly observed to precede actual response execution (i.e., reaction time) by 200-300 ms. For slow trials, however, with mean reaction times of 714 ms and 968 ms for hold and switch trials, respectively, the steep increase seems to occur too early to be tied to response execution proper, and therefore suggests that even on slow trials, the upcoming response hand is prepared: not in such a way as to lead to pre-stimulus lateralization, but so that lateralization can occur quickly post-stimulus.

Post-stimulus ERPs

Figure 2.5 shows grand-average post-stimulus ERPs for fast and slow switch and hold trials, with the 100 ms interval before stimulus onset serving as baseline. The P300 is larger for fast than for slow trials; this difference is found both for switch and hold trials and is maximal at central and parietal areas. Also, P300 amplitude for hold trials exceeds that for switch trials, for both fast and slow trials. These differences were tested using repeated-measures MANOVA with the same factors used in the analysis of the pre-stimulus effects. The mean amplitude in the interval from 275 to 375 ms post-stimulus was analyzed. Trial type ($F(1,10) = 50.4$, $p < .001$), speed ($F(1, 10) = 17.3$, $p < .005$), and channel ($F(4, 7) = 10.9$, $p < .005$) showed main effects. Channel interacted with trial type ($F(4, 7) = 15.3$, $p < .001$) and speed ($F(4, 7) = 13.0$, $p < .002$).

It should be noted that post-stimulus effects may be related to the baseline period, at which time sizable CNV effects were found. In these data, fast trials showed a greater pre-stimulus negative deflection relative to slow trials. Their greater post-stimulus P300 may be related to negating this baseline shift. The effect of trial type on P300 amplitude was not accompanied by a differential CNV effect.

We analyzed early post-stimulus ERPs (50-200 ms post-stimulus) for possible effects of modality that might indicate a dependence on relevant modality of perceptual processing of the compound stimulus. No significant effects were found.

Time-frequency analysis

The EEG was recorded using 125 electrodes. Data inspection revealed that some channels picked up an ECG signal. For the frequency-domain analyses (none of the channels used in the ERP analysis were contaminated), a selection of 66 channels was made from the original 128, that contained no evident ECG signal in any subject and gave a complete and evenly distributed representation of the scalp. The selected channels are Fp1, Fp2, F3, Fz, F4, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, Oz, O2, AFz, FC5, FC1, FC2, FC6, CP1, CP2, AF3, AF4, PO3, POz, PO4, F5, F1, F2, F6, P5, P1, P2, P6, FC3, FC4, C5, C1, C2, C6, CP3, CP4, FCz, TP7, CPz, TP8, FT7, FT8, T7, T8, AF1, AF2, T1, T2, CPP7, CPP3, CPP4, CPP8, CPP5, CPP1, CPP2 and CPP6. The cluster analysis on the selection of electrodes resulted in the following clusters (shown in figure 2.6), with the anchor followed by associated electrodes between brackets: F3 (AF3, F5); Fz (AFz, FC1, FC2, F1, F2, FCz, AF1, AF2); F4 (AF4, F6, FC4); T3 (TP7, FT7, T7, T1); T4 (TP8, FT8, T8, T2); C3 (C1, C5; C4 C2, C6); P3 (T5, P3, CP1, P5, CP3, CPP3, CPP5, CPP7); Pz (CP2, CPz, CPP1,CPP2); P4 (T6, PO4, P6, CP4, CPP4, CPP6, CPP8) and Oz (O1, O2, Poz).

The remaining electrodes (Fp2, Fp1, FC6, FC5, FC3, Cz, PO3, P1 and P2) failed to be consistently assigned to a cluster and were discarded.

Instantaneous amplitude

FDR was performed on the instantaneous amplitude (IA) data for a number of contrasts: 1) visual versus auditory, for fast switch trials; 2) visual versus auditory, for fast hold trials; 3) fast switch versus fast hold, for the visual and auditory tasks separately; 4) fast versus slow response; and 5) the interaction of response speed by trial type.

Of these contrasts, only the response speed factor yielded significant differences (figure 2.7). Theta IA (5-7 Hz) during the preparation interval is higher for fast trials, while post-stimulus theta IA is higher for slow trials. This suggests that this frequency band reflects processes that are necessary for task performance, but can be dealt with adequately prior to stimulus presentation, thereby allowing faster reaction times. Pre- and post-stimulus effects are distributed at anterior and posterior regions, respectively. Figure 2.8, top, shows the time course of theta amplitude for fast and slow trials, revealing these effects of response speed superimposed on a background time course of theta amplitude increasing after stimulus presentation and following a response.

The time-course of the beta-band (20-24 Hz) effect is shown in figure 2.8, bottom. Fast trials show lower beta-band amplitude (i.e., more beta-desynchronization) than slow trials in the preparation interval. Given the association of beta-desynchronization with motor preparation, this difference might indicate enhanced advance motor preparation on fast trials. The constant offsets, as found at the temporal and occipital regions that are particularly sensitive to EMG artefacts, seem likely to be due to effects of the lower frequencies of EMG activity.

The high-frequency (¿ 30 Hz) effects of response speed are in the EMG range; when subjects do not prepare, they may be fidgeting in some way.

The FDR-maps for the MRAA for switch and hold trials are given in figure 2.9, showing preparatory activity in the alpha and beta bands. The MRAA shows the lateralization of amplitude according to the relevant hand, changing sign for switch trials but not for hold trials.

The alpha-band (10 - 14 Hz) MRAA time course is shown in figure 2.10, top, for fast and slow switch and hold trials. This MRAA can be seen to behave quite differently from the traditional time-domain LRP (figure 2.4). In particular, for both fast and slow switch trials, it clearly reverses sign during the preparation interval to reach levels similar to those found for fast and slow hold trials. Also, its post-stimulus time course is markedly different from that of the LRP, peaking some 200-300 ms post-stimulus and then rapidly declining. The positive sign of the alpha-band MRAA signifies preparation-related alpha desynchronization in the motor cortex contralateral to the response hand or, equivalently, alpha synchronization in the ipsilateral motor cortex.

Figure 2.10, bottom, shows the beta-band MRAA time-course for fast and slow switch and hold trials. As can be seen in the FDR-maps, only switch trials are preceded by significant beta-band lateralization. This lateralization is achieved following a reversal that starts immediately after the previous response. Similarly to the alpha-band MRAA, the positive sign of the beta-band MRAA signifies preparation-related beta desynchronization in the motor cortex contralateral to the response hand, or beta synchronization in the ipsilateral motor cortex.

Note that the alpha- and beta-band MRAA's are not different for fast and slow trials. Thus, whereas both MRAA's seem to be associated with advance preparation, they do not predict response speed; that is, they do not predict success or failure, or relative effectiveness, of selective task preparation as manifested in reaction time.

Instantaneous phase-locking

Because of the large number of tests inherent in testing time by frequency by electrode combination datasets, testing of instantaneous phase-locking effects was restricted to three frequency bands, with FDR applied to each band separately; the three bands are theta (5 - 7 Hz), alpha (8 - 14 Hz) and beta (20 - 24 Hz). It should be noted that this increased the chances of false-positives above the nominal 5% rate, but, given the explorative nature of the present study, it seemed appropriate to preserve reasonable power to detect potentially important effects.

No FDR-significant differences in phase-locking were found between visual and auditory tasks, or in the interaction between modality and relevant response hand. Thus, no evidence was found for phasic changes in effective connectivity, expressed in phase-locking, of sensory cortices to other areas, e.g. frontal or motor cortices. Also, none of the other contrasts used previously for analysis of instantaneous amplitudes yielded significant results for instantaneous phase-locking.

When the factor response hand was taken into account, significant results for instantaneous phase-locking in the beta band were obtained, but only for switch trials. These results are schematically depicted in figure 2.11. Figure 2.11, top, shows the pattern of electrode-cluster pairs for which beta-band phase-locking was significantly higher during the preparation interval when the upcoming task was associated with the left hand as compared to the right hand. This pattern was centered on the right (i.e., contralateral) centroparietal region and indicates enhanced phase locking of beta-band activity in this region with beta-band activities in bilateral frontal regions. Figure 2.11, bottom, shows a similar pattern of enhanced beta-band phase locking, but now centered on left centroparietal regions, when the upcoming task was associated with the right hand as compared to the left hand. No such effects were found for hold trials. Indeed, an FDR-based interaction analysis showed the lateralized phase-locking patterns to be significantly stronger for switch as compared to hold trials; the results of this analysis are depicted in figure 2.12. This figure shows the (electrode-pair, time) points where the left - right hand difference was significantly greater for switch than for hold trials. That is, as seen in figure 2.11, left-hand preparation results in increased right-hemisphere phase locking. Figure 2.12, top, shows that this right-hemisphere increase is significantly greater when the previous response-set was on the left hand. The same goes for the negative plots in figures 2.11 and 2.12, which show a greater left-hemisphere increase preceding right-hand trials, which is again greater for switch trials. A similar interaction analysis yielded no indication of a possible dependence of these phase-locking results on response speed.

2.1.5 Discussion

This study aimed to explore ERPs, oscillations and phase-locking in the EEG during the preparation interval in a task-switching task, and to determine whether dividing trials into subsets on the basis of reaction time is relevant for psychophysiological studies of task switching. An interaction between reaction time and switch versus hold trials was of interest in testing the idea that anticipatory preparation may be different for switch and hold trials. The lateralization of activity (the LRP, MRAA and lateralized phase locking) was used as an index for motor-related preparation. The theta, alpha and beta frequency bands were studied to find evidence for, respectively, task-related amplitude topography, the inhibition of irrelevant modality and the frequency-domain aspects of lateralization due to hand preparation. Phase-locking was studied to determine whether task-related shifts in coupling could be measured using the PLV. As discussed below, various effects on phase-locking and oscillatory amplitude were found, as well as differences related to response speed and interactions of response speed and switching versus holding a task set.

The speed of the upcoming response was associated with both time- and frequency-domain effects. Both the CNV and pre-stimulus theta amplitude predicted whether a subject's response to a stimulus would be fast or slow. Pre- and post-stimulus theta amplitude was reversed for fast and slow trials. While fast trials showed increased anterior theta activity during the preparation interval, slow trials showed posterior theta activity post-stimulus. However, no fast - slow by switch - hold interaction was found on theta-band amplitude. In contrast, the CNV did show a fast - slow by switch - hold interaction. Fast switch trials showed increased frontal negativity pre-stimulus, relative to all other conditions. More centrally, fast trials were preceded by increased negativity, for both switch and hold trials. A frontal pre-stimulus negativity preceding switch trials was also found by Lorist et al. [137] and also seemed similar to an aspect of Wylie et al.'s [248] data (figure 4), in which the frontal negative slope between responses and stimuli was greatest between pre-switch and switch trials. Taken together with the present results, these effects could be interpreted to have been due to the fast subset of switch trials.

The LRP showed a pre-stimulus fast - slow by switch - hold interaction that seems to be best interpreted as preparation by release. When the same hand was to be used, post-response lateralization did not decay to a neutral baseline; the previous hand would then appear to retain an increased response tendency. The response - stimulus interval LRP was similar for the fast and slow subsets of hold trials. In contrast, when subjects were to switch hand, this pre-stimulus decay predicted response speed: if the level stayed with that for hold trials, subjects were slower than if the lateralization reached baseline. This loss of lateralization may index the release of the tendency to respond with the previously used hand. Motor preparation was also reflected in the time-frequency domain measures, but with qualitatively different time courses. The motor cortex associated with the responses that are part of the upcoming task set showed a decrease in mu and beta amplitude and, specifically preceding switch trials, participation in a pattern of increased beta-band phase-locking also involving frontal areas.

The timing of the frequency-domain effects (MRAA and lateralized phase locking) is notably different from that of the time-domain LRP, which is strongest around response, showing only rather subtle effects, in terms of differences in rate and asymptote of decay, during preparation. In contrast, the frequency-domain measures, especially phase-locking, seem to have a strong preparatory role.

The switch-specificity of preparatory beta-MRAA lateralization may be related to the modulation of an automatic post-response amplitude rebound, which is either reduced when the same hand must be used or enhanced when the other hand must be used. This may be an example of cognitive control working through the modulation of automatic processes. The interaction of lateralized phase locking with the switch - hold factor but not with reaction time suggests that this phase locking reflects an anticipatory switching process, but one that does not seem to fail, under the present experimental conditions.

No EEG effects were found that could be related to activation of task-specific brain areas in the theta-band, or to preparation via the selection of modality involving the alpha band. These null-findings could be due to a problem of measurability: by no means all brain processes were measured in this study. The way subjects performed this specific task may also have played a role. Because each response-hand was uniquely associated with a modality, choosing a hand could remove the need to select modality: incorrect responses could be blocked at response, and correct responses allowed, even if both responses would have been equally evoked by stimulation. A follow-up study [72] has been done to determine if modality-related oscillatory activity could be found when subjects were to perform tasks that differed only on relevant modality. In that study, two effects of modality over occipital regions were found. Switching to a visual task involved increased occipital theta-band amplitude during the preparation interval, while repeating an auditory task was associated with increased occipital alpha-band amplitude. So, the absence of those effects in the present study suggests that subjects did not prepare via biasing the relevant modality.

No evidence was found for a "remapping" type of preparation involving differences in phase locking between sensory and motor cortices relevant to the current task set. Again, various possible factors weaken the significance of this finding. The specific phase-locking measure used here is insensitive to varying phase differences over trials and cannot detect non-linear coupling. Statistical power is also a problem due to the large number of tests and the explorative nature of the study. The generation of more specific hypotheses and associated measures may yet lead to the discovery of EEG effects reflecting changes in the interactions between sensory, motor and controlling cortex in future studies. One characteristic of the design used here may be especially relevant to such studies. Because stimuli were uniquely mapped to responses, the individual stimulus - response mappings did not have to be changed on a trial-to-trial basis. It is conceivable that precisely that kind of switching could be associated with changing phase relations. So, while the task set did change - the response to the same total tone + letter stimulus could be different following a switch - the correct response per object only changed in terms of its being given or not (cf. the distinction between intentional and attentional set switching [200]). The shifting trial-by-trial intention could then simply be an intention to not move one or the other hand, as opposed to an intention of which the activation must result in changes within the communication pathways from stimuli to responses.

The combination of the motor-related effects and the null findings in the present study could be tentatively interpreted as an effect of the task context that led to preparation based on the motor component of the task. Further studies may reveal whether this is due to a conscious, strategic choice of subjects, if for example it is subjectively less effortful to bias response hand than perception, or that this kind of preparation arises more or less automatically in this task context. Similar motor-related effects as in the present study have been found in a follow-up study (in preparation) in which tasks differed only on response hand, without associated modality differences.

In summary, while the brain did show preparatory frequency-domain behavior in this task, fundamental questions remain as to what this behavior is accomplishing. No evidence was found for the idea that phase-locking, as measured by the PLV, binds together stimuli and responses. However, this may be due to the task, which subjects may have performed by concentrating on which hand to use. The potential importance of selecting trials on the basis of subjects' behavior was underscored by strong effects found by comparing fast and slow trials. Fast - slow by switch - hold interactions were found in the preparation interval, suggesting that preparation for switch trials differs from that for hold trials. Such interactions may help understand the mechanisms of voluntary / goal-directed behavior, and may be of interest in complementing post-stimulus results on task switching [92]. It seems that further study using the classification of trials on the basis of reaction time would be useful.

2.1.6 Acknowledgements

The authors would like to thank Prof. Dr. R. Ridderinkhof and two anonymous reviewers for their suggestions for improving this paper.

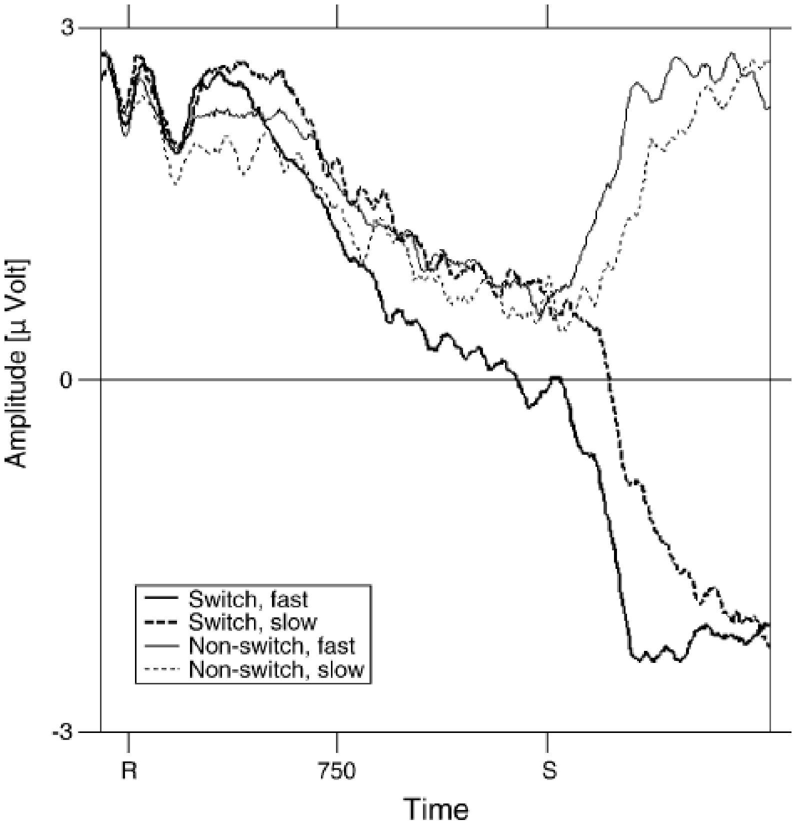


Figure 2.4: The LRP. The "correct" response hand was defined as the hand used on the previous task, so that the LRP becomes negative for switch trials and remains positive for non-switch trials. The conditions were first baselined at the previous response, so that the "positive", response-related value was zero. To acquire more intuitive values, the waveforms were shifted vertically (all by the same amount, + 2.5 micro volt) so that the new zero-value lay halfway between the post-stimulus responses for the switch and non-switch trials. Now, around plus-three is the value for a response with the hand used for the previous trial, and around minus-three is the value for a response with the other hand.

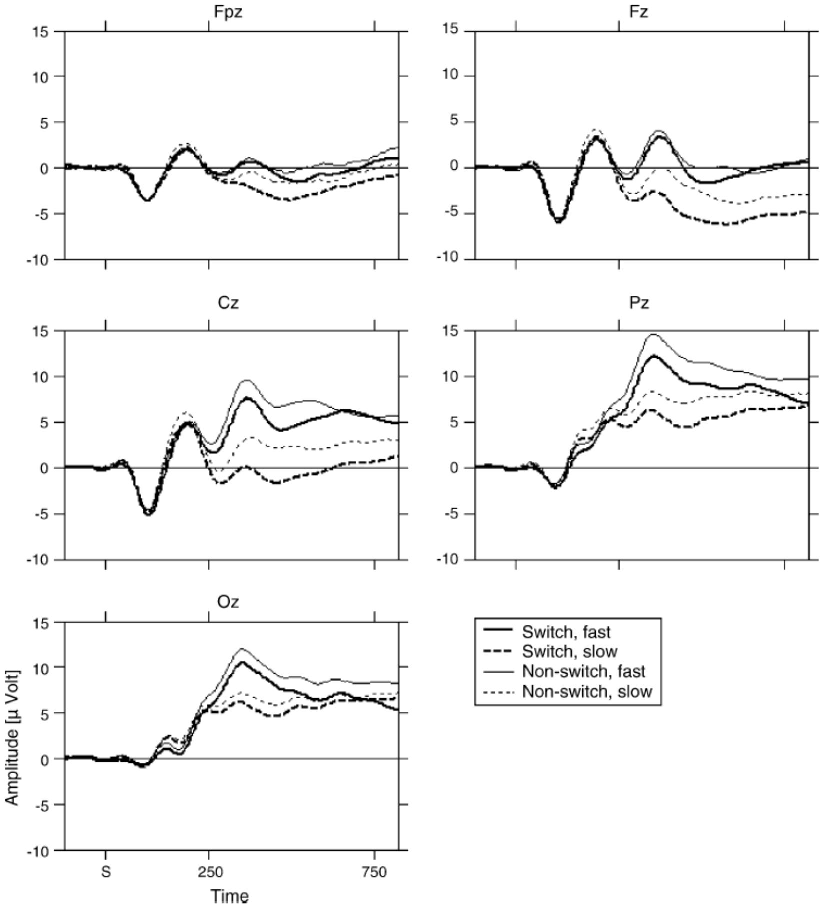


Figure 2.5: The ERP, locked to and baselined (from -100 to 0 ms) at stimulus onset, for switch and non-switch trials, separated for trials which will have fast and slow responses.

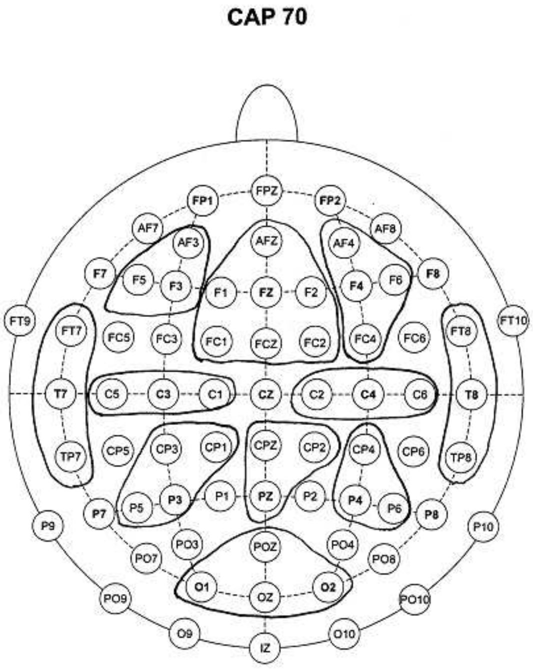


Figure 2.6: The electrode clusters used for time - frequency analyses. Electrode positions around which a line is drawn were averaged to form a cluster.

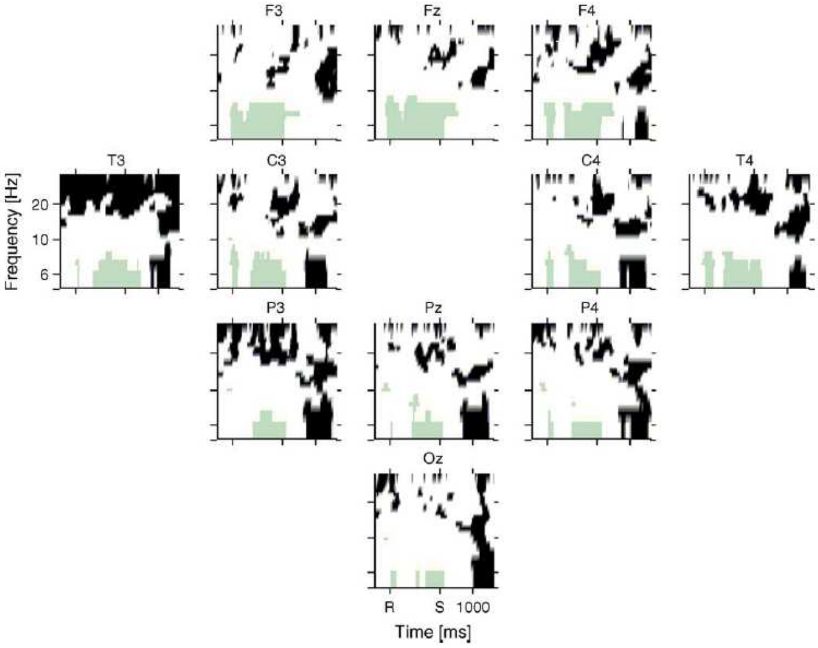


Figure 2.7: Significant amplitude differences between fast and slow trials. Amplitude was measured as described in the method section, using wavelet analysis. Each subplot is a time-frequency plot showing datapoints at which the difference was significant according to the FDR procedure. Time is plotted on the horizontal, frequency on the vertical axis. The gray and black datapoints show positive and negative effects respectively. The electrode names refer to the anchor-electrode of the cluster. The cut-off t-value for these results, given by the FDR procedure for this contrast, was 3.0.

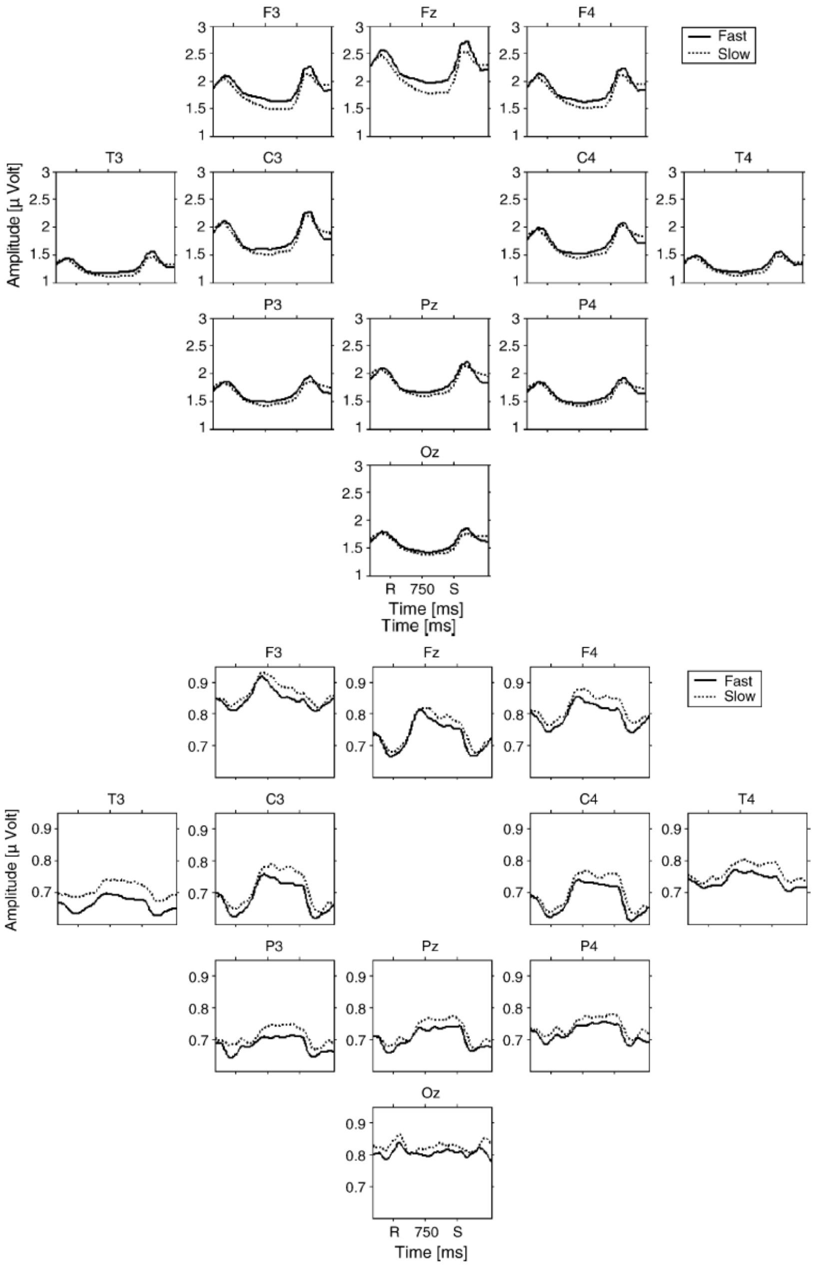


Figure 2.8: The time course of theta- (top) and beta- (bottom) band amplitude for fast and slow trials, from the response of the previous trial past stimulus onset of the upcoming trial.

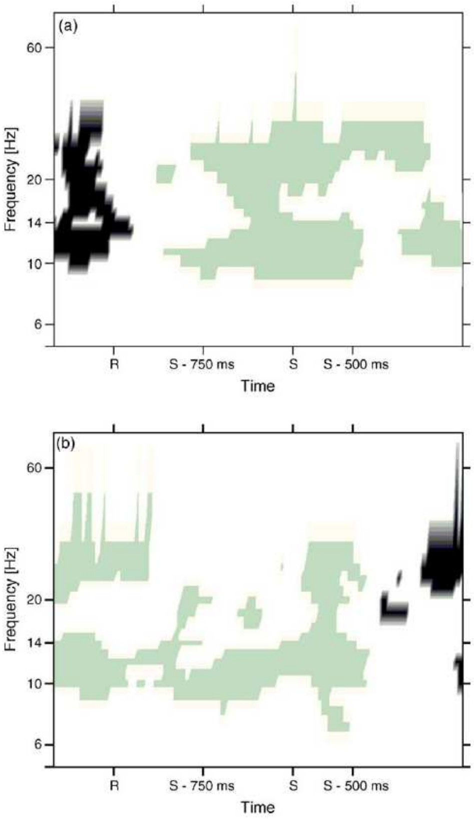


Figure 2.9: Significant lateralization of amplitude preceding switch (top) and hold (bottom) trials, related to upcoming response hand, as measured by the motor-related amplitude asymmetry (MRAA). Each time - frequency point reflects the MRAA at that point, as defined, similarly to the LRP, as the difference of the left - right lateralization when the upcoming response is left- as opposed to right-handed. Response-related desynchronization would, using this double-difference, lead to positive values for a response given with the upcoming response hand. Significant values indicate consistent lateralization related to the upcoming response hand, positive values indicating lateralization in the direction of the MRAA at response (that is, the left - right hemisphere amplitude difference is significantly different when the upcoming response is left- versus right-handed). Since for switch trials the previous response was given with the opposite hand, the MRAA around the previous response is negative for switch trials. Time - frequency points at which significant positive and negative differences were found are plotted in grey and black, respectively.

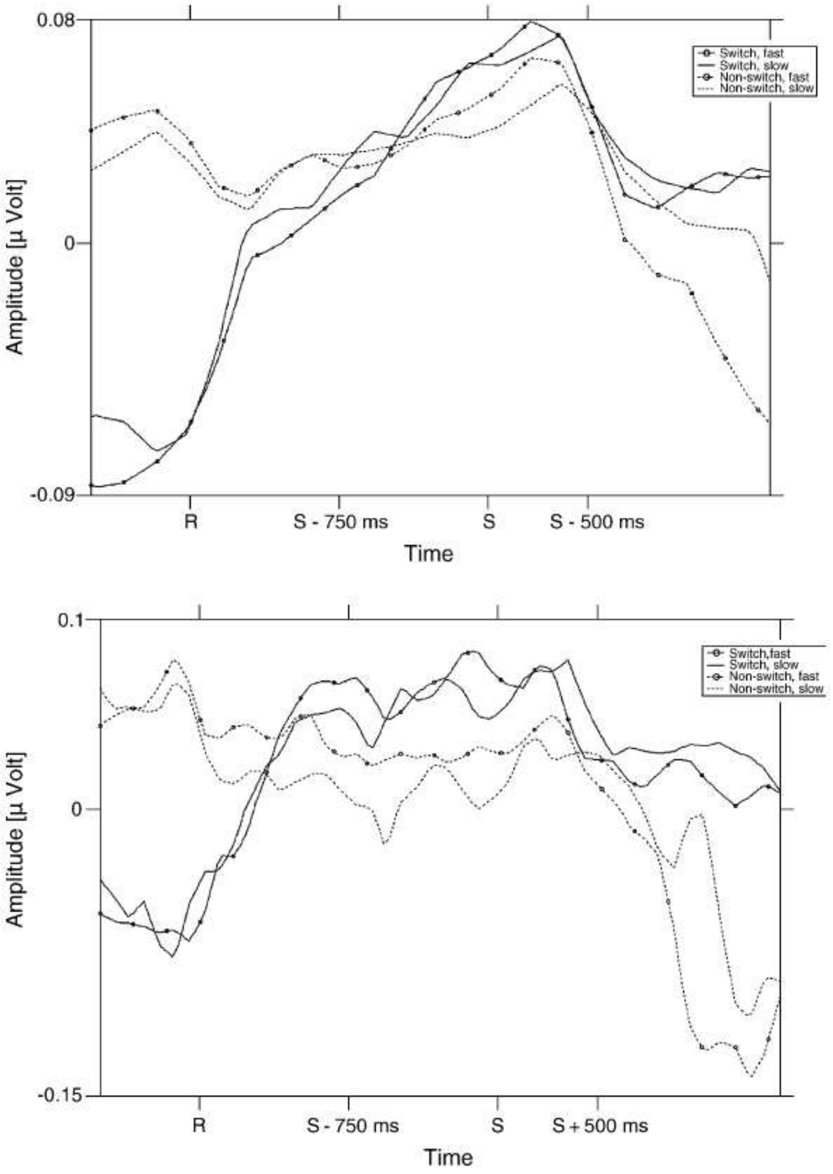
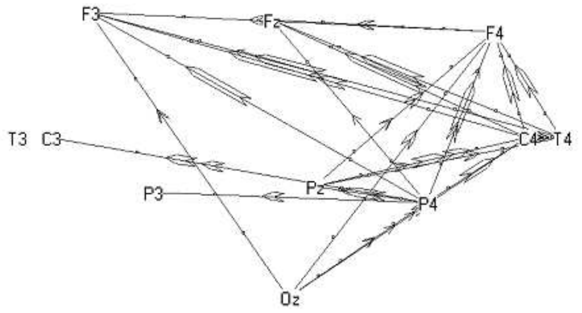


Figure 2.10: The time course of the MRAA in the alpha (top) and beta (bottom) band, plotted for the fast and slow switch and non-switch conditions.



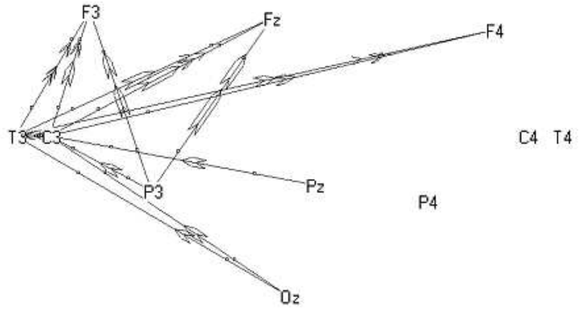


Figure 2.11: Positive (top) and negative (bottom) significant differences in phase-locking value when the upcoming task is left- and right-handed, in the beta band, for switch trials. The plot should be read as follows. Periods of significant datapoints with a positive sign are represented by the arrows on the line drawn between the involved regions. The regions are plotted at the average position of the component electrodes, viewed top-down, with anterior regions at the top of the picture, left and right plotted as such. The begin- and end-times of the periods are represented by the point and end of the arrow on the line. The arrow points in the direction of time, so if the arrow is close to the region it points to, the datapoints occur near the end of the trial. The two dots on each line represent the times of response and stimulus. The plots show that, during the response - stimulus interval preceding switch trials, phase-locking in the beta band occurs involving the hand with which the upcoming task is associated. The FDR cut-off t-value in these plots was 3.4.

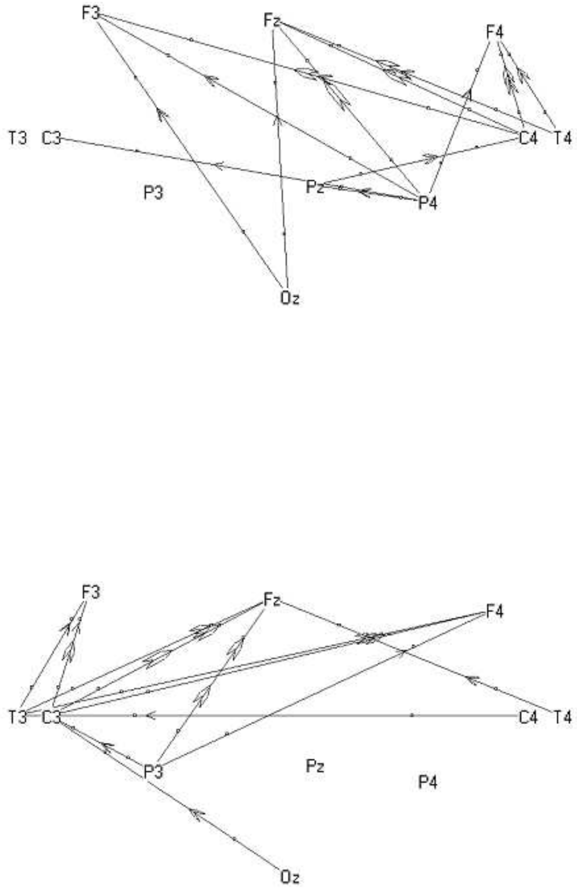


Figure 2.12: Interaction of left - right hand with switch - hold trial type. The plot should be read as in figure 13. The pattern of significant values now indicate where and when the effect of hand, shown in figure 13 for switch trials, remain when the left - right differences for hold trials is subtracted. The pre-stimulus lateralization can be seen to be significantly stronger for switch than for hold trials. The FDR cut-off t-value was 4.0.

2.2 Switching between visual and auditory tasks

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2.2.1 Abstract

The instantaneous amplitude of the theta and alpha bands of the electroencephalogram (EEG) was studied during preparation periods in a task-switching experiment. Subjects had to switch between tasks in which they were to respond to either the visual or the auditory component of the stimulus. 11 - 13 Hz occipital amplitude increased prior to auditory, relative to visual repetition trials. The effect was transient, ending well before presentation of the stimulus that was being prepared for. Alternation trials were preceded by an increase in occipital theta-band activity, relative to repetition trials. This effect was also transient and interacted with modality in one time window. The effects suggest tentative hypotheses for the function of transient bursts of alpha- and theta-band oscillations and indicate the possibility of a psychophysiological resolution of theoretical questions concerning the origin of switch costs.

2.2.2 Introduction

Before a task can be performed, the brain must somehow implement the correct task set: the set of all stimulus - response mappings necessary to perform that task [157]. For any task involving stimuli which are not always associated with the same responses, its task set must have a transient, context-sensitive implementation. However, while the brain has the ability to switch tasks, the replacement of one task set by another is associated with switch costs [103]: increased average response times on trials following a task switch, relative to trials requiring the same task as the previous trial. Subsequent experiments [3] have shown that switch costs diminish as the time available to replace task sets increases, but never completely disappear. The persistent difference between switch and repetition trials is called the residual switch cost.

According to the task-set inertia (TSI) hypothesis [3], switch costs are due to a conflict between task sets that share common features. While the influence of a previous task set decays over time, a full stimulus - response cycle seems to be necessary and sufficient for its complete replacement [197] [70]. Rogers and Monsell [197] propose that task-set reconfiguration (TSR), the required binding of stimuli to responses, does partially occur prior to stimulus presentation. The benefit of increasing preparation time derives from the opportunity to complete more of TSR. Residual switch costs are explained by an inability to completely prepare for an upcoming task: the actual stimulus is necessary to complete TSR, although not to initiate it. The TSI and TSR hypotheses do not seem to be incompatible; residual switch costs might be multiply determined, by both previous task interference and an inability to completely prepare. Such a combined explananation is of course less parsimonious than either separate hypothesis, and this added complexity of a combination has yet to be justified [70].

The failure-to-engage hypothesis [47] is based on reaction time distribution rather than average reaction time. The residual switch costs found when subjects are provided with the opportunity to prepare for a switch in task prior to stimulus onset have a distribution that consists of a mixture of reaction times drawn from two other distributions: those when subjects were already prepared and those when subjects had not had a chance to prepare. These distributions are estimated from repetition trials with long preparation intervals and switch trials with short preparation intervals, respectively. Residual switch costs may not, therefore, be due to an effect present on every trial when a switch must be performed, but to the proportions of prepared and unprepared trials. According to the failure-to-engage hypothesis, the subset of prepared trials are fully prepared, while the subset of unprepared trials follow from a failure to engage the intention to switch tasks.

This changes what must be explained about residual switch costs. Hypotheses must explain why trials are divided into a fast and a slow subset, instead of why a single average reaction time is slower. In the failure-to-engage hypothesis, a task set is either recalled or not, and the theoretical questions reduce to the way memory recall is implemented in general, and how the memory and recall of task sets are implemented in particular. How are task sets stored? How are they instantiated? How does the brain remember what to recall?

Theta-band (5 - 7 Hz) oscillations may be involved in one way to switch tasks, namely the reactivation of the memory of a task set. Theta oscillations are involved in a number of cognitive functions [106]. The phase of theta oscillations modulates long-term potentiation; hence, synaptic plasticity is partially determined by theta oscillations [93] [87]. The phase of theta oscillations in the hippocampus of rats has been shown to code for location [173] [213]. The power of theta oscillations measured by the electroencephalogram (EEG) increases with working memory load [69] [122]. As might be expected due to its role in synaptic plasticity, EEG theta power also increases when information is encoded to [114] or retrieved from [117] long-term memory. Hence, the theta band is of interest in this context because, first, preparation is in a sense the recall of the memory of what task to perform and, second, remembering what to recall is a situation involving working-with-memory (WWM [158]).

WWM refers to three operations of the prefrontal cortex on information. First, the organisation of information before it is encoded to memory; second, the strategic search for cues to activate associated information in memory; and third, the relation of information retrieved from memory to current goals. WWM has a dependent relation with automatic, associative memory. Before memory can be worked with, its content must have been determined by associative memory at a previous time - that is, the function of working with memory does not not include memory itself. WWM will therefore always include both the prefrontal cortex and activity in and relations between neuronal areas that represent a specific kind of information, e.g. occipital areas for visual information. In the case of task-switching, the memory being worked with is the task set: stimuli, responses and the relations between them.

If theta amplitude reflects WWM, effects specific to the areas being worked with should be found. In a study by Kirk and Mackay [112] linguistic and spatial task demands resulted in left and right hemisphere theta maxima, respectively, providing an indication that theta topography may be in part determined by the relevance of specific cortices. Task - region compatibility of effects on theta amplitude would provide some support for the suggestion that theta oscillations can occur as a cortical expression of hippocampal activity [115]. The present study provides data that is relevant for this hypothetical compatibility, for visual information and the occipital cortex.

Another way to switch tasks is to leave a set of stimulus - response mappings intact, but to block a subset of either stimuli or responses so that the remaining paths form a task set. Alpha-band (8 - 12 Hz) oscillations may be involved in such a function, as they are related either to simply the absence of processing [187] [23] or to the active and selective inhibition of external sensory influences [40]. Bastiaansen et al. [17] found anticipatory event-related desynchronization (i.e., a drop in amplitude) in the alpha-band when visual feedback was expected, which was explained in terms of a thalamo-cortical gating mechanism [82] [31] [214]. Temporal desynchronization due to auditory preparation was found only using magnetoencephalogram (MEG) recordings; the EEG does not seem able to register such activity. A general hypothesis on the effect of alpha oscillations, that fits with either of the ideas mentioned above, is based on a consequence of large-scale synchrony, namely that enforced synchronous firing diminishes the parallel processing that a large number of neurons would otherwise be able to perform [168]. A simple cause of synchronous oscillations in the alpha band is rhythmic inhibition due to excitatory-to-inhibitory-back to-excitatory feedback combined with long-lasting (NMDA) post-synaptic dynamics [237]. Such an interaction, due to the periods of uniform inhibition, also seems likely to cause a decrease in the information a neuronal population undergoing synchrony could transmit or transform.

These theories and results suggest hypotheses concerning effects in the theta and alpha frequency bands related to the implementation of task sets. This is not to say that other frequency bands, for instance the gamma band [228], might not be of interest, or even be intimately related to the same processes associated with the theta and alpha bands. The present study, however, is focused on the theta and alpha frequency bands because of their known relevance for memory and inhibition / idling, respectively, and the possible importance of these processes in understanding task-switching.

In the present study, subjects were confronted with ambiguous stimuli: a letter and a tone, presented simultaneously. Subjects had to perform one of two tasks using these stimuli, either responding to the letter or the tone (see Methods for details). The period of interest is the interval during which subjects could prepare to respond in the correct way to the upcoming stimulus. In this interval, effects related to the next kind of trial - visual versus auditory, alternation versus repetition - could be related to the recall of a task set.

The final focus of the present study is the occipital region. Although both the visual and auditory modality were relevant in the task, the occipital region was chosen due to the sensitivity of the EEG to activity in visual cortex, as opposed to auditory cortex (see above). This selection of frequency bands, period and location allows the following hypotheses to be formulated.

First, preparing to switch to the visual task is expected to involve increased occipital theta amplitude in the preparation interval. This expectation follows from the relation of theta activity to memory and the hypothesis that switching to a new task can be considered to be the recall of the memory of the task-set. By letting subjects switch between a visual and auditory task, effects associated with the recall of a visual task might be found, and such effects can be contrasted with the recall of a non-visual task.

Second, effects on occipital alpha amplitude might be expected in this interval, in the case that switching in this task is achieved by inhibiting irrelevant cortices, as opposed to recalling memories involving relevant cortices. Such inhibition would be expected to cause increased occipital alpha amplitude - associated with increased inhibition - when preparing for the auditory task, in which situation information in the visual cortex is irrelevant.

2.2.3 Methods

Subjects

Subjects were eight paid volunteers (age 18 - 25 years), with normal or corrected-to-normal vision. Four subjects were male. All subjects were right-handed.

Task

A version of a Rogers and Monsell [197] task-switching task, implemented in MEL [150], was used. In this task, visual stimuli were presented for 200 ms in one of four cells in a two by two matrix. Auditory stimuli, which were either a high (400 Hz) or a low (1200 Hz) tone, were presented simultaneously and for the same duration. The visual stimuli were the letters H and L. Subjects (all Dutch speakers) were instructed to think of these letters as standing for the Dutch words for "high" and "low" ("hoog" and "laag"). All "high" and "low" stimuli were coupled to responses with the right or left index finger, respectively. Responses were given through a keyboard, using the 'z' and '/' keys. The mapping of "high" and "low" stimuli to keys was randomized over subjects. In the visual and auditory tasks, subjects were to respond to the visual and auditory stimuli respectively. Each cell in the matrix was associated with the visual or the auditory task, and the letter appeared in a clockwise sequence, so tasks were always predictable. Tasks of the same modality were always assigned to adjacent cells, so that subjects performed the tasks in a task 1 - task 1- task 2 - task 2 rhythm. The task - cell assignment was kept constant for each subject and counterbalanced over subjects. Counterbalancing included whether tasks were assigned to the left versus right cells or the top versus bottom cells, as well as which task was to be performed within these assignment patterns.

After a response, a delay of one of three lengths of preparation interval (150, 750 or 1500 ms) prior to the next stimulus, of which the visual dimension was presented in the cell clockwise to the previous one. Intervals were varied per trial, within blocks. The proportions of the preparation intervals were 33 %, 17 % and 50 %, for 150, 750 and 1500 ms respectively. The high percentage of long intervals was chosen because only these trials would be used in the analysis. Short-preparation intervals were used for estimation in the mixture model, so a reasonable number of these were also needed. Medium-length intervals, however, were only needed to keep subjects' attention on the task during long preparation intervals, so only a relatively small number of these were presented.

Subjects were explicitly instructed to use the delays to prepare for the next task. They were told to direct their attention to the correct modality and recall the correct task-mapping. They were also instructed to respond as quickly and accurately as possible. Subjects were trained for around 45 minutes. Training was provided in sessions which started with pure-task blocks, one for each task, followed by six mixed blocks. Subjects were encouraged to respond as quickly and accurately as they could. At the end of training, visual inspection of reaction times showed a reduction in switch costs over increasing preparation-interval duration for all subjects, indicating that subjects were preparing for upcoming tasks. The task proper consisted of a short repetition of the training session with only one mixed block, followed by eight mixed and two pure blocks of 100 trials each. The order of blocks was randomized. Subjects were instructed to take as much time as they needed to rest between blocks.

Due to the simultaneous presentation of a visual and an auditory stimulus, the combined stimuli are either congruent or incongruent. Stimuli are termed congruent if both the visual and auditory stimuli demand the same response. Since congruence is only defined post-stimulus, this factor cannot influence the preparatory effects that the hypotheses are concerned with. It is included in the behavioral results for completeness and because it may be of interest in the interpretation of preparatory effects.

EEG measurement

The following electrode positions were measured: Fp1, Fpz, Fp2, F3, Fz, F4, FC3, FCz, FC4, FT7, FT8, C3, Cz, C4, T7, T8, TP7, TP8, P3, Pz, P4, O1, Oz and O2. Impedance was kept below 2 kΩ. PAS amplifiers (Instrumentation Service Psychology (IDP) of the University of Groningen) and the acquisition program Ada (IDP) were used for data acquisition. The sampling frequency was 250 Hz, high-cut filtered with a pass frequency of 80 Hz and stop frequency of 125 Hz. The voltage range was 500 mV sampled using 12 bits, providing a resolution of 0.1 μV.

Data analysis

Brain Vision (Brain Products, 1998) was used for visual inspection and artefact rejection, segmentation and ocular correction. Segmentation was based on a selection of trials determined by mixture-model analysis software [47] as described next.

A distribution-based view of task-switching data suggests using reaction times to determine the odds of preparation per trial and using this information to separate subsets of prepared and unprepared trials. The mixture model specifies that the cumulative distribution function (CDF) of the reaction times t for long interval, alternation trials is a linear combination of the CDF's of the prepared and unprepared trials:

$CDF-mixed(t) = \alpha * CDF-prepared(t) + (1-\alpha) * CDF-unprepared(t)$

The prepared and unprepared CDF's were estimated using the long interval, repetition and the short interval, alternation reaction times. The α parameter stands for the proportion of alternation trials in which subjects successfully switched, and could therefore be said to have been actively preparing. Only the fastest 100 * α % of trials in the conditions (both alternation and repetition) were used in the EEG analysis, to select trials of which the EEG activity are likely to reflect preparation. The multinomial maximum likelihood model (MMLM, Yantis, 1991) was used to estimate the α parameter as well as, in separate models, an additional δ parameter which is a shift of the prepared distribution, adding a minimum increase of reaction time due to switching. For more details on the mixture model see Nieuwenhuis and Monsell (2002).

Note that only the very fastest subset of trials would be expected to be uncontaminated by unprepared trials, which is why, for example, a persistent effect of alternation is to be expected. Using the fastest α * 100 % trials is a trade-off between preparation odds and the number of trials remaining for EEG analysis that provides a well-defined comparability of the selection process over subjects. For all subjects, although the number of trials removed was different, the estimated minimal preparation odds (that is, one) were the same. For subjects with a low switching parameter, a large proportion of trials will be lost to EEG analysis, but if hypotheses are concerned specifically with preparation this would seem preferable to including trials of which the odds of preparation are bad.

Wavelet analysis [124] was performed on the data using the program Gamma [66]. Wavelet analysis is based on the convolution of signals with wavelets: oscillatory functions which have finite energy and are therefore localized in time. Wavelets have a mean and standard deviation in time and frequency, specifying their location and the uncertainty of their localization. In this study, the Morlet wavelet was used, which is the product of Gaussian curve and a (co)sine. By convolving a signal twice, once with a cosine- and once with a sine-based wavelet, the amplitude of the signal around the time - frequency mean of the wavelet (i.e. the instantaneous amplitude IA) can be found. The convolutions measure the similarity of the signal to a cosine and a sine; using these measures as Cartesian coordinates defines a vector of which the length abstracts the amplitude from phase. As the phase changes, the vector rotates as the signal's similarity shifts to and from the cosine and sine-based wavelet, but its length does not change. The signal's amplitude is equal to the vector's length multiplied by 2 / (σ_t) * sqrt(2 * pi)), with σ_t the standard deviation of the Gaussian involved in the wavelet. The vectors over time of IA for each trial were averaged to measure the typical amplitude time courses related to specific periods.

The frequencies from 5 to 16 Hz were chosen as mean frequencies, all with a 1 Hz uncertainty parameter (standard deviation in frequency). The associated width, expressed as the standard deviation in time, is 159 ms. The IA's over groups of electrodes were averaged to create the following regions: frontal (Fp1, Fpz, Fp2, F3, Fz and F4), central (FCz, Cz, CPz), parietal (P3, Pz and P4) and occipital (O1, Oz and O2). Matlab (The MathWorks, Inc, 1984) and SPSS (SPSS Inc., 1989) were used for statistical testing and visualization.

The relative difference (RD) was taken when comparing within-subject instantaneous amplitudes in the following manner: $RD = 2 * (IA1 - IA2)/(IA1 + IA2)$, where IA1 and IA2 are the instantaneous amplitudes of the conditions to be compared, at the same times, frequencies and positions. In this way, the differences between the values for two conditions were normalized by their average so that overall variance of absolute amplitude over subjects was removed. Prior to calculating differences, the data were smoothed using a running average over 3 Hz and 140 ms. The degree of smoothing was chosen to deal with possible intersubject variability in the precise location of effects; more precise effects would be lost in the data reduction explained below.

Due to the large number of tests that could be performed on the data, a two-step procedure was used to focus analyses on those parts of the data relevant to the hypotheses. The first step of the statistical analysis is aimed at reducing the data to a small set of relevant times and frequencies. This step is based on contrasts of interest determined by the hypotheses: the effect of modality, given both alternation and repetition; and the effect of alternation, given a visual task. These contrasts were concerned specifically with the theta and alpha bands respectively, the preparation interval and the occipital region, and specified the direction of effects. The data were reduced by replacing 3 Hz by 140 ms-sized sections of time-frequency by the mean value in that section. This reduced the number of tests to be performed. The t-scores of the averaged RD's were computed, and these remaining multiple tests were analyzed using the false discovery rate (FDR) procedure (Benjamini and Hochberg, 1995). This procedure controls the proportion of rejected null hypotheses which are rejected falsely when multiple differences are being tested. A false discovery rate with a one-sided error rate of 1.25 % was chosen, so that the overall rate over the four selection contrasts was controlled. The second step of the analysis is to examine effects in the location (in time and frequency) indicated by the FDR procedure. To do so, repeated measures analyses were performed and the time courses of instantaneous amplitude studied. Only mixed blocks and fast (see above) and accurate trials following a long preparation interval were used in the analysis. These analyses were performed using the frontal, central, parietal and occipital regions.

2.2.4 Results

Behavior

Figures 2.13 and 2.14 show the reaction time data. An important effect is the diminishing difference between alternation and repetition trials, which indicates that subjects were preparing for the upcoming task during preparation intervals.

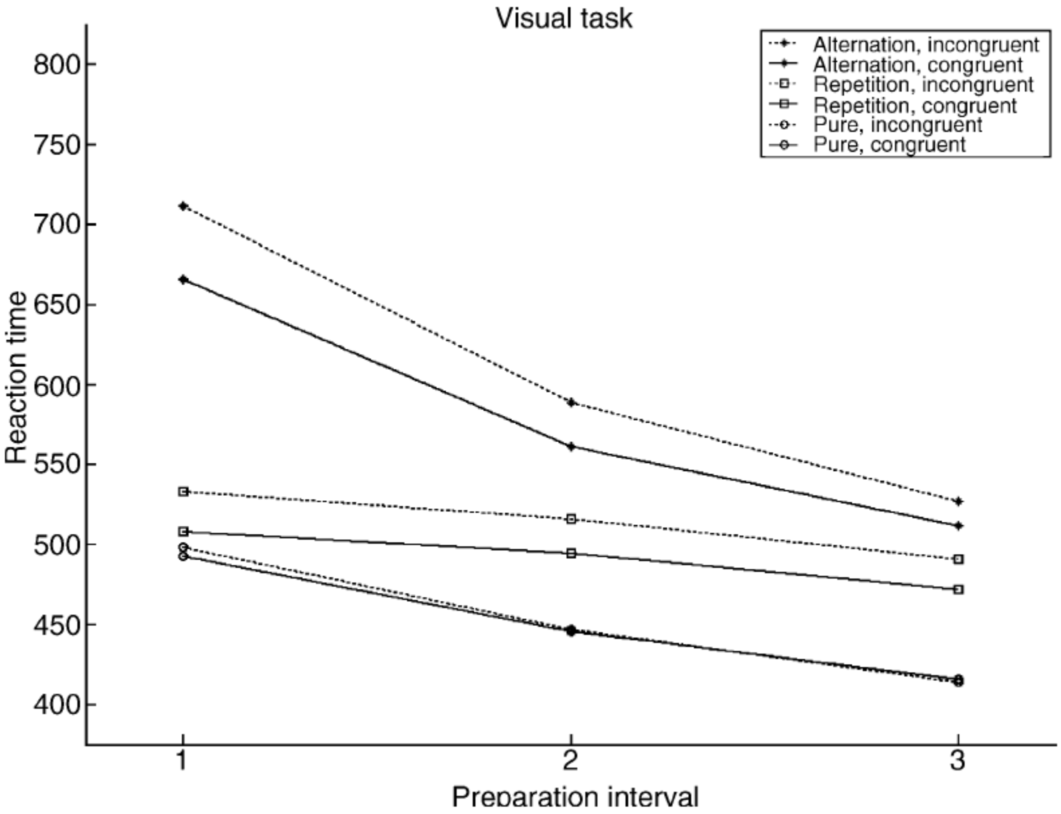


Figure 2.13: Reaction times, visual task

Repeated measures analysis was performed on the reaction time data using the factors congruence, modality (visual versus auditory task), alternation (alternation versus repetition trial) and preparation interval.

Congruent stimuli caused faster reaction times than incongruent stimuli (F (1, 7) = 11.8, p = .011), the visual task was performed more quickly than the auditory task (F (1, 7) = 5.6, p = .05), alternation trials were slower than repetition trials (F (1, 7) = 51.2, p < .000) and longer preparation intervals led to faster responses (F (2, 6) = 14.1, p = .001). Relative to repetition trials, alternation trials showed a larger effect of congruence (F (1, 7) = 10.4, p = .014) and preparation interval (F (2, 6) = 13.5, p = .003). A weak interaction was found suggesting that the alternation - repetition effect was larger for the auditory task (F (1, 7) = 4.1, p = .083).

Figures 2.15 and 2.16 shows the accuracy scores. The same repeated measures analyses as done for reaction times was performed for accuracy. Congruent trials were more accurate than incongruent trials (F (1, 7) = 48.5, p < .000), visual trials were more accurate than auditory trials (F (1, 7) = 5.8, p = .046) and repetition trials were more accurate than alternation trials (F (1, 7) = 34.8, p = .001). Preparation interval had a weakly significant effect (F (2, 6) = 3.2, p = .071). Congruence effects were greater for auditory versus visual trials (F (1, 7) = 7.5, p = .029) and for alternation versus repetition trials (F (1, 7) = 12.6, p = .009). The effect of preparation interval is greater for incongruent trials (F (2, 6) = 4.6, p = .029). The effect of alternation versus repetition was, with weak significance, greater for auditory trials (F (1, 7) = 5.2, p = .057).

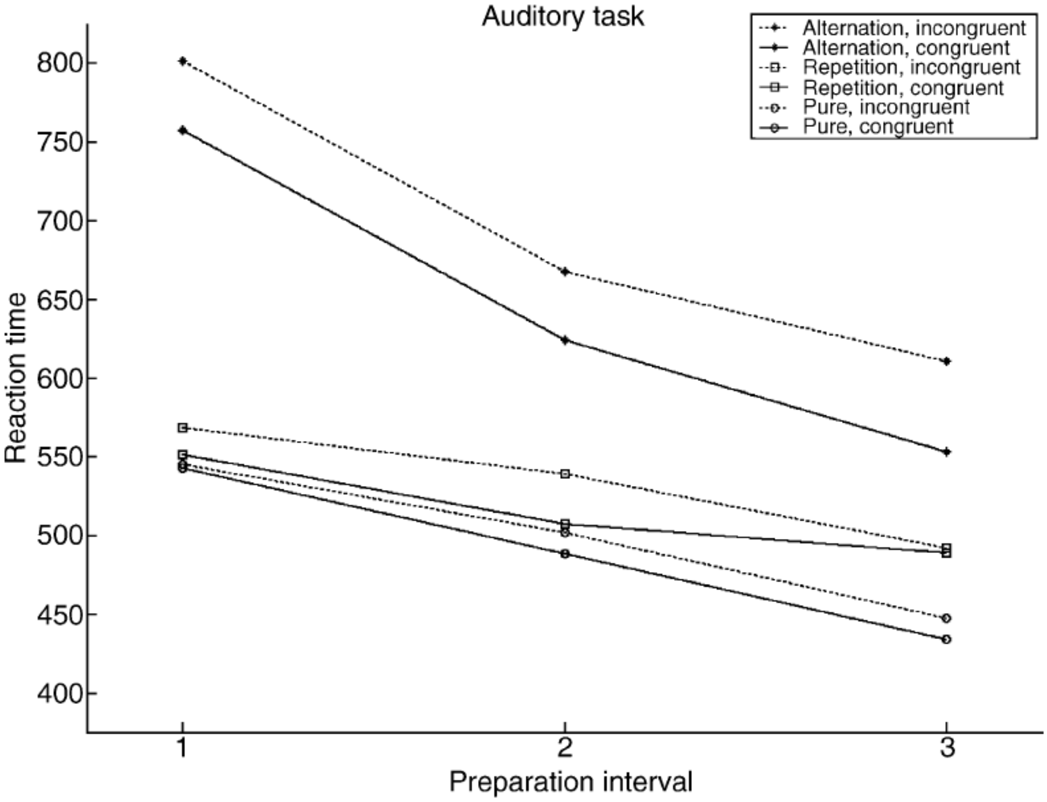


Figure 2.14: Reaction times, auditory task

The behavioral data suggest that auditory trials are not only more difficult to perform quickly and correctly, but also more sensitive to incongruence and the need to switch. One explanation of these results is that they are due to the need to perform eye movements to follow the stimuli around the cells, and the subsequent changes in the visual field. The auditory task may have a disadvantage due to this general importance of the visual modality.

The results of the mixture model analysis are as follows. The α-only, or restricted, model did not give a good fit for the overall data ($G^2(24) = 52.01, p{=}.0008$). The estimated α was .72 with a standard error of .065, giving a 95 % confidence interval (CI) of [.59 .86]. The bad model fit was due to one subject with an extremely high $G\hat{2}$; the overall fit without this subject had a $G^2(21) of 24.64, p{=}0.2631$.

The model including a δ parameter provided a good overall fit including all subjects ($G^2(16) = 21.74, p{=}.1516$), with an α of .703 (CI = [.51 .9]) and a δ of -16.375 (CI = [-58 25]). Because the delta parameter should show an increase in reaction times, and the confidence interval contains zero, no overall additive effect seems to be present. For individual subjects the restricted model sometimes gave a better fit in terms of p-value than the model including a shift. The α used to estimate the proportion of prepared trials for a subject was taken from the model which had the higher p-value for that individual. The alpha's used for trial selection were .47, .75, 1 .9, .8, .6, .7 and .4. On average, around 30 % of trials were rejected based on α. Taking an average accuracy of around 90%, this resulted in a loss of around 40% of trials due to selection based on behavioural

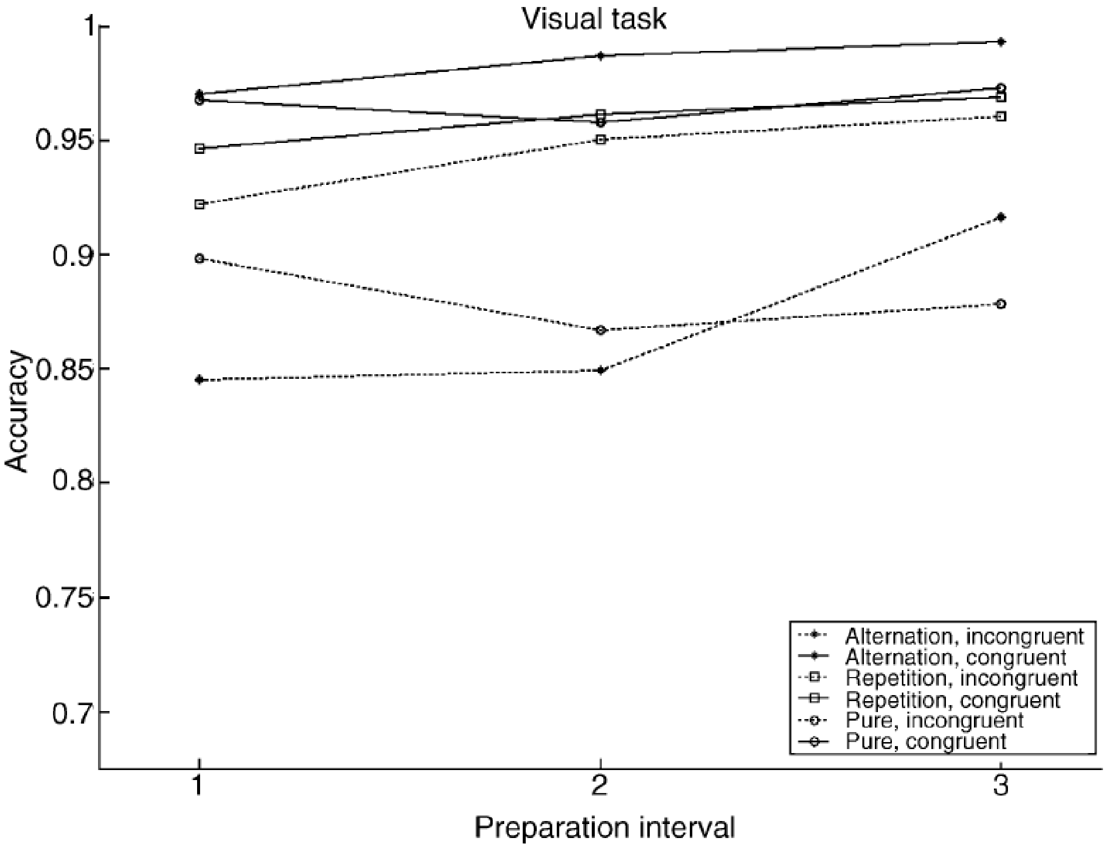


Figure 2.15: Accuracy, visual task

measures. As argued above, while the average proportion of rejected trials is high, the inclusion of trials of which the estimated preparation odds are low seems unlikely to increase the signal to noise ratio of preparatory effects.

Taking the fastest $\alpha * 100$ % of a subject's trials can be seen as selecting the trials that are more likely to be prepared than not. This aspect of likelihood implies that even within this selection of trials a proportion will be unprepared. Repeated-measures analysis on the trials that will be used in the EEG analyses (that is, those with fast response times and a long preparation interval) show that this is the case. With factors congruence, alternation - repetition and visual - auditory, the following effects on reaction time were significant. Incongruent trials were slower than congruent trials (F (1, 7) = 21.5, p = .002), and this effect was greater for alternation trials (F (1, 7) = 20, p = .003). The effect of alternation versus repetition was still significant (F (1, 7) = 81.6, p < .0005) for the selected trials. For accuracy, the main effects of congruence (F (1, 7) = 12, p = .011) and alternation (F (1, 7) = 7.5, p = .029) were significant. Congrence interacted with with modality (F (1, 7) = 6.9, p = .035), where the effect of congruence was greater for auditory trials, and with alternation (F (1, 7) = 8.8, p = .021), where the effect of congruence was greater for alternation trials. Because the EEG will be analysed during the period between response and subsequent stimuli, differences in the mean accuracy of trials preceding those trials to be analyzed could bias results. However, no significant differences between the mean accuracies preceding trials

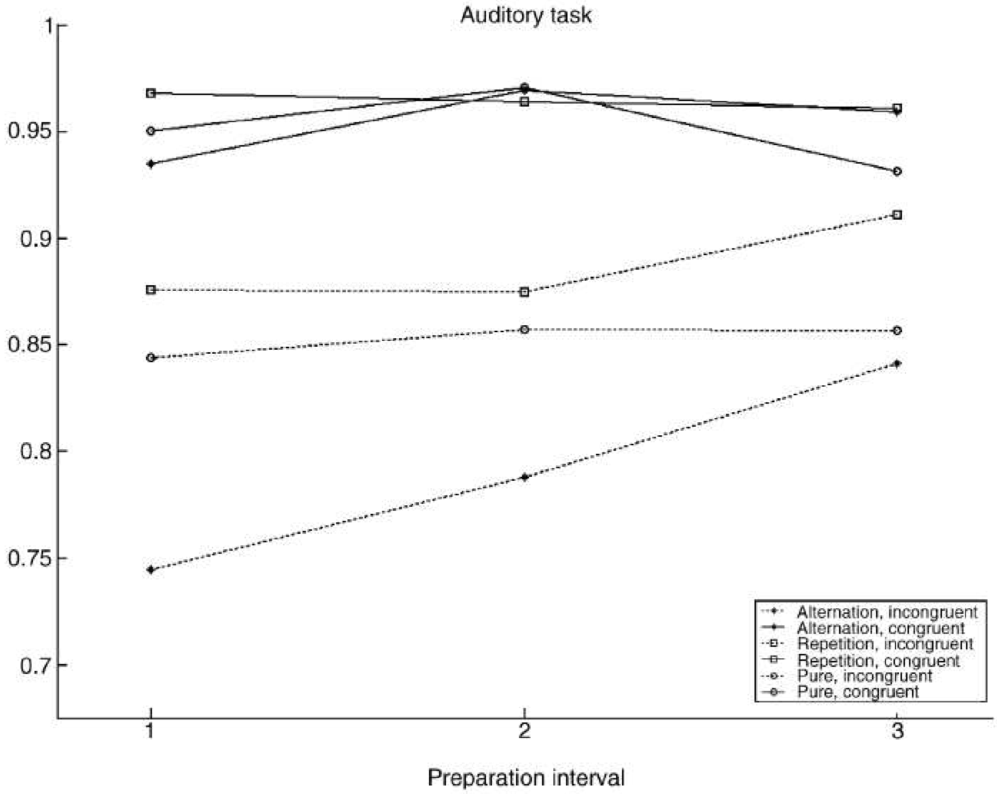


Figure 2.16: Accuracy, auditory task

in the conditions to be compared in EEG analyses (that is, modality and alternation, given a long preparation interval) were found.

Instantaneous amplitude

The FDR procedure selected two data regions as containing significant differences between conditions. In the "visual - auditory, given repetition" contrast, auditory trials show higher amplitude 560 - 700 ms into the preparation interval, in the 11 - 13 Hz band. The most extreme t-value in this range is -7.6. Alternation trials show higher amplitude than repetition trials in the 560 to 980 ms range at 5 - 7 Hz for the "alternation - repetition, given visual task" contrast (most extreme t-value = 5.6). The amplitude signal in these frequency bands is plotted in figures 2.17 and 2.18.

The time course of occipital theta IA (figure 2.17, bottom) shows an increase for around 500 ms after stimulus-presentation. The IA's of alternation and repetition intervals start to diverge during the preparation interval as the high amplitude due to the previous trial drops. The IA curves for auditory trials, however, lose their divergence while for visual trials the divergence increases to a maximum at around one second post-response.

The spatial distribution of theta band amplitude (figure 2.17, top) shows that the theta-band has its highest overall amplitude centrally, but the alternation - repetition effect in the 560 - 980 ms period is strongest over the occipital region, with parietal sites showing a smaller effect.

Repeated measures analysis of theta-band IA averaged over the 560 - 980 ms period showed

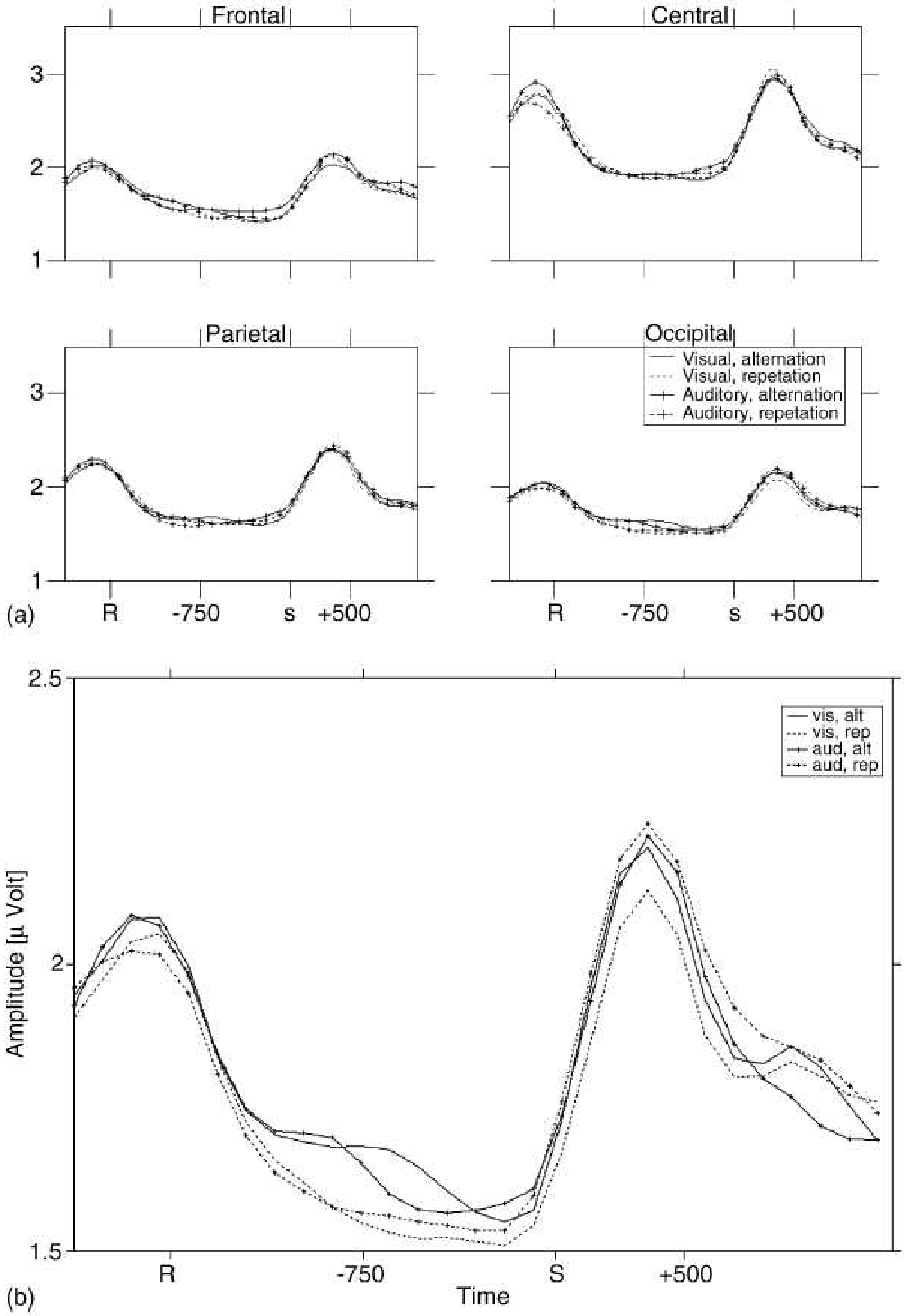


Figure 2.17: 5 - 7 Hz, all regions (top) and occipital region (bottom)

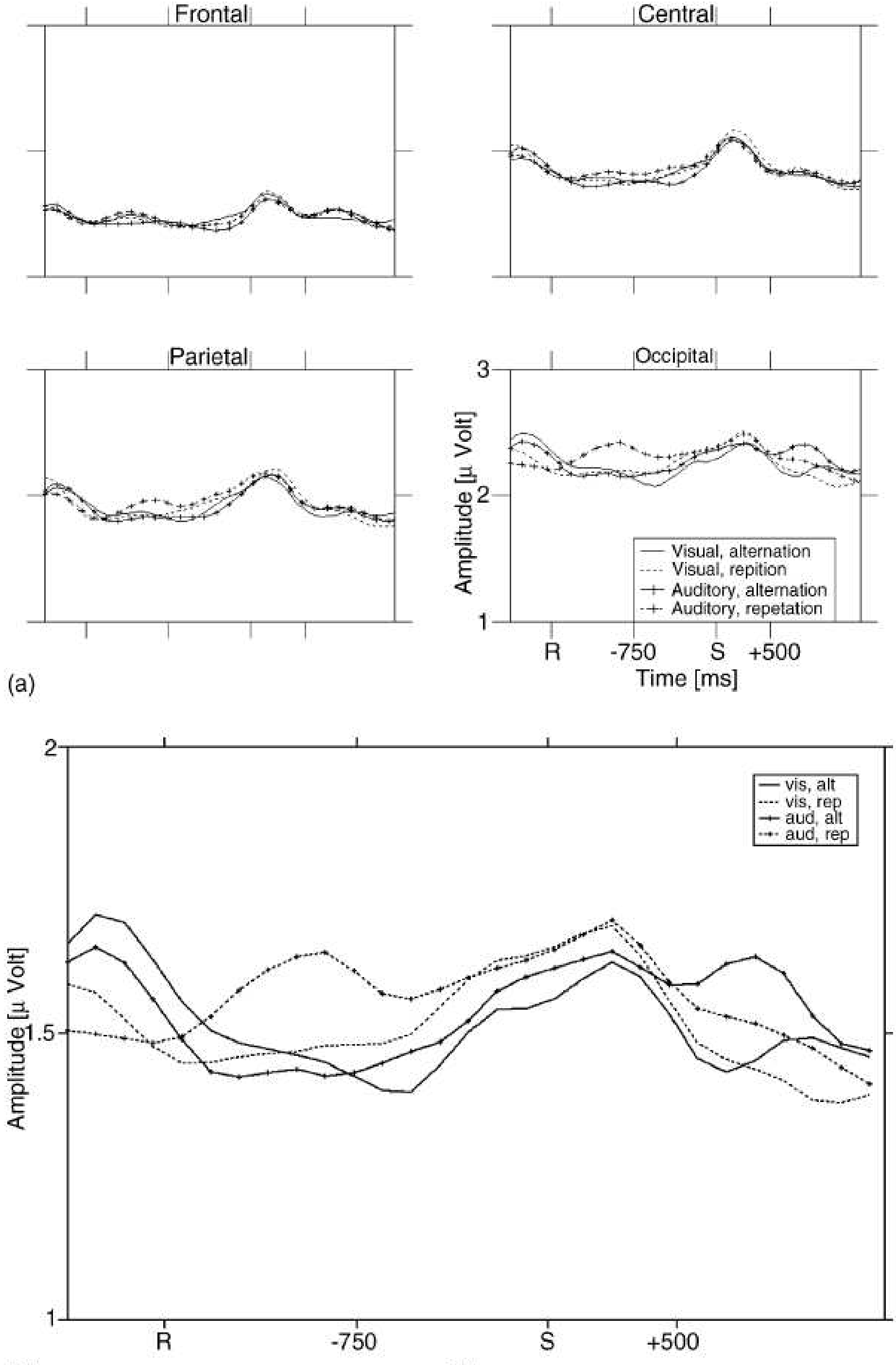


Figure 2.18: 11 - 13 Hz, all regions (top) and occipital region (bottom)

significant effects of alternation (F (1, 7) = 11.4, p = .012) and region (F (3, 5) = 34.4, p = .001). The following exploratory analyses were performed to obtain more information on this effect. In the period where the divergence of the visual and auditory alternation curves is strongest (840 - 980 ms post-response), the effects of alternation (F (1, 7) = 8.9, p = .02), region (F (3, 5) = 36.4, p = .001) and the alternation by region interaction (F (3, 5) = 6.5, p = .035) were significant. Restricting the analysis to the occipital region, alternation (F (1, 7) = 10.4, p = .014) and the interaction of alternation by modality (F (1, 7) = 5.6, p = .05) were significant.

In figure 2.18, bottom, the high-alpha band effect can be seen to be due to an increase for the auditory - repetition condition. The effect occurs at roughly 600 ms post-response and disappears in the second half of the preparation interval. The overall time-course shows peaks around stimulus presentation, and a decrease during the preparation interval.

The distribution of high-alpha amplitude (figure 2.18, top) shows that the visual - auditory repetition effect is largest occipitally, although it is still visible over the parietal region. The effect of region (F (3, 5) = 7.0, p = .03) and the interactions of modality by alternation (F (1, 7) = 5.8, p = .046) and modality by alternation by region (F (3, 5) = 5.4, p = .05) were significant.

Event-related potentials

For completeness the event-related potentials (ERP's) for the conditions studied using wavelet analysis are shown in figure 2.19. The same statistical procedure as used for IA was used, with a lighter smoothing and windowing interval of 20 ms to preserve the faster dynamics of the ERP. The four midline electrodes Fz, Cz, Pz and Oz were included in the FDR selection procedure. No areas with significant differences were found in this step. Due to the potential interest of effects on N1, the mean voltage over 100 - 120 ms post-stimulus was tested separately using repeated measures analysis. Only the factor electrode was significant (F (3, 5) = 7.4, p = .027).

The response-stimulus interval ERP's (figure 2.20) seem to suggest that visual repetition trials, which were, based on behavioral data, the easiest to perform, had the least negativity, especially occipitally, while the more difficult auditory alternation trials were most negative frontocentrally. However, no effect, other than that of electrode (F(3, 5) = 7.0, p = .031), was significant, using repeated measures analysis on the average voltage over the second half of the response-stimulus interval and electrodes Fz, Cz, Pz and Oz.

2.2.5 Discussion

Two experimental effects on instantaneous amplitude were found using the FDR procedure. First, an increase in occipital theta amplitude was found for alternation versus repetition trials, but only for the visual task. The lack of an effect of alternation for the auditory task may be partly due to low statistical power, as the theta-amplitude time course preceding alternation trials is initially similar for both modalities and no alternation by modality interaction was found over the whole period selected by the FDR procedure. However, the visual and auditory alternation time courses diverge around 1s into the preparation interval, and the interaction between alternation and modality is significant at the occipital region in this period. Second, an occipital increase in high alpha amplitude was found for the auditory versus the visual task, but only for repetition trials. Stimulus-locked ERP's did not show significant effects. This may be due to low statistical power, but visual inspection of the N1 in particular shows no trends related to attention-related negativity. While not the focus of the present study, this contrast between preparatory frequency-

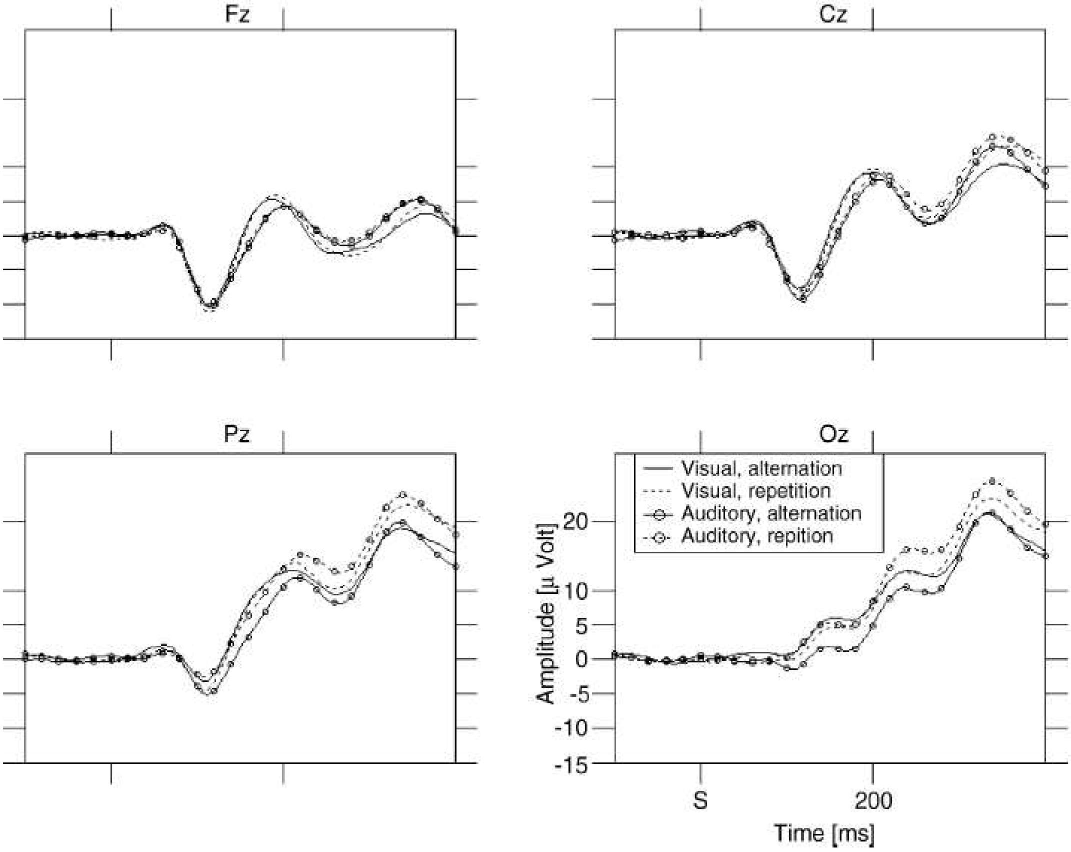


Figure 2.19: Event-related potentials

domain effects and stimulus-locked ERP's, if it can be replicated, may be interesting in terms of what kind of preparation is not necessarily associated with the processes measured in the present study. Since the N1 is related to the early modulation of input [55] [241], the absence of N1 effects suggests that the theta and alpha effects reflect processes which achieve something other than that kind of modulation. Tentative hypotheses on what these processes might be are given below.

The theta-band effect may reflect, as the literature suggests, part of the recall of the task memory, as it occurs most strongly (although apparently not exclusively; see below) when the previously irrelevant visual task must be reactivated. If this is the case, this effect suggests that switch costs are at least partially due to preparation of the upcoming task, as opposed to interference from the previous task. If the memory recall possibly indexed by the theta-band increase has not had time to take place, or if subjects fail to reactivate the memory of the task set, then they will be unprepared for the next trial.

Because the theta effect ends well before stimulus presentation, it seems that the underlying process must cause an enduring change in the state of the brain that is not itself associated with measurable theta oscillations. What could provide theta oscillations with such a toggle function? Hypothetically, the function of such periods of strong oscillations may be to force an excess of neuronal activity into a certain region of phase-space; for instance, the representations of all letter stimuli could be rhythmically activated. If local competition subsequently selects a subset of this

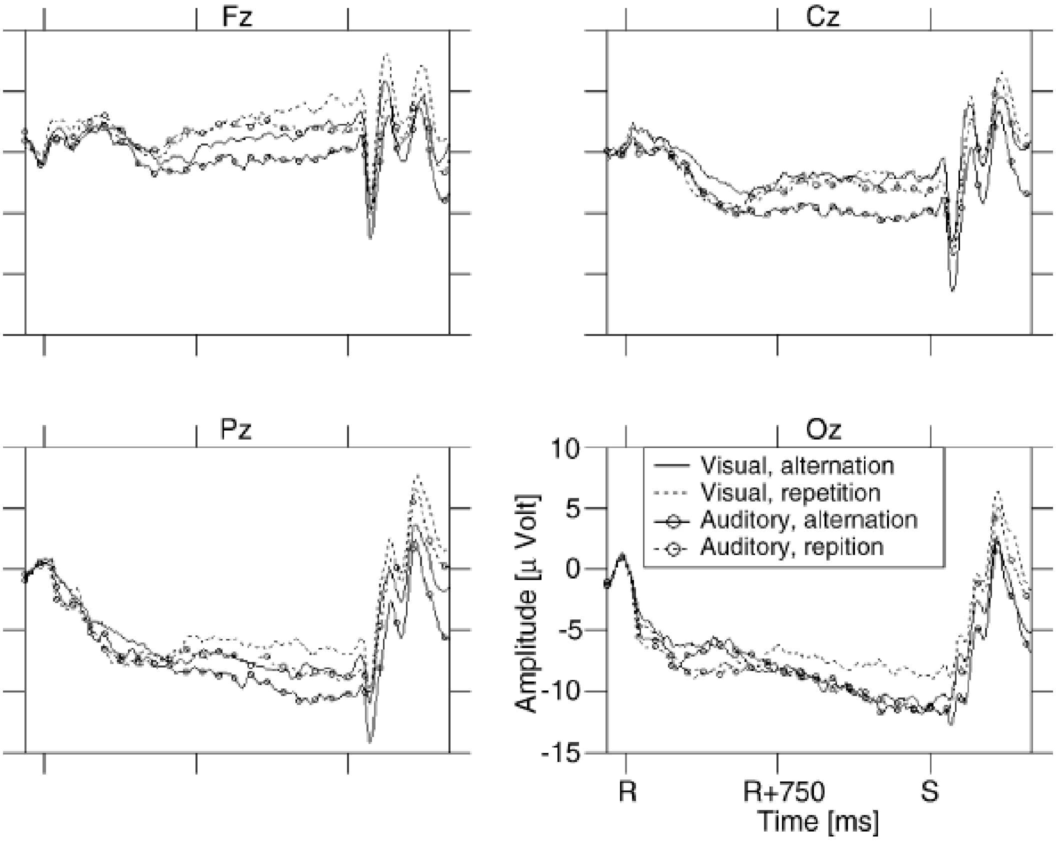


Figure 2.20: Response-stimulus interval event-related potentials

activity, such as the letter "H", then that subset will take over the phase-region, phasically inhibiting competition. That subset will be active in phase with whichever distant subsets, such as ones coding for responses, won their local competition. In this way, an initial overkill of theta oscillations could implement phase coding [95] [212]. A set of stimuli and responses containing stimulus - response pairs with shared phase space may be involved in the realization of task sets.

Such a mechanism could be generalized to explain why an initial alternation-effect on occipital theta amplitude was found for auditory trials. In this case, the whole visual and auditory modalities might be the elements that are initially activated, of which the occipital subset subsequently wins the competition given that a visual task is being prepared for. One important alternative hypothesis, namely that the theta effects are due in some way to eye movements, would seem to be weakened by the topography of the effect, which in the case of an ocular artefact would be expected to be strongest frontally. Nevertheless, further research is clearly necessary to determine the value of the speculative hypothesis formulated above. One potentially interesting question, if such posterior "toggle" effects prove to be a robust phenomenon, is what their relation is to frontal theta oscillations that endure up to stimulus presentation [231].

The increase in occipital alpha-band amplitude between subsequent auditory trials fits with an inhibitory function of alpha oscillations, as performance of the auditory task would benefit from the inhibition of visual input. However, two questions arise: how could a transient effect be relevant to preparation, and why is it not found for alternation trials?

The transience of the effect suggests that, if it does reflect a preparatory function, that function is indirect; at stimulus presentation, no amplitude difference is left to influence stimulus processing. Such an indirect function may be to prevent the initiation of a process starting in the visual cortex during the preparation interval. For instance, the eye movements between trials cause changes in visual input, to which the brain may respond by increasing its sensitivity to the visual modality. Such an advantage for visual stimuli would also explain the absence of the effect on alternation trials as well as the borderline-significant interactions in behavioral data suggesting the auditory task to be more sensitive to incongruence and switching. After a visual representation has been selected for determining the response, feedback mechanisms might further increase the influence of activity in visual cortex. This hypothetical explanation is clearly in need of further research, but it does at least seem possible that the pattern of results could be caused by preparory processes.

Although more research is needed to test and improve the specific speculations given here, it seems that the frequency domain may contain answers to theoretical questions concerning switch costs, which are elusive without the aid of neuroimaging and neuroscientific theory. The results of this study, while limited, are sufficient to suggest that there may be different possible ways to switch tasks, each of which might contribute to switch costs. The theta-band effect, if it does reflect memory retrieval, measures a process aimed at instantiating the upcoming task; if this process is disturbed, switch costs would be expected. The lack of an alpha-band effect for alternation trials suggests an inability to suppress the irrelevant modality, again supplying a cause for switch costs, but now based on previous-task interference. Hence, an interplay of processes reflecting interference, reconfiguration and engagement, dependent on the abilities of subjects and the opportunities afforded by the task, may produce the behavioral results found in task-switching experiments. The need to explain psychophysiological data may justify a cross-theoretical approach to generating hypotheses and designing future experiments, in which for instance the influence of previous-task interference on the chance of a failure to prepare could be studied.

Future research using the kind of approach used in the present study would seem worthwhile. Dealing with both behavioral data and time-varying frequency-domain characteristics demands hypotheses that can make logical connections between specific temporal relations and behavioral emergent properties. Adding other measures such as the BOLD response, the ERP or coherence can further constrain hypotheses. Research using fMRI has shown effects related to switching tasks [28] [35] [53], of which perhaps the most important result is the association of increased activity of lateral prefrontal cortex with alternation. Preparatory ERP effects have been studied by Lorist et al.[137], who found frontal negativity preceding alternation trials and parietal negativity preceding repetition trials. Recent research in our group has revealed effects of phase-locking in a similar design as used in this study.

It is worth noting that the design used here has disadvantages for EEG analysis, especially for calculating ERP's, because of the continuous sequence of response, preparation and stimulus presentation. There is no quiet baseline to use as a common zero-voltage point for all conditions. The continuity also introduces a possible confound because every condition is preceded by a specific other condition. Explicitly cued switch and repeat trials may therefore be a preferable design to use for further psychophysiological research, especially if aimed at using ERP's. The behavioral effects of modality and congruence found in this study may similarly be undesirable. Studies primarily concerned with post-stimulus measures would seem to have to analyze the congruent and incongruent conditions separately, which would leave each condition with half the initial number of trials. In this study, the auditory task seemed more difficult to switch to and more sensitive to incongruence than the visual task. While this may be interesting in itself, it confounds the modality being prepared with the difficulty of the task being prepared. This problem might be dealt with by using separate visual mixed and auditory blocks. Alternation would then involve a change in the mapping of stimuli to responses. An adaptive task that adjusts the discriminability of the visual task might also reduce the modality effects. Finally, using a central explicit cue would remove the eye movements between trials and in that way perhaps reduce the benefit for visual input.

In conclusion, future research could draw on various measures to study task-switching and more generally the ways in which the brain works with memory. The relevance of using multiple measurements to generate explanatory hypotheses is illustrated by the lack of significant effects on ERP's in the present study, contrasted by the strong, if not yet well-understood, effects on amplitude. Results such as those found in the present study may in particular help modelling studies by providing detailed clues as to mechanisms used by the brain in certain situations, as well as constraints models should comply with. Without such studies, it seems unlikely that hypotheses at the same level of detail as the data, providing logical, causal links between emergent behavioural effects and frequency-domain characteristics, will be able to be either formulated or adequately tested.

2.3 Cued chiastic switching

2.3.1 Introduction

In the experiments of sections 2.1 and 2.2, task sets differed on relevant modality and / or hand. Preparation for the different tasks could in those cases involve processes involved in increasing the probability of responding with one or the other hand, or making information in one or the other modality more likely to be eventually encoded into a response. The data appeared to reflect such selections: when switching to one or the other hand for responding, beta-band activity lateralized; when preparing for a visual versus auditory modality, patterns of theta- and alpha-band activity were found over occipital areas. The tasks allowed good performance to be achieved by biasing the influence or sensitivity of whole stimulus or response sets.

When the tasks to be switched between involve a remapping between identical stimuli and responses, task selection must involve more subtle mechanisms. In the present study, stimuli were always one of two shapes and responses were always given with the left or right index finger. So, biasing between modalities or hands is no longer sufficient; now the element-to-response links between the stimulus and response sets, however they are implemented neurally, must be changed to switch tasks. The aim of the study was to explore EEG activity in the context of this crossing of stimulus - response mappings. Of special interest was the question whether something like the switch-related phase-locking found for hand-switches could be found for such "chiastic" switches.

The present task uses explicit task cues, providing a quieter baseline period for ERP's than available in the alternating runs paradigms of the previous studies. It also brings up the question of what effect cue repetition and cue change might have. In the behavioral study by Mayr described in section 1.2, in which cue- and task-switching were disentagled, the cost of cue switching interacted with cue - stimulus time, while task switch costs did not. The four simplest sequence types were distinguished: hold - hold, switch - hold, hold - switch, switch - switch. So, for instance, activity preceding a hold trial could be considered when preceded by a hold versus a switch trial.

Finally, reaction time was used to compare activity preceding stimuli to which fast versus slow responses would be given. This comparison may provide clues on what makes preparation effective, as in section 2.1. This contrast also provides a further test of the interpretation of theta-band time courses found when visual and auditory tasks were used (section 2.2). It was hypothesized in that study that switching involves a transient increase in theta-band oscillations, that decreases once switching is completed. Since effective preparation, defined as activity followed by fast responses, seems likely to involve a prompt completion of switching, an elongated period of increased theta band amplitude was expected for slow versus fast switch trials. By the above hypothesis this pattern should be absent for hold trials. Finally, slow trials seem more likely not to have been preceded by much preparation at all, and so considering only a fast subset of trials is a way to try to increase statistical power, as was done in 2.2.

2.3.2 Method

Subjects

Nine subjects, of college age, were tested. Five of the subjects were male. All subjects were informed of the experimental procedures and gave written consent. Subjects received 20 euros fee. Two other subjects were not allowed in the EEG analysis due to an inability to adequately perform the task.

Task

The task was programmed in MEL [150]. Trials consisted of a cue followed 1500 ms later by a stimulus to which one of two responses had to be made. The cues were either a red or green, or blue or gray '*', centered on the screen, presented up to stimulus presentation. Color coding is explained below. The imperative stimuli were white symbols, either a '-' or a ':', centered on the screen, until a response was given. Stimuli subtended around 1 degree visual angle. Responses were either a left- or a right-hand response, given by pressing the keys 'z' or 'm'. If an error was made, subjects saw an '=' sign for the 1000 ms intertrial interval. The size of the stimuli was around 1 degrees visual angle.

Subjects were trained on the day prior to the EEG measurements. The training started with two single-trial blocks of 25 trials. Cues were the same color - red or green - on these trials. Subjects were instructed verbally and through on-screen instructions that the color of the cue specified the correct stimulus - response mapping. The mapping of color to stimulus - response mapping, e.g., "red specifies ':' to left and '-' to right", was counterbalanced over subjects and kept consistent within each subject.

Following these two blocks, four blocks or 25 trials were trained in which the mapping changed during a block. The change was indicated by two new colors for the cue, gray and blue, which signaled subjects to either switch or hold their previous S-R mapping. The meaning of gray and blue cues was counterbalanced over and kept constant within subjects. Red or green start-up cues were given on the first trial of a block, and following an error.

On the experiment day, subjects had electrodes and cap placed (see below) and practiced three blocks of 25 trials, two non-switching blocks and one switching block. Then subjects then performed 12 blocks of 25 trials of the switching condition while their EEG was recorded. Following this set of blocks, subjects performed the same task but now with only 200 ms between cue and stimulus. This task consisted of three practice blocks of 25 trials and six blocks of switch blocks.

EEG measurements and analysis

Reference electrodes were clamped to the ears. Scalp electrodes were placed using an electrode cap. Electrodes Fp1, Fpz, Fp2, F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, Oz, O2 were used. PAS amplifiers (Instrumentation Service Psychology (IDP) of the University of Groningen) and the acquisition program Ada (IDP) were used for data acquisition. The sampling frequency was 100 Hz. The voltage range was 250 μV sampled using 4096 bits, providing a resolution of 0.06 μV. All electrode impedances were kept below 5 kΩ.

Brain Vision was used for segmentation, artifact correction and ocular correction. Time-frequency information was extracted using a wavelet-based approach (Lachaux et al., 1999), as described in section 2.1. The frequencies and σ_f's (in parentheses) were 5 - 16 Hz (1 Hz) in 1 Hz steps, 18 - 30 Hz (2 Hz) in 2 Hz steps, and 35 Hz (2 Hz). Statistical analyses were done in Matlab and SPSS. The false discovery rate procedure [22] was used as described in section 2.1, to select points at specific times and frequencies for further analysis. Only the long CSI condition was used in the EEG analyses. The first four trials of a block, trials on which an error was made, and trials following errors, were excluded from the EEG analyses. Fast and slow trials were defined by a median split.

2.3.3 Results

Behavioral data

The factors cue type (shift versus stay), CSI and change / repetition of cue, stimulus or response were included in a repeated measures MANOVA. The repetition effects were included in separate repeated measures models because of logical interactions, e.g. a cue change and a stimulus change cannot, given a correct response, be followed by a response change.

The following results were found on reaction time. Error trials and trials after error trials were excluded from these data, as were the first four trials of each block.In the response change model (figure 2.21), mean effects were found for CSI (F(1, 8) = 26, p = .001) and cue type (F(1, 8) = 17, p = .003); interactions were found for cue type by CSI (F(1, 8) = 11, p = .01), cue type by response repetition (F(1, 8) = 45, p < .0005) and the three-way interaction (F(1, 8) = 15, p = .005). The results can be described as a larger effect of switching tasks when responses are repeated. Testing the cue type effect separately for the response repetition conditions, a significant effect of trial type on reaction time was found only for response repetitions (for the short CSI: t(8) = 5.5, p = .001 for response repetition and t(8) = .8, p = .4 for response change; for the long CSI: t(8) = 3.3, p = .012 for response repetition and t(8) = .2, p = .8 for response change). So, even in the short CSI condition, no effect of switching was found on RT when the response changed, that is, when the stimulus was repeated but had to be responded to differently. In contrast, when a different stimulus was presented to which the response had to be given that was previously given to the other stimulus, reaction times were slowed. Analysis of the long-CSI condition showed a main effect of cue type (F(1, 8) = 7.0, p = .03) and an interaction between cue type and response repetition (F(1, 8) = 7.8, p = .024).

In the cue change model (figure 2.21), main effects were found for all factors, CSI (F(1, 8) = 24, p = .001), cue type (F(1, 8) = 15, p = .005) and cue change (F(1, 8) = 7.3, p < .027). All two-way interactions were significant: CSI by cue type (F(1, 8) = 7.7, p = .024), CSI by cue change (F(1, 8) = 7.5, p = .026) and cue type by cue change (F(1, 8) = 8.7, p = .019). The three-way interaction showed a trend (F(1, 8) = 5.0, p = .056). Inspection of the plot (figure 1c) shows that the effect of cue type was attenuated when the cue changed. Equivalently, the results could be described as an increase of the effect of cue type given a certain sequence, i.e., the second response in a switch - switch sequence is slower than that in a hold - switch sequence, while the second response in a hold - hold sequence is faster than the second response in a switch - hold sequence. The reaction advantage of the hold - hold sequence was markedly faster in the short CSI condition. Analysis of the long-CSI condition showed main effects of cue type (F(1, 8) = 6.3, p = .036) and an interaction of cue type with cue change (F(1, 8) = 5.9, p = .041).

In the stimulus change model (figure 2.21), main effects were found for all factors, CSI (F(1, 8) = 26, p = .001), cue type (F(1, 8) = 17, p = .003) and stimulus change (F(1, 8) = 26, p < .0005). Interactions were found between CSI and cue type (F(1, 8) = 11, p = .01) and CSI and stimulus change (F(1, 8) = 15, p = .05). The results concerning stimulus changes were due to faster responses for repeated stimuli, regardless of cue type. This effect was smaller for the long than the short CSI (73 ms versus 252 ms). Notably, this type of change was the only change-variable that did not interact with cue type. A separate analysis of the long-CSI condition showed main effects of cue type (F(1, 8) = 7.0, p = .03) and stimulus change (F(1, 8) = 7.8, p = .024), but no interaction.

The same analyses were performed for accuracy. For the response change model (figure 2.22),

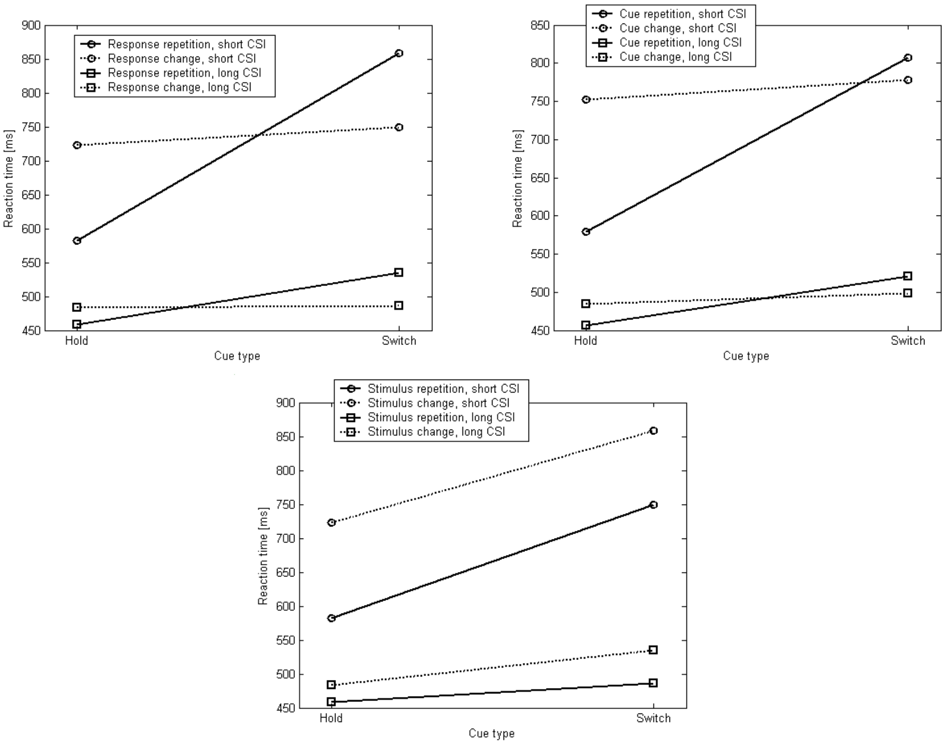


Figure 2.21: Reaction time. From top to bottom: response change, cue change and stimulus change model.

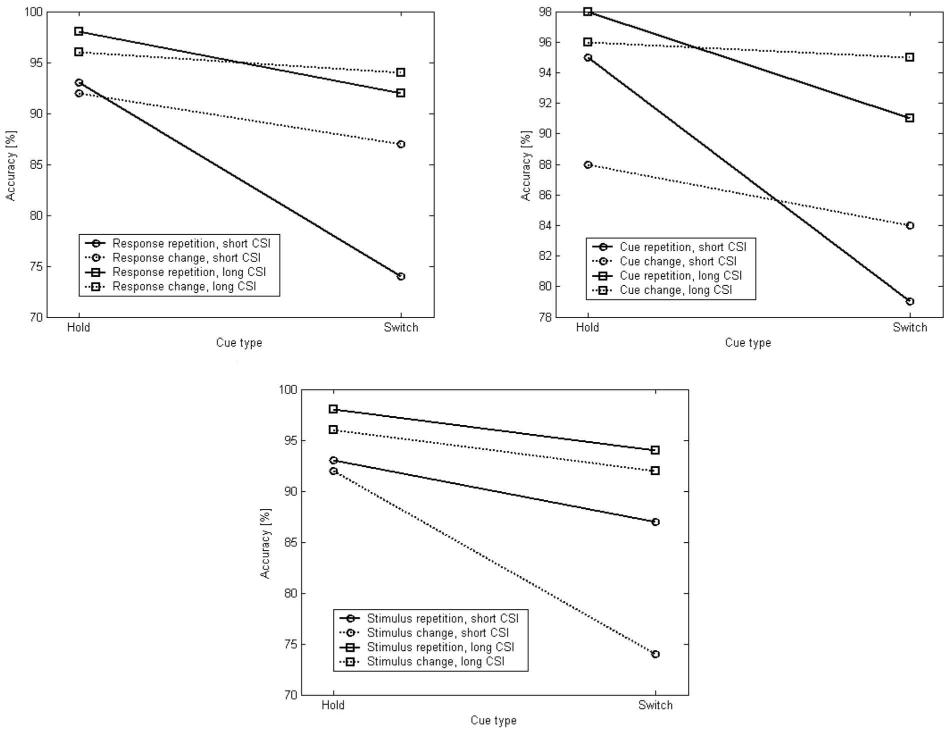


Figure 2.22: Accuracy. From top to bottom: response change, cue change and stimulus change model.

main effects were found only for CSI (F(1, 8) = 9.2, p = .016) and cue type (F(1, 8) = 11, p = .011). Borderline significant interactions were found for CSI by cue type (F(1, 8) = 4.1, p = .078) and cue type by response change (F(1, 8) = 4.7, p = .061). Post hoc tests show that the effect of response change was not significant for either the switch or hold cue types in the long CSI condition. The effect showed a trend for the short CSI, but only for the switch cue types (t(8) = 1.8, p = .11). The large decrease in accuracy in the switch cue, short CSI condition (and the absence of an associated significant interaction) was due to a subset of subjects, the lowest scores being only 20%, 50% and 70% accuracy. The subject with 20 % accuracy had the lowest overall accuracy, but still reached 84% accuracy in the hold cue, short CSI condition, and in the long CSI condition reached 96% accuracy in the hold cue and 84% accuracy in the switch cue conditions. It seems that some subjects, who otherwise seemed to be able and willing to perform the task, had exceptional difficulty with this condition. Analyses restricted to the long-CSI condition showed a significant effect of cue type (F(1, 8) = 17, p = .003) and a borderline significant cue type x response change interaction (F(1, 8) = 3.9, p = .085).

In the cue change model (figure 2.22), the main effects of CSI (F(1, 8) = 11, p = .01), cue type (F(1, 8) = 13, p = .008) on accuracy were significant. The interaction between cue type and cue change was significant (F(1, 8) = 8.1, p = .022) and the interaction between CSI and cue type was borderline significant (F(1, 8) = 4.5, p = .066). The figure shows a greater effect of cue type on accuracy if the cue was repeated, as for the reaction time data. The low accuracy for the switch cue, short CSI was again due to the same subset of subjects scoring badly (50 - 80%) in this condition. In the long CSI condition, the main effect of cue type (F(1, 8) = 15, p = .005) and the cue type x cue change interaction (F(1, 8) = 9, p = .017) were significant, and the main effect of cue change was borderline significant (F(1, 8) = 5.0, p = .055).

In the stimulus change model (figure 2.22), the main effects of CSI (F(1, 8) = 9.2, p = .016), cue type (F(1, 8) = 11, p = .011) on accuracy were significant and the main effect of stimulus change was borderline significant (F(1, 8) = 4.7, p = .061). No interaction was significant. A borderline significant interaction was found for CSI and cue type (F(1, 8) = 4.1, p = .078). Note that the "problem" condition (stimulus changes in the switch cue, short CSI condition) contains the same scores as the response repetitions in the switch cue, short-CSI condition described above. Within the long-CSI condition, the effect of cue type was significant (F(1, 8) = 17, p = .003) and the effect of stimulus change was borderline significant (F(1, 8) = 3.9, p = .085).

Event-related potentials

The ERP's are plotted in subsets of the eight conditions, to allow visual evaluation of the 56 relations. The top plot of figure 2.23 shows the cue-locked ERP's for fast trials, so that preparatory activity should be most clear. The middle and bottom plots show the ERP's for the cue change and cue repetition subsets, respectively.

The most striking result in the fast group is a broader positive peak, in the middle of the cue - stimulus interval, for the cue-change conditions; or equivalently, a negative shift for cue-repetition at that time. At posterior sites, the conditions showed an ordering in voltage, hold - switch and hold - hold sequences having the most and least positive voltage respectively. Repeated measures ANOVA (Huynh-Feldt corrected) was performed on the average voltage over 500 - 900 ms post-cue, for the four plotted midline electrodes, with task switching, cue repetition and response speed as factors. Significance was found for cue repetition (F(1, 8) = 5.7, p = .045), electrode (F(3, 24) = 7.8, p < .008), task switching by cue repetition (F(1, 8) = 5.6, p = .046), response speed by cue

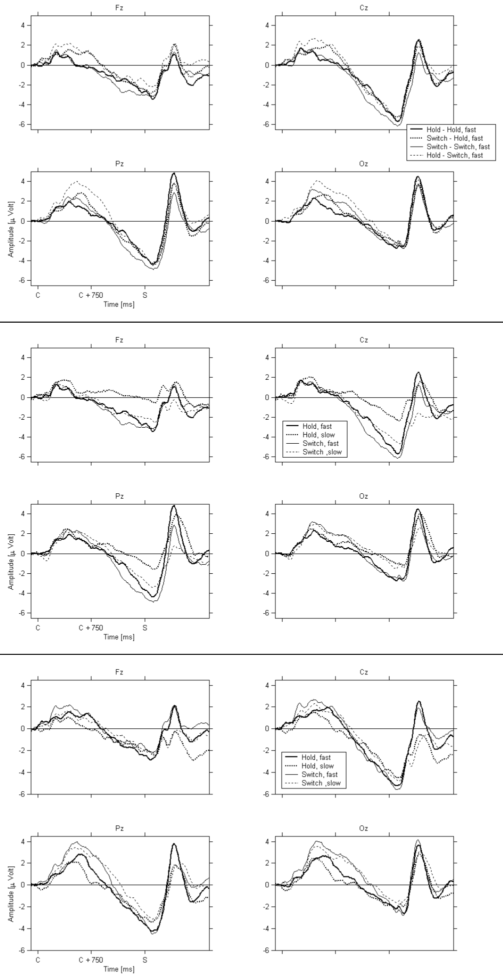


Figure 2.23: ERP, fast conditions (top), cue repetition conditions (middle), cue change conditions (bottom)

repetition (weak: F(1, 8) = 3.9, p = .085), task switching by electrode (F(3, 24) = 5.9, p = .024) and response speed by electrode (F(3, 24) = 15, p = .015). The figures containing subconditions per cue condition (2.23, middle and bottom) show that the interactions are due to greater effects of response speed and task switching when the cue changes, fast and switch trials being more positive than their opposites.

The terminal CNV was tested over the last 100 ms of the cue - stimulus interval. Significance was found for response speed (borderline: F(1, 8) = 4.8, p = .059), electrode (F(3, 24) = 14, p < .0005), task switching by cue repetition (F(1, 8) = 10, p =.012), task switching by response speed (weak: F(1, 8) = 4.0, p = .082), cue repetition by response speed (F(1, 8) = 5.4, p =.048), electrode by task switching (F(3, 24) = 4.7, p =.013) and electrode by response speed (F(3, 24) = 3.5, p =.046). The visually dominating feature late in the cue - stimulus interval is the weak CNV for slow hold trials in a hold - hold sequence. A potentialy important feature of the data is that effects on the terminal CNV may be obscured due to differences in the height and width of the middle-period positive peak. Towards the end of the interval in the cue change conditions, the curves for switch trials can be seen to have a greater, negative slope.

Amplitude

Effects in the amplitude data were analyzed by using FDR on the three contrasts fast - slow, cue change - cue repetition and switch - hold, both on all electrodes and on the midline selection Fz, Cz, Pz and Oz. Each contrast was tested separately for each of the four combination of the other variables. No effects were found at a 5% false discovery rate. At a 10 % rate, restricted to the midline selection, differences were found for the cue change - cue repetition contrast, preceding fast hold trials, in the frequency bands 6, 8 and 15 Hz. Of these effects, those at 8 and 15 Hz were found to be due to baseline differences. Differences were also found between fast and slow trials, preceding cue-repetition switch trials (that is, switch trials following a switch trial), in the frequency bands 6 and 18 Hz. The cut-off t-values were 6.6 and 6.9 for the cue repetition and response speed contrasts, respectively.

In the 6 Hz band (figure 2.24, top), on cue-repetition switch trials, the fast - slow difference is due to the lower amplitude at Cz around 900 ms post-cue for fast trials. This appears to be due to a delayed peak for slow trials. On fast hold trials, the cue change - cue repetition difference is due to higher amplitude for the cue change condition (or switch - hold condition) at the end of the preparation interval, at Fz and Cz. At 18 Hz (figure 2.24, bottom), the fast - slow difference, given a switch - switch sequence, was found at around 1 s post-cue, due to a peak in amplitude for slow trials.

Phase locking

Over the pairs between electrodes F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, and Oz, no significant differences were found using FDR at a 10 % rate, for the set of contrasts also used for amplitude data. To simplify the data, they were clustered into frontal (F3, Fz, F4), central (C3, Cz, C4) and parieto-occipital (P3, Pz, P4, Oz) groups. Only fast trials were considered. Inspection of the data showed time - frequency regions in which conditions diverged, in the theta and alpha bands.

In the theta band (5 - 7 Hz), shown in figure 2.25, around 400 - 700 ms post-cue, a low frontal-central PLV was visible for the hold - hold condition. This was tested using repeated measures ANOVA (Huynh - Feldt corrected), that showed a task switching by cue repetition by

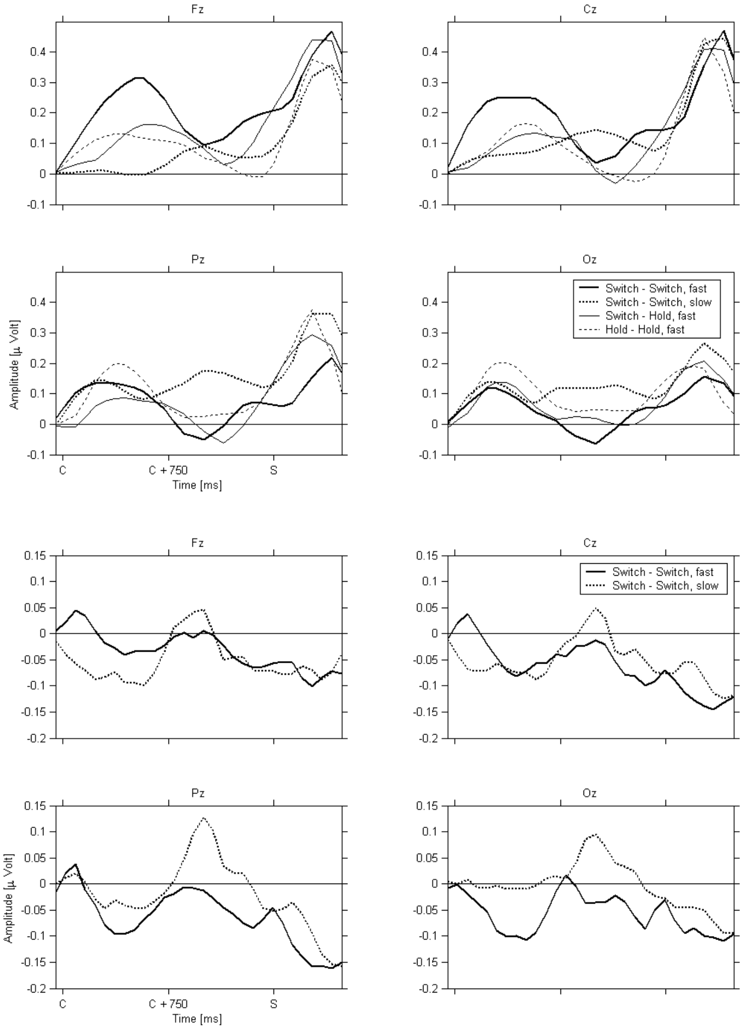


Figure 2.24: Instantaneous amplitude, 6 Hz (top) and 18 Hz (bottom)

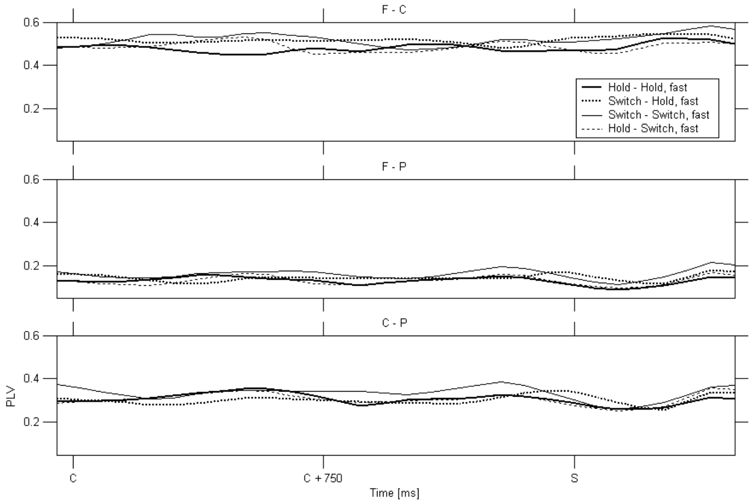


Figure 2.25: Phase-locking values, 5 - 7 Hz

pair interaction (F(2, 16) = 7.1, p = .017). The only other effect was of pair (F(2, 16) = 284, p < .0005), although the pair by task switching (F(2, 16) = 4.3, p = .055) and pair by cue repetition (F(2, 16) = 3.2, p = .09) interactions showed trends. In the second half of the cue - stimulus interval, frontal- and central-parietal phase-locking was high for the switch - switch condition. ANOVA on the 800 - 1300 ms post-cue period gave significant differences for pair (F(2, 16) = 5.1, p = .05) and task switching by pair (F(2, 16) = 5.1, p = .05). The spatial patterns associated with the switch - switch condition, relative to the average of the other sequences, over the 800 - 1300 time period are shown in figure 2.26. Notably, right-frontal phase-locking is low and posterior, especially interhemispheric central - parietal, phase-locking is high for the switch - switch condition.

In the alpha band (8 - 12 Hz), the most apparent feature was a different PLV time course for the fast hold - hold condition, which was low in the first half of the cue - stimulus interval and then rose, especially for central - parietal phase locking. The same time periods were tested as for the theta band. Over 400 - 600 ms post-cue, only the effect of pair was significant (F(2, 16) = 137, p < .0005). Over 800 - 1300 ms post-cue, significance was found for pair (F(2, 16) = 155, p < .0005) and the task switching by cue repetition interaction (F(1, 8) = 12, p = .009).

2.3.4 Discussion

Even though trials were separated by a 750 ms intertrial interval, an explicit cue and a 1.5 s cue - stimulus interval, robust switch costs were found of around 30 ms. The switch - switch sequence was most difficult, in terms of slowness, errors and the effect of introducing the short cue - stimulus interval condition. Note that stimulus - response associations in that condition have had less opportunity to be strengthened than in hold - switch sequences, despite suggestions that such associations may cause switch costs [247]. This suggests that other factors are relevant to switching behavior, at least in this design. Subjectively and anecdotally, switch - switch sequences required the most effort, and felt potentially confusing. Hypothetically and paradoxically, the lack of a well-established task set (i.e. stimulus - response associations) may make it more difficult to switch, because the relative stability of the tasks may provide a cue as to which task is no longer

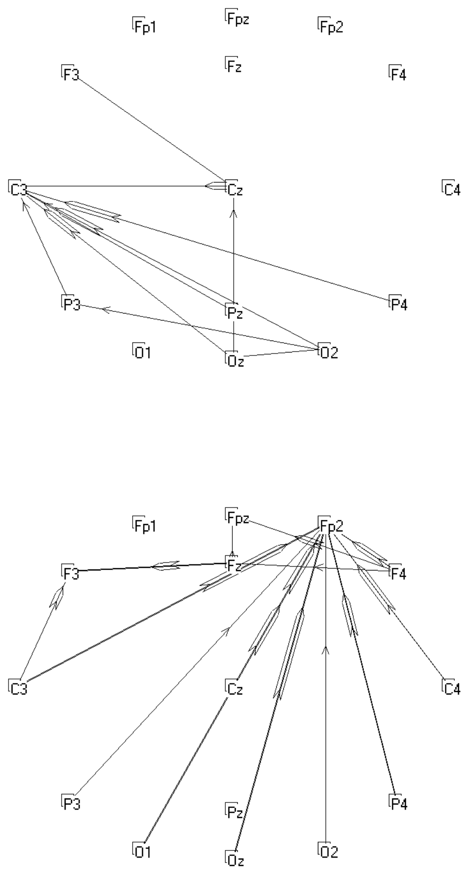


Figure 2.26: Phase-locking pattern of switch - switch trials relative to the other conditions, 5 - 7 Hz, positive (top) and negative (bottom) differences. Plotted values were selected based on being extreme within the data set (z > 2), mean and variance being calculated over the set of positive difference-values over time and electrode pair. This plotting method emphasizes spatiotemporal patterns in the data.

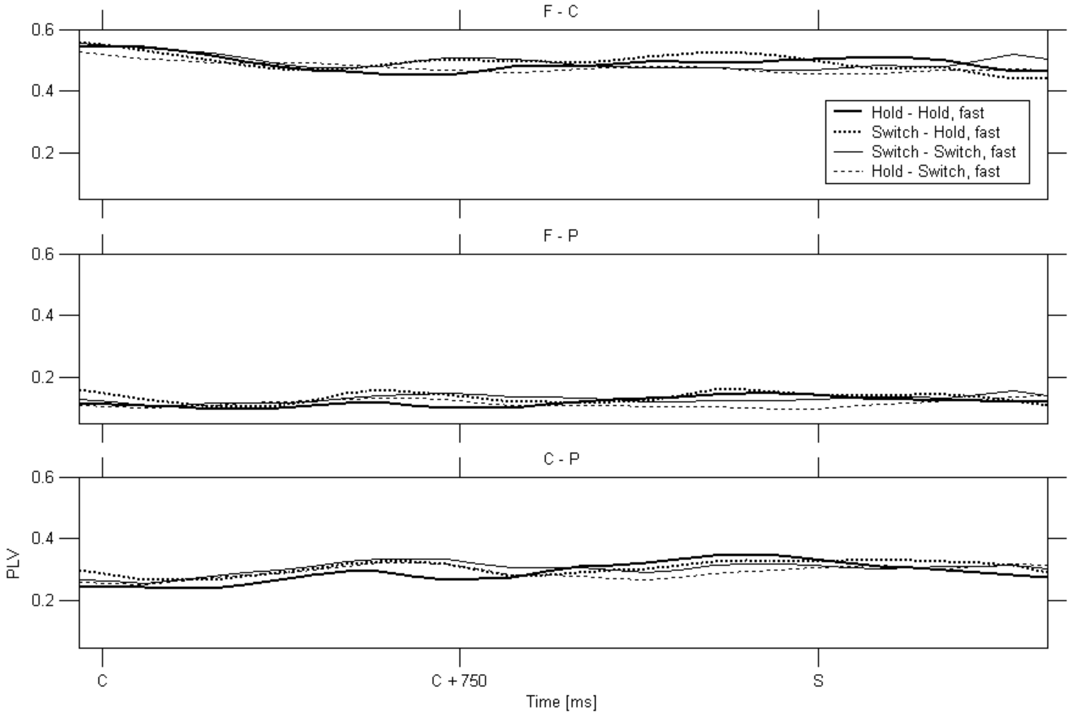


Figure 2.27: Phase-locking values, 8 - 12 Hz

irrelevant. Relative stability could even be the characteristic used to select tasks when switching, as discussed in section 3.

A further behavioral effect that may be interesting in terms of further study is the possible attenuation of switch costs when the responses differ on the subsequent trials. However, in that condition the stimulus always repeats, so the condition is confounded. The confound leads to two interpretations. First, that attempting to repeat a response to a different stimulus re-triggers an error signal, defined by the previous task rules concerning that response. The unused response would then have a weaker association within the task rules. Such an interpretation would emphasize the effect of stimulus - response associations [247] (or, equivalently, sensorimotor integration [25] (section 1.4.3), or "event files" consisting of of perception - action bindings [88]). Alternatively, the physical presentation of a stimulus could initiate the overwriting of the associated response rule, as part of exogenous switching [197]. If the previously-used rule produces most interference, then stimulus-repetition would by hypothesis provide a more relevant external drive than stimulus-change (in which case the response to be given remains part of a non-overwritten rule).

The short cue - stimulus interval condition cannot be directly compared with the long-interval condition, as it was always presented at the end of the session and was performed with less training. The condition was initially only included as a check on whether the cue - stimulus interval had any effect at all, which was clearly the case. The condition may be interesting as an apparently ethically responsible "shock" condition, in which, apart from the decreased opportunity for preparation, perhaps fatigue and the loss of the comfort of knowing the task well must be overcome. Note that the condition had been announced beforehand. Although all subjects were generally able to deal with the condition, the switch - switch sequences especially showed a large performance decrease. Such sequences also showed a number of effects on physiological measures, as described below.

The presence of cue-locked switch - hold differences replicates previous findings [201], in which the post-cue peak was localized in ventromedial and dorsomedial prefrontal cortex. The peak was interpreted to reflect intentional set switch initiation, and was emphasized to occur prior to the availability of task stimuli. Three further patterns in the ERP's stood out. First, there was an increased post-stimulus positive peak following changed cues, broadly distributed in time and location but most strong at occipito-parietal sites around 600 ms post-stimulus. Second, following cue changes, the differences between switch and hold, and between fast and slow conditions were larger than following cue repetitions. Third, slow hold - hold conditions showed a diminished CNV relative to the other conditions. So, all three variables appear to be important in explaining pre-stimulus activity.

Increased post-cue positive peaks were found in two other cued paradigms, described in sections 2.6 and 2.5. In both cases, the peak was found when more information was provided by the cue. So, from parsimony, the peak here is interpreted as an increase in information processing that is for some reason evoked by a changed cue. Note that, from the task requirements, cues would not be expected to be dependent on trial sequences. Possibly, the sub-task of preparation - task A being " hold" and task B being " switch" - is also subject to task-switching phenomena. The cue-change effects may then reflect switching at a higher level of control than the task (as in the cascade of control in frontal cortex [119], described in section 1.3.2).

The amplitude time course in the theta-band was different than expected. Instead of a longer period of theta-band amplitude, slow switch trials showed a delay in the post-cue peak relative to fast switch trials. The trend was found only for the switch - switch sequence, which was, as described above, the most difficult condition. Nevertheless, that a switch-related effect was found in terms of the timing of a transient peak in theta-band amplitude is globally in line with the results of the modality-switching experiment (section 2.2). Finally, an 18 Hz peak at Pz around 900 ms post-cue, exceeding baseline values, was found for slow relative to fast cue-repetition switch trials. The peak may reflect, based on the idling and holding hypotheses described in section 1.6, some kind of internal freezing in an attempt to deal with a confusing switch - switch sequence.

The phase-locking data appear to support the idea of controlled sensorimotor integration involving phase coding in the theta band (section 1.4). Frontal-parietal and central-parietal theta-band phase-locking is high for the fast switch - switch sequence, over the second half of the cue - stimulus interval. Note that, again, it is the subjectively difficult switch - switch sequence that involves distinct preparatory activity. Frontal - central theta-band phase-locking, in contrast, is relatively low for this sequence. Early post-cue frontal-central phase locking is low for the fast hold - hold condition, and it is this cue which involves neither preparatory- or task-level switching. The fast hold - hold cue condition also showed high central - parietal alpha-band phase locking late in the cue - stimulus interval, which may be a reflection of little preparation being needed in this condition, other conditions having greater alpha-band ERD.

In conclusion, various measures showed effects of and interactions between cue types, task sequences and response speed. Cue switching, or the sequence of preparation-tasks (e.g. hold - switch), appears to be important, both in terms of early activity and of interactions with the effect of task switching. Further research is needed to determine whether cue-related effects are due to cue-stimulus or cue-task sequence effects. Perhaps most important in relation to the other task-switching experiments described in this text, switch - hold effects were found, for cue repetition, in both theta-band amplitude time course and phase-locking. In relation to the motor preparation tasks, the 18 Hz peak in the slow switch - switch condition may be interesting. In the choice - nogo task (section 2.6), a similar effect - a transient lateralization in beta-band ERS - was found when go probability was low. In both cases, a transient cue - stimulus interval burst of beta ERS was found in conditions in which a lower response tendency could be assumed.

2.4 Switching between response hands

Article (T. E. Gladwin, B. M. 't Hart and R. de Jong) in preparation.

2.4.1 Introduction

In the experiment described in section 2.1, subjects switched between tasks that differed on two dimensions: the relevance of the visual versus the auditory modality, and the hand to respond with. The tasks were presented in an alternating runs paradigm, with an AABB scheme. Three types of lateralization in the EEG were found that were related to preparing to respond with the left versus the right hand, especially if the hand had to be switched. First, the lateralized readiness potential (LRP [131] [37]) could not be shown to lateralize in the direction associated with the upcoming response hand. A greater decay was found in the response - stimulus interval preceding fast switch trials than any other condition, i.e. slow switch trials, fast hold trials and slow hold trials. Second, a positive motor-related amplitude asymmetry (MRAA; this is a lateralization measure defined as the LRP but using amplitude data) arose in the same interval, signifying a relative desynchronization over the hemisphere contralateral to the upcoming response hand. This pre-stimulus MRAA was found in the mu and beta bands, did not differ for fast and slow trials and, in contrast to the LRP, reflected clear pre-stimulaus lateralization. Finally, the hemisphere associated with the upcoming response hand showed increased pre-stimulus phase-locking, especially with frontal areas, specifically on switch trials.

The motor-related results were found in a complex task in which it was not certain how subjects prepared in terms of stimulus - response mappings: e.g., subjects could switch between modalities, inhibit the irrelevant response hand or change the associations between stimuli and responses. The absence of modality-related effects spoke against preparation-via-modality, and the finding of measurable modality-related effects in modality-switching (section 2.2) provided this null-finding with more weight. The lateralization effects showed that the hand of the upcoming task set was associated with pre-stimulus motor activity, but it could be the case that such activity would be different when only hand could be used to prepare. For instance, perhaps the only decay-like pre-stimulus LRP is not a feature of switching between hands, but of some consequence of the hand - modality combination.

The present study aims, first, to replicate the potentially interesting motor-related findings of the previous study in a simplified experiment, and second, to compare the pattern of motor-related lateralization between the complex hand - modality switching task, and a hand-only switching task. The results will be extended by the inclusion of EMG channels on the muscles of the left and right arms, so that EEG - EMG phase locking can be studied. As described in section 1.6.3, EEG - EMG phase locking has been found in the beta band, and is apparently related to holding stable postures [80]. Such phase locking has been shown to change on a within-trial time scale [110] [13], and so may play a role in preparation in a task switching context.

2.4.2 Methods

Subjects

Sixteen right-handed subjects, of college age (mean 25 years old), were tested. Seven of the subjects were male. All subjects were informed of the experimental procedures and gave written consent. Subjects received a fee for participation.

Task

A version of the alternating runs task [197] task-switching task, implemented in MEL [150], was used. In this task, visual stimuli were presented for 250 ms in one of four cells in a two by two matrix. The stimuli were the letters X and O, subtending around 1 degree visual angle, which were coupled to the index and middle finger respectively. Responses were given through a keyboard, using the 'z', 'x', '.' and '/' keys. The top and bottom two cells were assigned to different hands, counter-balanced over subjects. In this way, subjects switched hands when crossing from the top to the bottom or the bottom to the top of the matrix.

After a response, there was a delay of one of two lengths (500 or 1000 ms) prior to the next stimulus. The visual stimuli were presented in the cell clockwise to the previous one. Intervals were varied per trial, within blocks. The proportions of the preparation intervals were 1 / 3 and 2 / 3, for 500 and 1000 ms respectively. The higher percentage of long intervals was chosen because only these trials would be used in the analysis. The shorter intervals were included to keep subjects' attention on the task during long preparation intervals.

Subjects were explicitly instructed to use the delays to prepare for the next task. They were also instructed to respond as quickly and accurately as possible.

Procedure

Subjects were trained on this and two other tasks for around 45 to 60 minutes. The other tasks are described in sections 2.5 and 2.6. Training involved performing runs of each single-task and the mixed task blocks, each block containing 15 trials. Errors were indicated by a beep, during training only. Training ended when at most one error was made, and the switch cost on mixed blocks was less than 50 ms. Training was followed by electrode placement. Three refresher blocks of 20 trials were provided before the experiment: two single-task and one mixed block. This was followed by eight mixed blocks of 75 trials each. Subjects were instructed to take as much time as they needed to rest between blocks.

EEG and EMG measurement

Ag-AgCl electrodes were used for both EEG and EMG recordings. The following EEG electrode positions were measured: Fp1, Fpz, Fp2, AFz, F3, Fz, F4, FC3, FC1, FCz, FC2, FC4, C3, Cz, C4, CP3, CP4, P3, Pz and P4. EEG impedance was kept below 5 kΩ. The sampling frequency was 250 Hz. The voltage range was 500 μV sampled using 4096 bits, providing an EEG resolution of 0.12 μV. EMG was recorded from electrodes positioned lengthwise along the lower arm, at around one and two thirds of the length of the left and right flexor digitalis superficialis. The difference between the two channels was taken, per arm, and this signal was rectified to produce the EMG signal. EMG impedance was kept below 10 kΩ.

2.4.3 Data analysis

Statistical analyses were done using Matlab [141] and SPSS [219]. Brain Vision [26] was used for visual inspection and artefact rejection, segmentation and ocular correction. A wavelet analysis approach [124] was used to further analyze the EEG data, using the program Gamma [66]. For further details, see section 2.1. The frequencies from 5 to 38 Hz were chosen as mean frequencies, with a 1 Hz uncertainty parameter (standard deviation in frequency, σ_f) up to 16 Hz, and 2

Hz for higher frequecies. The distance between frequencies was equal to the standard deviation. Higher-frequency activity was sampled at 40 and 80 Hz, with standard deviations of 5 Hz.

For time-frequency analyses, t-scores were computed for all electrodes, combinations of frequencies (for phase measures), frequencies and time points, and these multiple tests were analyzed using the false discovery rate (FDR) procedure [22]. This procedure controls the proportion of rejected null hypotheses which are rejected falsely when multiple differences are being tested. A false discovery rate with a two-sided error rate of 5 % was chosen.

Lateralization measures were calculated as described in section 2.1: (left - right hemisphere activity, given left-hand responses) - (Left - right hemisphere activity, given right-hand responses).

2.4.4 Results

Behavioral data

The mean reaction times were 541 ms for alternation and 453 ms for repetition trials, t (15) = 5.5, p = .000. The mean accuracies were .93 and .96, respectively, t (15) = 2.9, p = .011.

Event-related potentials

Effects on the mean voltage of the ERP on the midline electrodes Fpz, Fz, Cz, Pz (figure 2.28) were tested at the end of the preparation interval, between 100 ms pre-stimulus and stimulus presentation. Repeated measures ANOVA with Huyn-Feldt correction was used. The increased negativity between alternation and repetition trials was significant (F (1, 15) = 15.2, p = .001), as was the factor electrode (F (3, 45) = 14.7, p =.000) and the interaction electrode by trial type (F (3, 45) = 5.9, p =.01). The interaction is due to a larger alternation - repetition difference centrally than at frontal or parietal electrodes. Note that, due to the alternating runs design, the baseline forms a problem for ERP's because the preparation interval starts immediately after the previous response, and the baseline for switch and repetition trials is confounded with the preceding trial type.

The LRP (figure 2.29) showed no significant difference between trial types (F(1, 15) = 1.6, p = .2), tested in the same period. As in the hand - modality switching experiment, switch trials do not show pre-stimulus lateralization related to the upcoming response hand, while a residual lateralization appears to be present for repetition trials.

Amplitude

The midline electrodes Fpz, Fz, Cz, Pz were tested for alternation - repetition differences. FDR only marked differences as significant around responses, in the theta band, when repetition trials showed higher theta amplitude over parietal and central areas (figure 2.30). The MRAA did show clear preparatory effects (figures 2.31, top and middle plots). For alternation trials, positive mu and beta band lateralization occurred from around 500 ms into the response - stimulus interval. The positive values reflect lower amplitudes, i.e. greater ERD, over the hemisphere contralateral to the upcoming response hand. Mu and beta lateralization was also present but less extensively on repetition trials. For repetition trials, a negative theta-band lateralization occurred immediately after the response. The negative sign implies higher amplitudes over the just-used (and so also upcoming) response hand. The differences in lateralization between alternation and repetition trials were significant, as shown in figure 2.31, bottom. The figure shows the FDR results of the

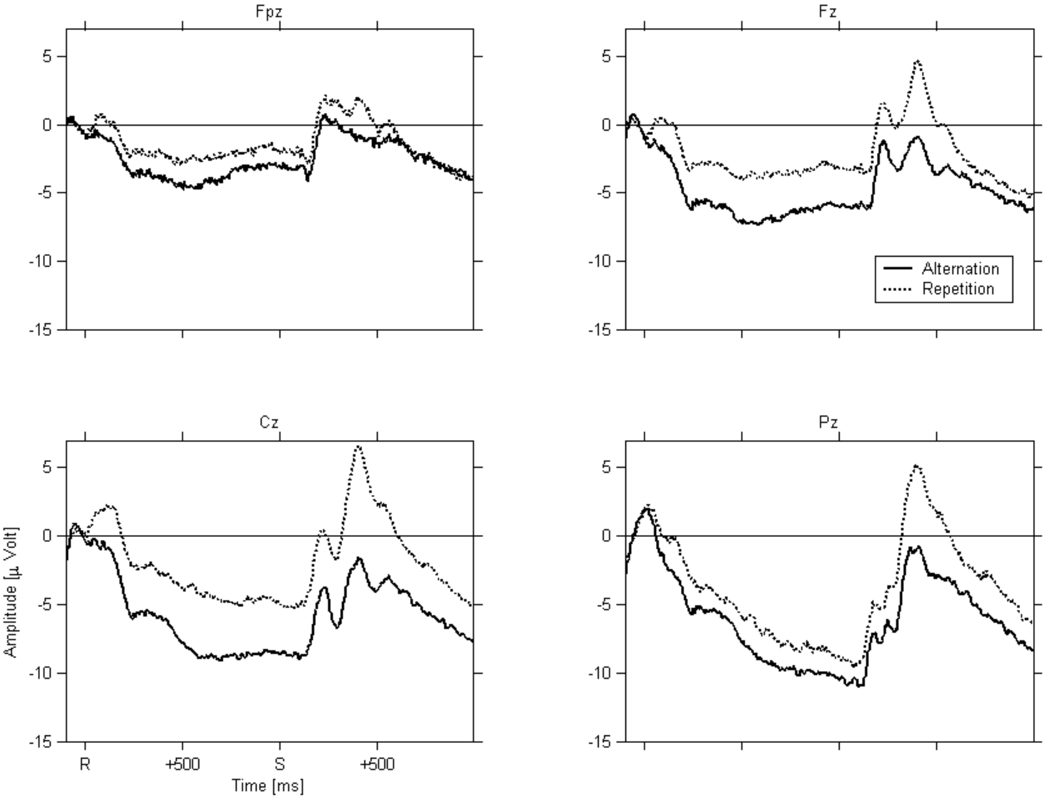


Figure 2.28: Event-related potentials.

contrast between the MRAA for alternation minus that for repetition trials. The positive values in the beta band towards the end of the response - stimulus interval indicate that the MRAA was more positive for alternation than for repetition trials at those time - frequency points. The early negative values in the theta band indicate that the positive MRAA in repetition trials was selective to that trial type. Time course for these frequency bands are shown in figure 2.32. The time courses show a reversal for the early theta-band lateralization effect for alternation and repetition trials, although as described above only the positive lateralization for repetition trials was significant. In the mu band, both alternation and repetition trials showed a rise starting around 500 ms post-response and continuing past stimulus presentation. The beta band showed a pre-stimulus peak for alternation but not repetition trials.

Phase-locking, scalp electrodes

No main effects of alternation versus repetition were found on PLV. Left versus right response hand did show significant preparatory differences for alternation trials. Preceding alternation trials, the hemisphere of the motor cortex that would be relevant after the preparation interval showed broad increases in beta-band phase-locking (figure 2.33), which were absent for repetition trials.

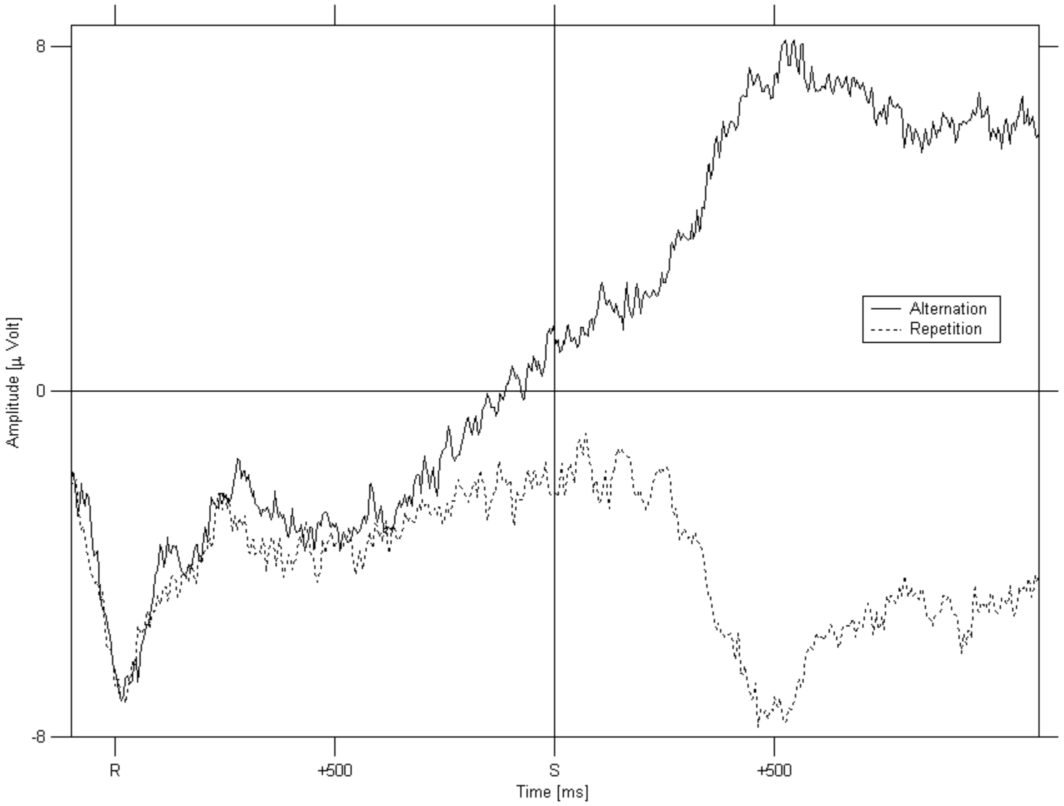


Figure 2.29: Lateralized readiness potentials. The LRP's are shifted so that the zero line lies between the post-stimulus response peaks. While this is only a rough approach to determining a zero-point, the pre-stimulus LRP's, especially in comparison to the mu- and beta-band MRAA time courses, only appear to reach a zero-level, rather than pre-stimulus lateralization, during a hand switch. More sophisticated methods of estimating the true zero-point of the LRP's (in preparation) support this characterization.

Phase-locking, EEG - EMG

Figure 2.34 shows the theta-band (5 - 7 Hz) time courses for EMG - EEG phase-locking values. During response, the PLV is high between EEG channels, especially over the contralateral hemisphere, and the EMG channel of the arm being used. The PLV is highest for the contralateral parietal channels. The pattern was tested using repeated measures Huyhn-Feldt corrected ANOVA, over the 100 ms around response, and for the twelve plotted channel-pairs. Hand and alternation - repetition were used as factors. Significant effects were found for hand (F(1, 15) = 5.7, p = .031), alternation - repetition by pair (F(11, 165) = 2.5, p = .017), and the three-way interaction (F(11, 165) = 23.7, p = .000). No consistent effect was found in the alpha band. The beta-band (18 - 24 Hz) PLV time courses show a preparatory effect, in which the contralateral central electrode shows high PLV's with the EMG channel of the arm not to be used (figure 2.35 . The effect is strongest and most consistent for alternation trials. This effect was tested as in the theta-band, over 300 -

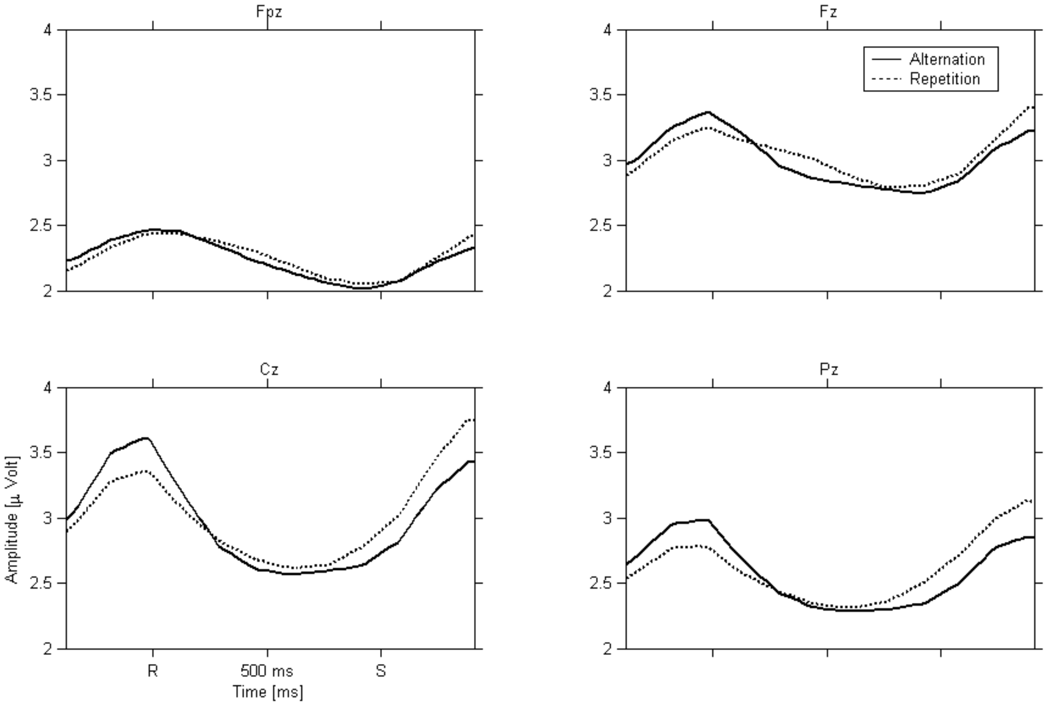


Figure 2.30: Theta band amplitude

600 ms into the response - stimulus interval. Significance was found for pair (F(11, 165) = 3.1, p = .002), hand by pair (F(11, 165) = 5.0, p = .000) and the three-way interaction (F(11, 165) = 4.4, p = .001).

2.4.5 Discussion

Preparatory motor-related lateralization was found on amplitude and phase-locking. Amplitude lateralization was found for the theta, mu and beta bands. For the mu and beta bands, ERD was greater over the hemisphere concerned with the upcoming response hand, from around 500 ms post-cue. The theta-band showed higher amplitudes over contralateral central channels at the start of the response - stimulus interval, for repetition trials. The lateralization of theta- and beta-band amplitude showed significant interactions with the alternation - repetition contrast. The early theta-band lateralization, as it reflects increased activity over relevant motor cortex just after the response, is in position to be related to evaluating feedback. Although speculative, this would indicate a potentially interesting difference between alternation and repetition trials. If the contralateral increase in theta activity should be interpreted as some kind of error sensitivity, then error detection and learning would be predicted to be impaired following a switch trial. A hypothetical origin of the beta-band lateralization is the modulation of the beta rebound, the increase of beta amplitude activity following responses (section 1.6). The suppression of this beta rebound may bias the response tendency towards the hand just used to respond, while letting it occur, or strengthening it, could be used to help switch response hands by inhibiting the previously used one. The widespread beta-band phase-locking between frontal and left or right central and

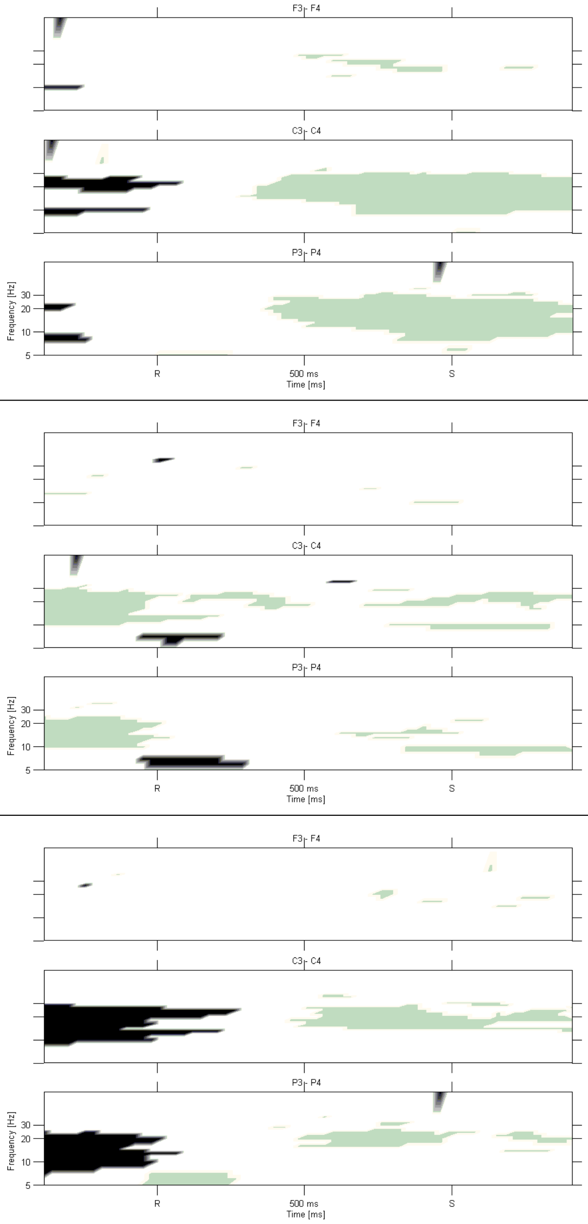


Figure 2.31: Lateralized amplitude, alternation trials (top), repetition trials (middle), alternation - repetition (bottom)

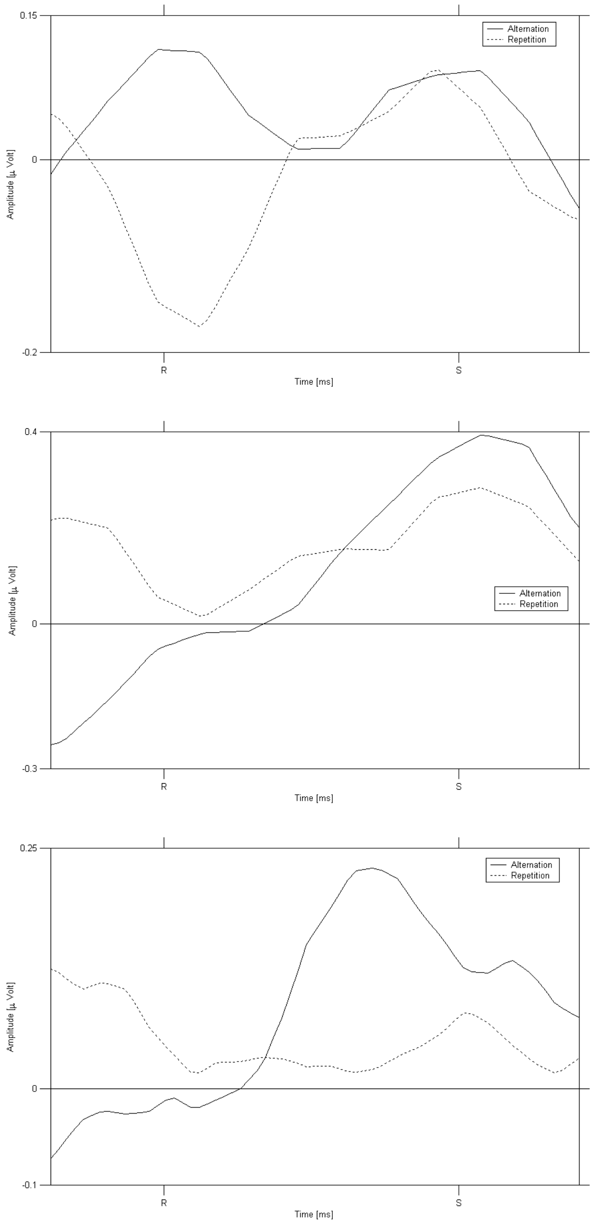


Figure 2.32: MRAA time courses, for frequency bands 5 - 7 Hz (top), 8 - 10 Hz (middle) and 18 - 24 Hz (bottom).

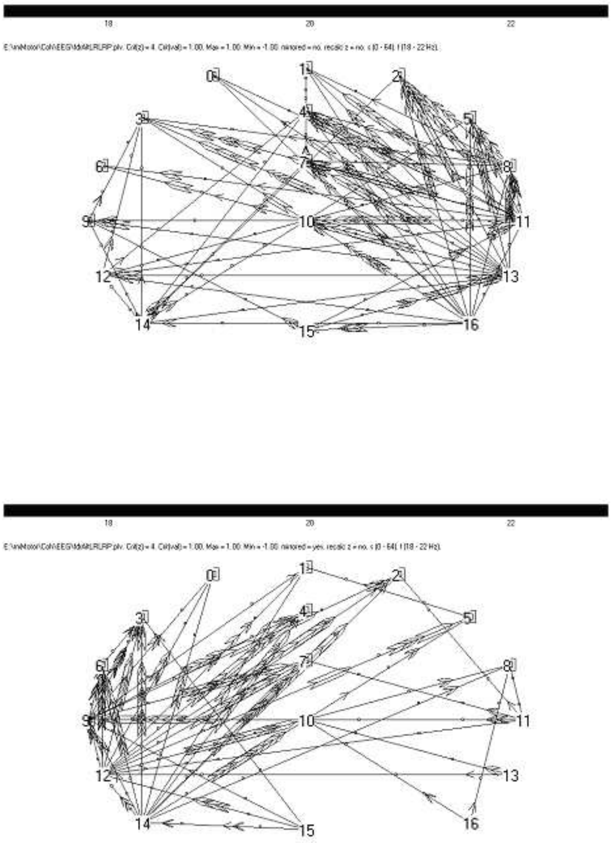


Figure 2.33: Phase-locking values for the left minus right hand contrast preceding alternation trials, positive (top) and negative (bottom) significant values. The plot should be read as follows. Periods of significant datapoints with a positive sign are represented by the arrows on the line drawn between the involved electrodes. The begin- and end-times of these periods are represented by the point and end of the arrow on the line. The arrow points in the direction of time, so if the arrow is close to the region it points to, the period of significance occurs near the end of the trial. The two small dots on each line represent the times of response and stimulus.

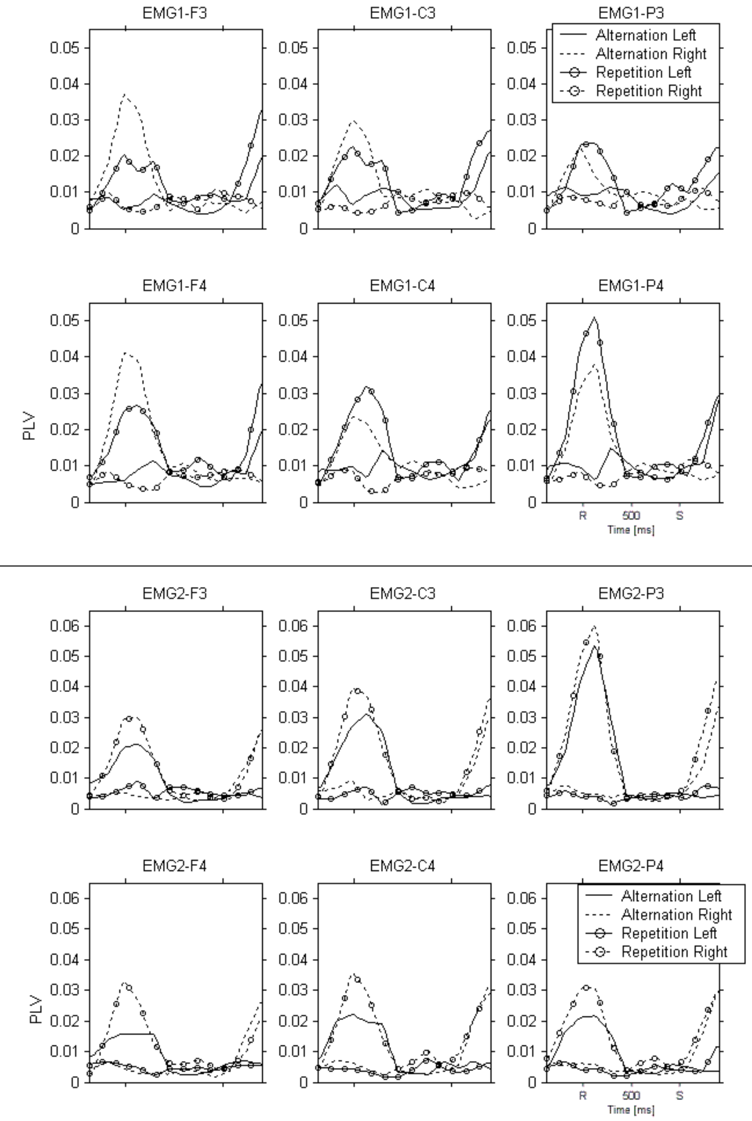


Figure 2.34: EEG-EMG theta-band phase-locking values, with the left arm (top) and right arm (bottom)

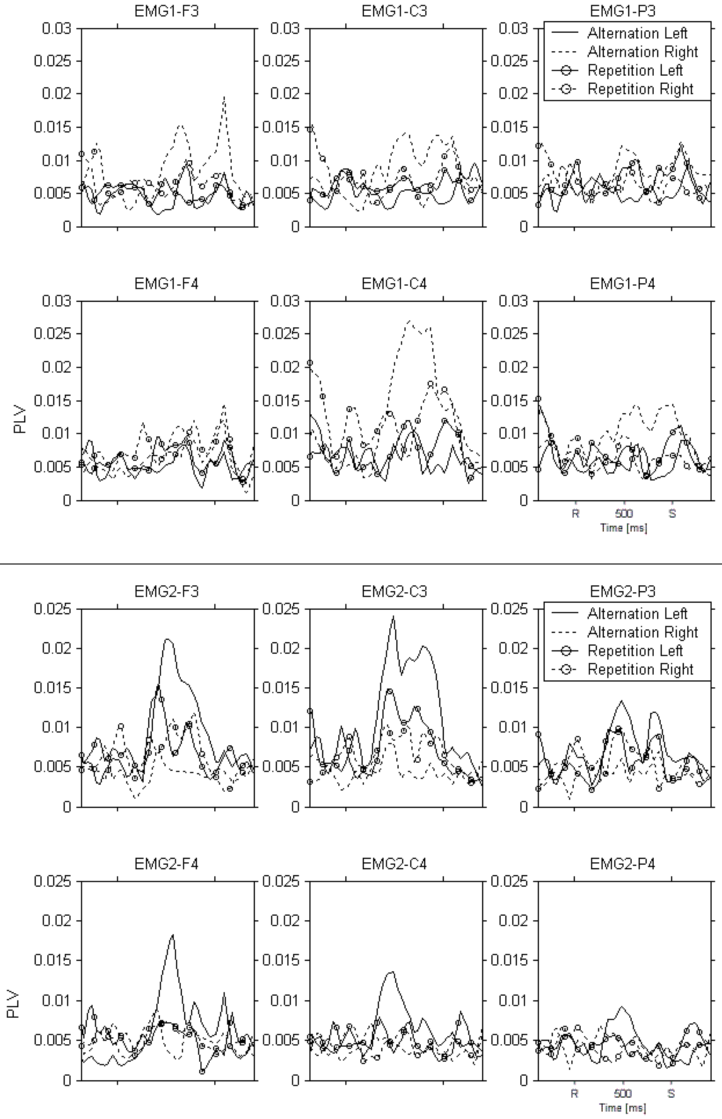


Figure 2.35: EEG-EMG beta-band phase-locking values, with the left arm (top) and right arm (bottom)

parietal areas is consistent with an influence of frontal cortex on posterior areas when working with memory, although of course the nature of this influence or even its directionality is not provided by the data. No alternation - repetition difference was found for the PLV.

The results provide a replication of the conspicuous patterns of beta-band motor-related lateralization, in which ERD and increased phase locking arise during the response - stimulus interval, found when subjects had to switch between both modality and hand (section 2.1). Further, the contrast of an apparently only decaying LRP with lateralizing mu- and beta- (for alternation trials) band MRAA was found in the present, hand-only switching task. So, the motor-related pattern found for hand - modality switching is not specific to the situation in which task sets also differ on modality. Together with the lack of modality-related effects that could be found when subjects switched between modalities, the results support the suggestion that preparation in the complex hand - modality task was based on switching between response hands. Whether this motor-based preparation is due to conscious, strategic or voluntary choices of subjects seems to be an interesting avenue for further study. To allow detailed comparisons including effects of response speed, a within-subject design could be used in which the full mixture model approach is also used for hand-only and modality-only switching. Further, instructions for or variations to the complex task could be varied to study whether subjects can voluntarily change the way they prepare. Subjects could simply be instructed to shift their attention between modalities and not prepare responses. Alternatively, the difficulty of discriminating stimuli could be manipulated to try to force attention to sensory input.

The previous findings are extended by the inclusion of phase-locking data with the left and right arms' EMG activity. Again, the beta band showed preparatory effects related to hand and switching, now with contralateral EEG phase-locking, in the beta band, with EMG activity of the arm that must not be used for the upcoming trial. This is in agreement with the idea that corticomuscular beta band activity plays a role in postural stability (section 1.6.3). Preparation would then seem to involve reducing the likelihood of responding with the irrelevant hand. Further study is needed to determine whether such inhibition is the goal, in terms of the control of underlying causal mechanisms, of preparation, or only an epiphenomenal consequence of, e.g., cortical processes.

Alternation trials showed lower theta-band amplitude post-stimulus. Whether or not this effect is phase-locked to the stimulus (and could therefore be described as a P3 component), it could be hypothesized that it reflects a slower or somehow less efficient integration of stimulus information into a sensorimotor framework such as that provided by, e.g., a hippocampal theta-band reference oscillation (see section 1.4).

The present results suggest that patterns of rhythmic activity in the beta band are part of the way information about future response requirements is communicated, from the moment that the memory of the upcoming trial is retrieved, to stimulus presentation. This communication must at some point take the form of a neural state into which stimulus information can be integrated such that the task is correctly performed. Although the conjunction between rhythmic neural activity and task performance and demands seems strong, neither the cause nor computational relevance of this association is yet clear. Future research will hopefully reveal what the relationship is between rhythmic activity and preparatory states of the brain and the rest of the nervous system.

2.5 Sequence cueing

2.5.1 Introduction

Other sections have described experiments in which subjects prepared simple movements or rules for movements. The present study is concerned with preparation for motor programs, in particular movement sequences. A sequence such as "wiggle the index finger, then shake the wrist" can be described as a recipe, from which movements can be read. Such a recipe is called a motor program [199], which is usually considered to be a metaphorical representation of complex movements in the brain, similar to perceptual schema's. A schema is a generalized representation of a class of stimuli or movements, extracted from the experience of instances belonging to a defining class [183]. Once learned, a motor program, or other kind of schema, can be used to recognize or generate instances. The motor program concept is considered here to primarily serve to define the contours of unknown organizational principles of the mind, as has been argued elsewhere [221].

When subjects choose between movement sequences of varying lengths, the time before the first response, and between subsequent responses, increases with sequence length [199]. Further, when subjects have to choose between sequences of different lengths, initiating the shorter sequence was still slowed when the other sequence was longer. Finally, decisions between sequences are faster when the sequences are similar (e.g. the same finger sequence but for the left and right hand). The results have been explained, or at least the behavioral pattern requiring explanation was clarified, by the motor-program editor model [199]. In the model, preparing a motor program is decomposed into preparing a sequence of subprograms. The subprograms are partially specified elements in the response sequence, and contain the shared features of the possible choices. When the information for the response decision becomes available, the unshared motor features are specified. Reaction time is a consequence of how many features must be specified by the imperative stimulus. The behavioral data and model help characterize the (temporal) organization of movements. However, many of the terms remain badly defined. Expressions such as "specifying a movement feature" make sense when a person is imagined to do so, for instance by saying "it is the left hand", but what does it mean when it happens within the mind?

The question of how features in motor recipes are filled in can be broadly restated in neural terms as how motor-related activity is organized. A distinction between movements and their organization fits well with the organization of frontal cortex as described in section 1.3.2; motor programs furthermore involve the temporal organization attributed to the function of prefrontal cortex. Damage to areas anterior to primary motor areas results in what could be described as a disruption of the control of motor programs; such effects are called the apraxias [59]. Patients, despite unaffected basic sensation and movement, may be unable to use objects which they are able to recognize, imitate gestures, perform movement sequences in the incorrect order, or confuse actions, e.g. combing hair instead of brushing teeth [59].

The various EEG and EEG-EMG measures described in the introduction and used in the other experiments presented in this thesis may be useful in understanding the mechanisms of organization involved in movement sequences. Using left- and right-hand responses allows lateralizion measures to be used, of potentials, amplitude and phase locking. The present study is concerned with the mapping of responses to a two-step motor program. Different parts of the program were filled in, and subsequent preparatory activity was measured. The program cues could inform subjects of the first, second, both or neither responses. Because cues could logically be used to prepare in at least two ways - either in the preparation of the actual response representation, or to decrease the amount of perceptual processing at stimulus presentation - an important role in the data analysis was reserved for lateralization. If cueing involves motor preparation, the hemisphere that innervates the cued hand should be involved in building up a response representation.

2.5.2 Method

Subjects

Sixteen right-handed subjects, of college age (mean 25 years old), were tested. Seven of the subjects were male. All subjects were informed of the experimental procedures and gave written consent. Subjects received a fee for participation.

Task

Subjects were required to give a two-response sequence using their left and right index fingers (keys 'z' and '/' on the keyboard). The sequence was signalled by two letters ('L' or 'R' for left and right) one above the other near the centre of the screen. The upper and lower letters indicated the first and second response. All four combinations of L and R were possible, so the sequences were left - left, left - right, right - left and right - right. Stimuli remained on screen until response. Subjects were instructed to respond as quickly as possible, with no further specifications.

1.5 s before stimulus presentation, a cue was presented that provided part of the upcoming stimulus. Each element had an independent 50 % chance of being cued. Uncued elements were represented by an asterisk. The possible cues were: no element information, only the first or only the second element or both elements given. Cues were presented in gray, and stimuli in white. So, when all information was cued, presentation of the imperative stimulus involved only a color change; in the other conditions, at least one additional unknown element was added to the display. Cues remained on screen until stimulus presentation. Trials were separated by a 750 ms intertrial interval.

Procedure

Subjects were trained on this and two other tasks for around 45 to 60 minutes. The other tasks are described in sections 2.4 and 2.6. Training blocks contained 30 trials and were repeated until reaction time was under 500 ms and two or fewer errors (2 % error rate) were made. Errors were indicated by beeps during traiing only, and reaction time and error rate were displayed after each block. Training was followed by electrode placement. The experimental session contained eight blocks of 100 trials.

EEG and EMG measurement

Ag-AgCl electrodes were used for both EEG and EMG recordings. The following EEG electrode positions were measured: Fp1, Fpz, Fp2, AFz, F3, Fz, F4, FC3, FC1, FCz, FC2, FC4, C3, Cz, C4, CP3, CP4, P3, Pz and P4. EEG impedance was kept below 5 kΩ. The sampling frequency was 250 Hz. The voltage range was 500 μV sampled using 4096 bits, providing an EEG resolution of 0.12 μV. EMG was recorded from electrodes positioned lengthwise along the lower arm, at around one and two thirds of the length of the left and right flexor digitalis superficialis. The difference between the two channels was taken, per arm, and this signal was rectified to produce the EMG signal. EMG impedance was kept below 10 kΩ.

2.5.3 Data analysis

Statistical analyses were done using Matlab [141] and SPSS [219]. Brain Vision [26] was used for visual inspection and artefact rejection, segmentation and ocular correction. A wavelet analysis approach [124] was used to further analyze the EEG data, using the program Gamma [66]. For further details, see section 2.1. The frequencies from 5 to 38 Hz were chosen as mean frequencies, with a 1 Hz uncertainty parameter (standard deviation in frequency, σ_f) up to 16 Hz, and 2 Hz for higher frequecies. The distance between frequencies was equal to the standard deviation. Higher-frequency activity was sampled at 40 and 80 Hz, with standard deviations of 5 Hz.

For time-frequency analyses, t-scores were computed for all electrodes, combinations of frequencies (for phase measures), frequencies and time points, and these multiple tests were analyzed using the false discovery rate (FDR) procedure [22]. This procedure controls the proportion of rejected null hypotheses which are rejected falsely when multiple differences are being tested. A false discovery rate with a two-sided error rate of 5 % was chosen.

Lateralization measures were calculated as described in section 2.1: (left - right hemisphere activity, given left-hand responses) - (Left - right hemisphere activity, given right-hand responses).

2.5.4 Results

Behavior

The reaction times and accuracies of the first and second responses were analyzed separately, using repeated measures MANOVA. The factors in the analysis were whether the first and second elements were cued or not and whether the elements were the same or different. The second reaction time is measured from the time of the first response. Reaction times were taken only from trials on which both responses were accurate. The range of reaction times that were analyzed was 150 to 2000 ms for the first response and 10 to 2000 ms for the second response.

Cueing the first (F(1, 15) = 480, p = .000) and second (F(1, 15) = 112, p = .000) response, the interaction of the first- and second-element cues (F(1, 15) = 5.7, p = .031), the interaction of repetition with the second cue (F(1, 15) = 24, p = .000) and the three-way interaction (F(1, 15) = 21, p = .000) had significant effects on the first reaction times (figure 2.36, top). Cueing the second element reduces the first-response reaction time, even when the cued hand is "wrong" in terms of the actual first response. This suggests that preparation occurs that is not directly related to movement generation. Whether the preparation is motor-related at all will be seen in EEG measures. The interactions appear to be due to faster different- than repeated-element sequences, only for partially-cued sequences.

The inter-response interval (figure 2.36, bottom) was influenced by repetition (F(1, 15) = 81, p = .000), and the interaction of repetition with cueing the first (F(1, 15) = 7.6, p = .014), second (F(1, 15) = 6.2, p = .025) or both (the three-way interaction: F(1, 15) = 5.7, p = .031) sequence elements. For different-element sequences only, cueing the second element can be seen to reduce reaction time. The shortest response - response time was found for the fully specified sequence. Note that when the same responses had to be given, the same finger had to be used, which seems likely to have caused the conspicuous delay relative to different-element sequences.

The accuracy of the first response (figure 2.37, top) was sensitive to the first (F(1, 15) = 17, p = .001), second (F(1, 15) = 6, p = .024) and combination (F(1, 15) = 8, p = .012) of cues, and to repetition (F(1, 15) = 10, p = .006). These results are due to the following patterns. First, more

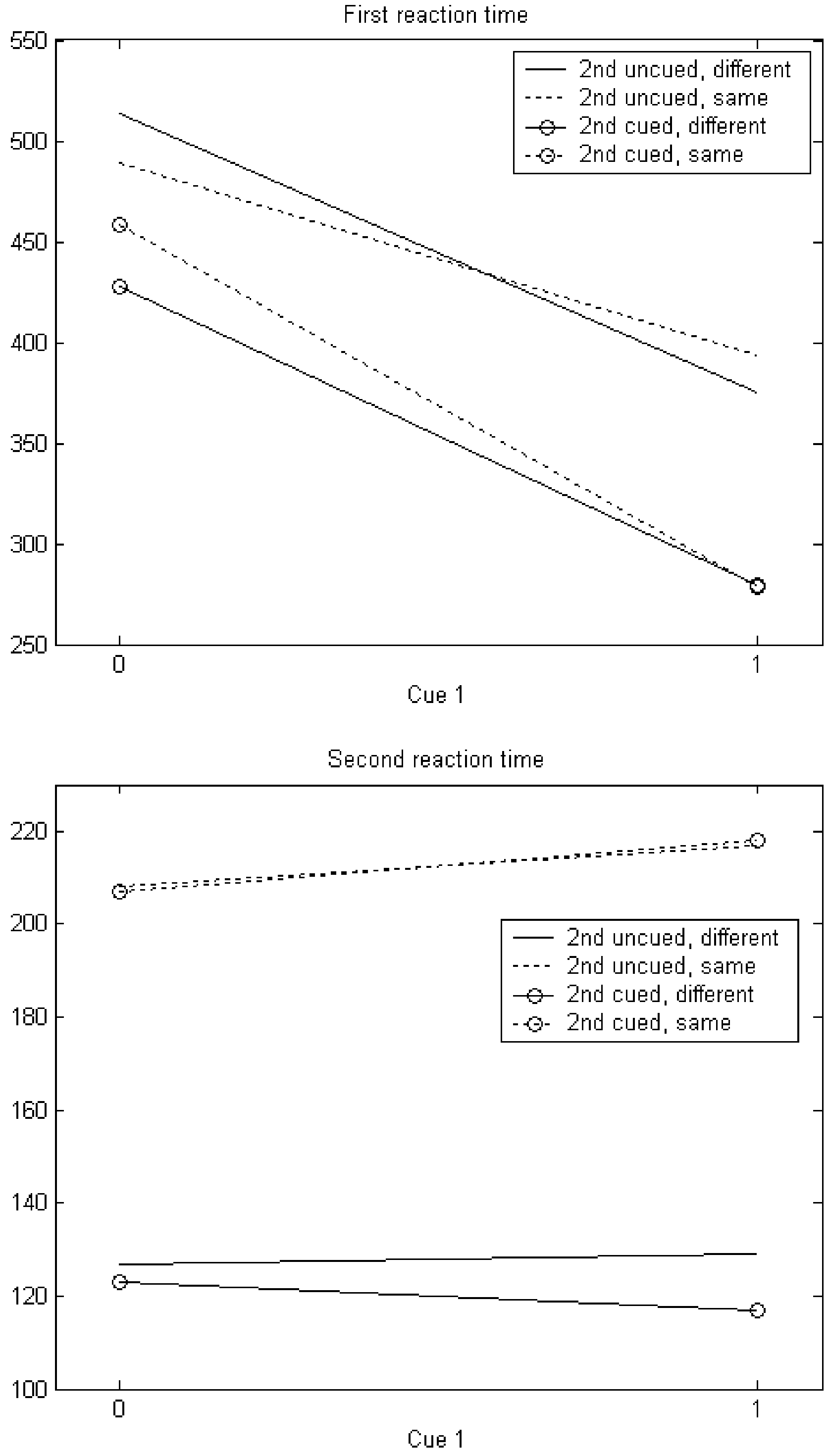


Figure 2.36: Reaction times, from imperative stimulus to first response (top) and the inter-response interval (bottom)

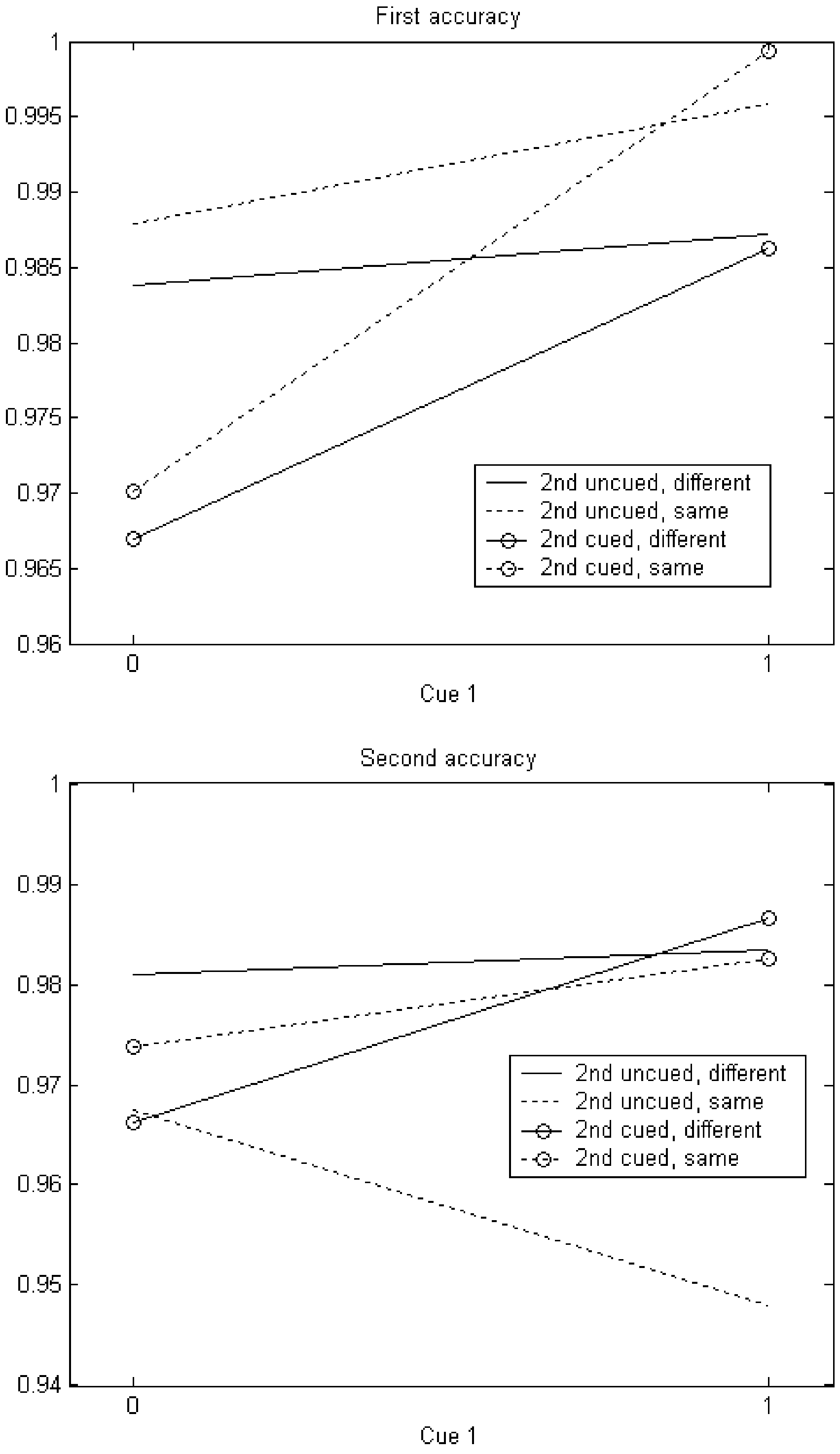


Figure 2.37: Accuracy of the first (top) and second (bottom) response

prior information results in higher accuracy. Second, the coordination of two different responses results in more errors. Third, cueing the second element reduces the accuracy of the first response.

The second response's accuracy (figure 2.37, bottom) showed effects of the second cue (F(1, 15) = 4.8, p = .044), the combination of cues (F(1, 15) = 15, p = .002) and the interaction of repetition with the first (F(1, 15) = 4.6, p = .049) and second (F(1, 15) = 16, p = .001) cue. This seems to be due to the result, similar to that found for the accuracy of the first response, that cueing only the first element decreases the accuracy of the second response on repetition trials.

ERP's

Figure 2.38, top, shows the ERP's for the different cueing conditions, for the midline electrodes Fpz, Fz, Cz and Pz. The post-cue positive peak was tested over 500 to 700 ms post-cue, using Huynh-Feldt corrected repeated measures, with the type of cued information (fully specified different elements, fully specified same elements, first element, second element, no information) and electrode as independent variables. The interaction of cue type and electrode was significant (F(12, 180) = 8.2, p = .000), as was the effect of electrode (F(3, 45) = 5.5, p = .005). Inspection of the ERP's shows a higher and broader peak at Pz for the all-information cues. The CNV during the second half of the preparation interval was also tested. Significance was found for electrode (F(3, 45) = 13.7, p = .000) and the interaction between electrode and cue type (F(12, 180) = 2.2, p = .047). This could be seen to be due to a division between the partially cued and fully cued, different sequences and the fully cued, same and uncued sequences.

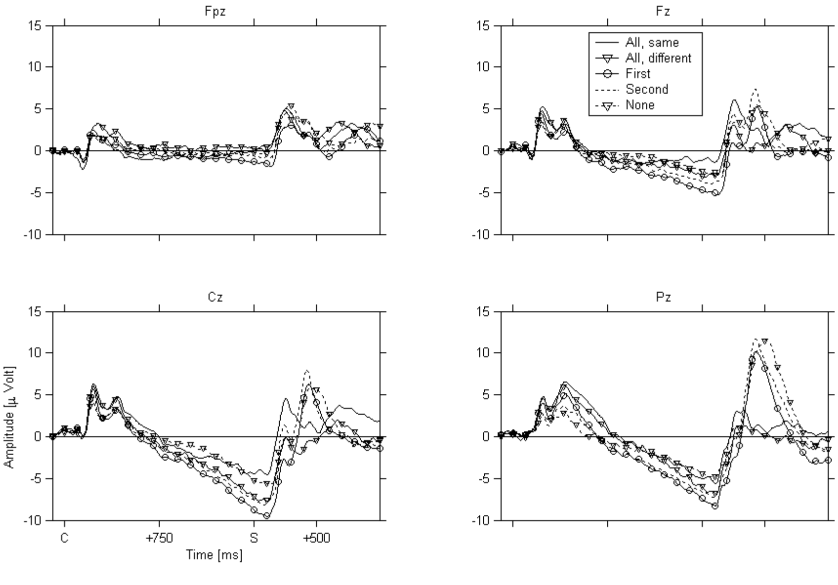


Figure 2.38: Cue-locked ERP's

Differences of the P3 component were also tested, averaged over 375 - 425 ms post-stimulus. The following effects were significant: information (F(4, 60) = 7.7, p = .001), electrode (F(3, 45) = 5.6, p = .015) and the interaction of electrode by information (F(12, 180) = 19.7, p = .000). These effects were caused by a low P3 when all the sequence information was cued. Note that in that condition only the onset of the stimulus needed to be detected for the response sequence to be given.

LRP's

Figure 2.39, bottom, shows the LRP's for different information cues, separated for repeated- and different-element sequences when all information was given. Repeated measures ANOVA shows significant differences between the conditions, tested over the last 100 ms of the response - stimulus interval (F(4, 60) = 3.0, p = .032). The main preparatory effect is a pre-stimulus LRP for the full information, different element sequence. Another preparatory effect can be seen for the full information, same element cue, for which the LRP can be seen to start rising prior to stimulus presentation.

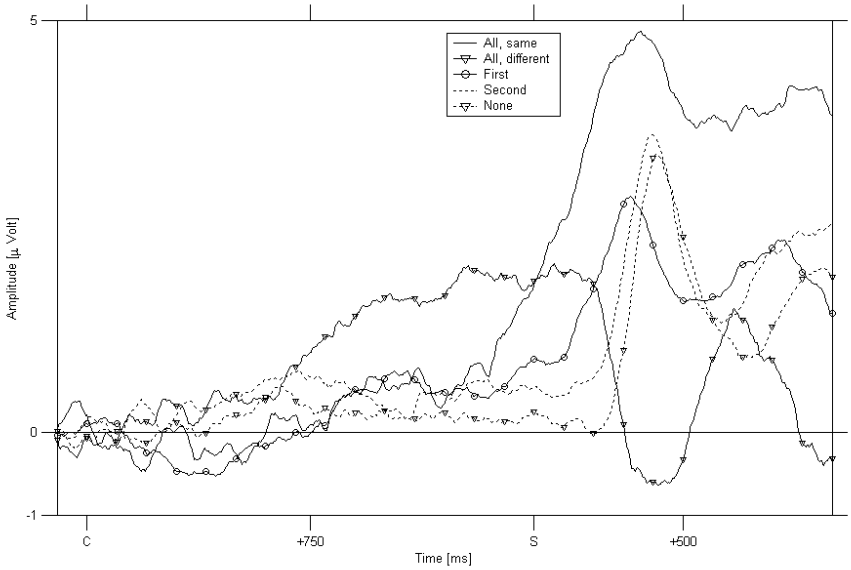


Figure 2.39: Cue-locked LRP's (defined by the cued response, or first response for full-sequence cues)

Amplitude

The FDR results of contrasts between the informative cue types and the no-information cue are shown in figures 2.40 and 2.41. The same midline electrodes were analyzed as for the ERP. All informative cues showed preparation-interval decreases in the beta band centered on central electrodes, relative to non-informative cues. Full-sequence cues showed an additional preparatory amplitude decrease in the alpha band. Full sequences also showed lower post-stimulus theta, where their P3 was lower. The amplitude time courses are shown in figure 2.42.

The motor-related amplitude asymmetry (MRAA; see section 2.1) was calculated using the same double-subtraction approach as the LRP. Left- and right-hand conditions were defined by the cued hand for first- and second-element cues, and by the hand coupled to the first element for full information and no-information cues. Only fully specified, same-element cues showed significant

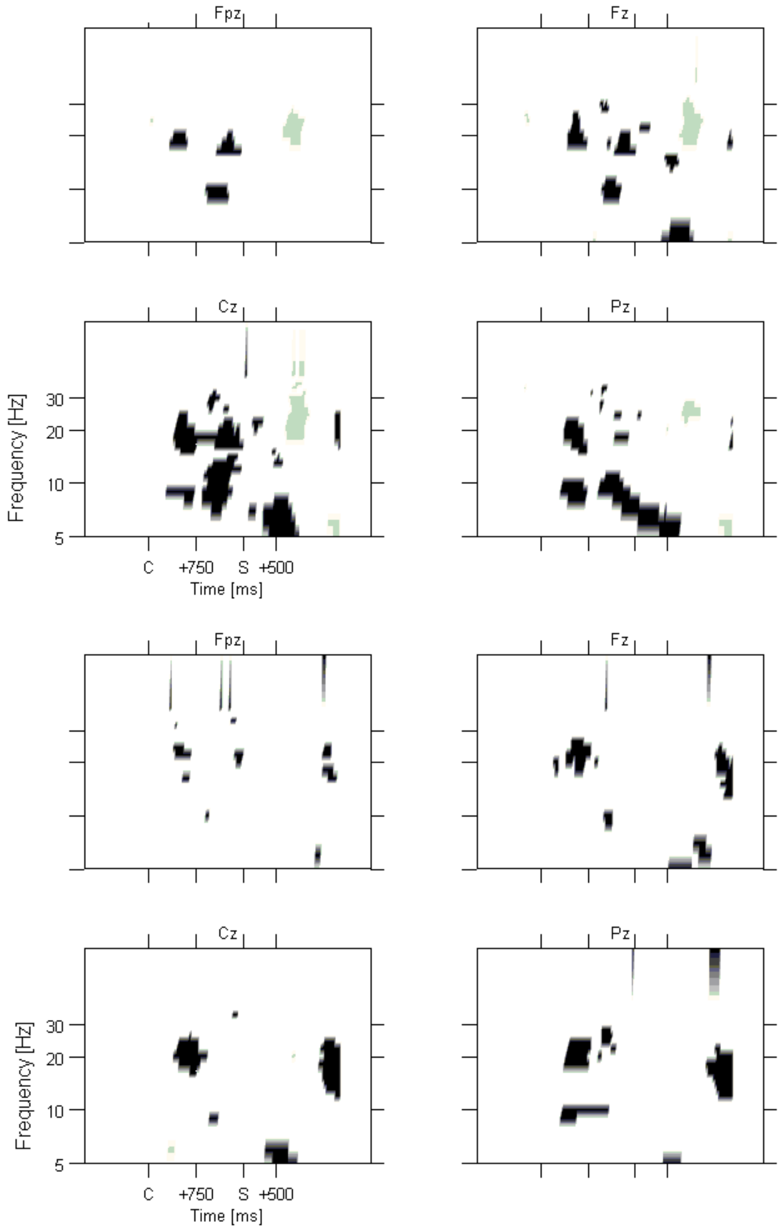


Figure 2.40: Full information minus neutral cue, different (top) and same (bottom) responses

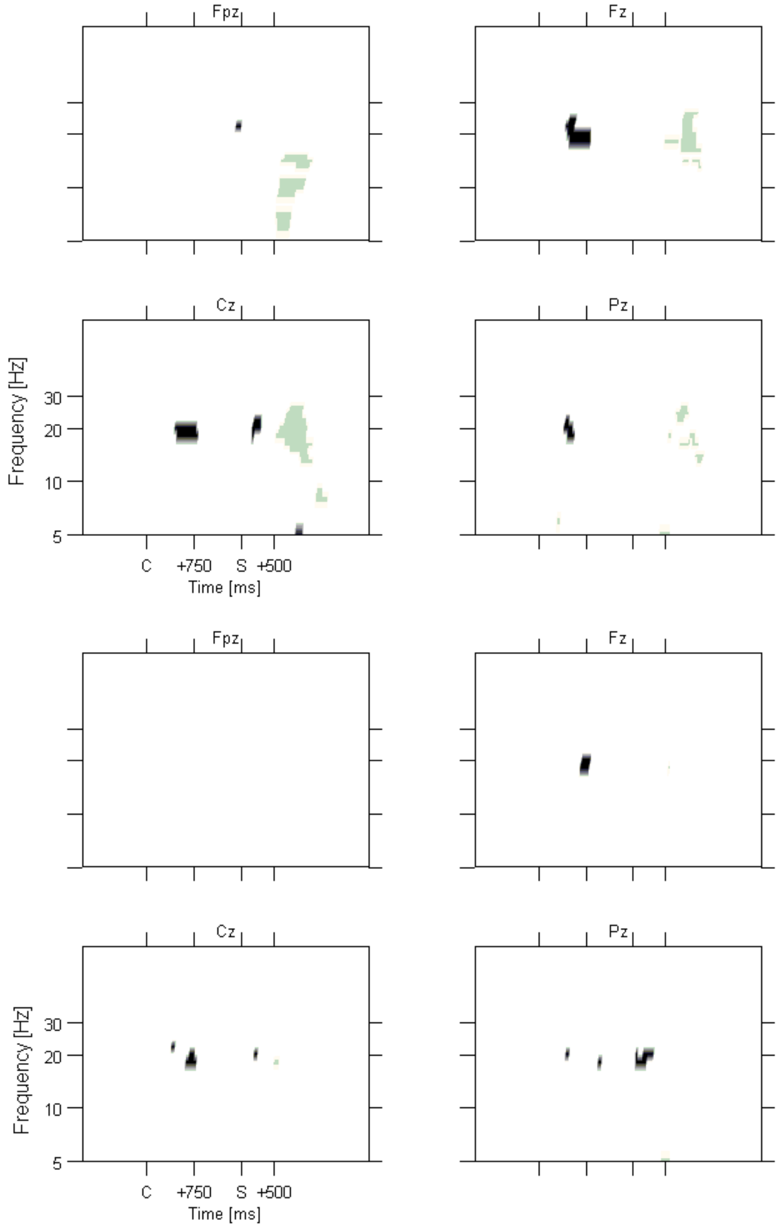


Figure 2.41: First (top) and second (bottom) response cued minus neutral cue

effects (figure 2.43). Both high-alpha band and beta band amplitude lateralized during the preparation interval. Notably, this condition showed no preparatory LRP, but did rise very quickly at, of even preceding, stimulus presentation. The effects found in the MRAA may measure the processes that allowed that kind of "trigger" preparation. MRAA time courses are shown in figure 2.44.

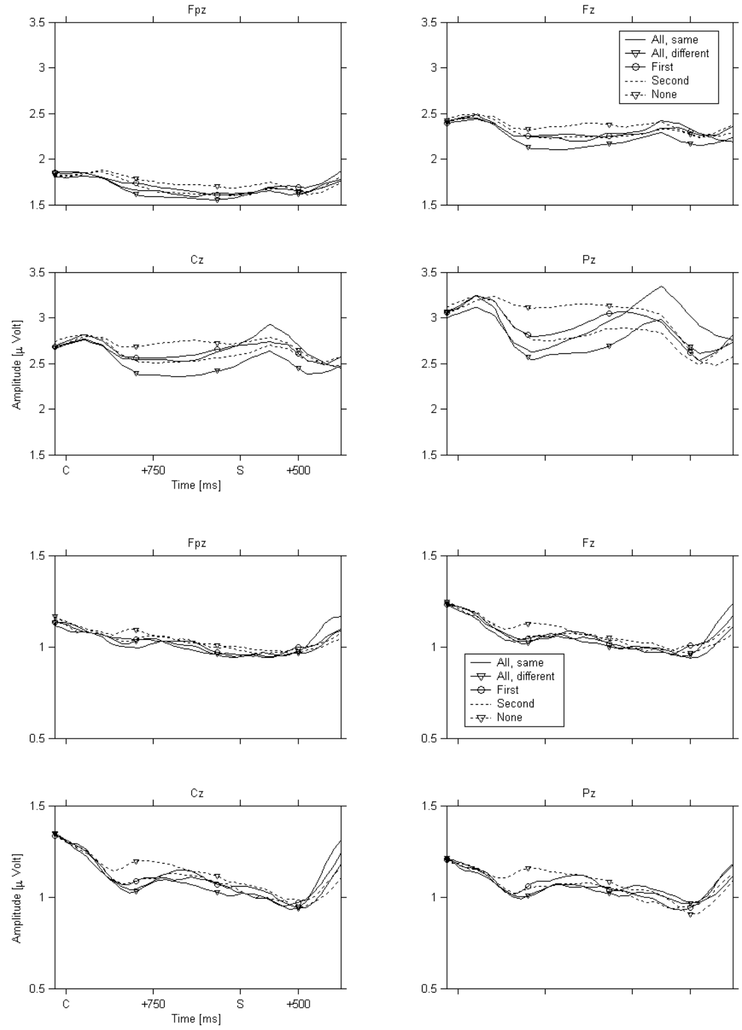
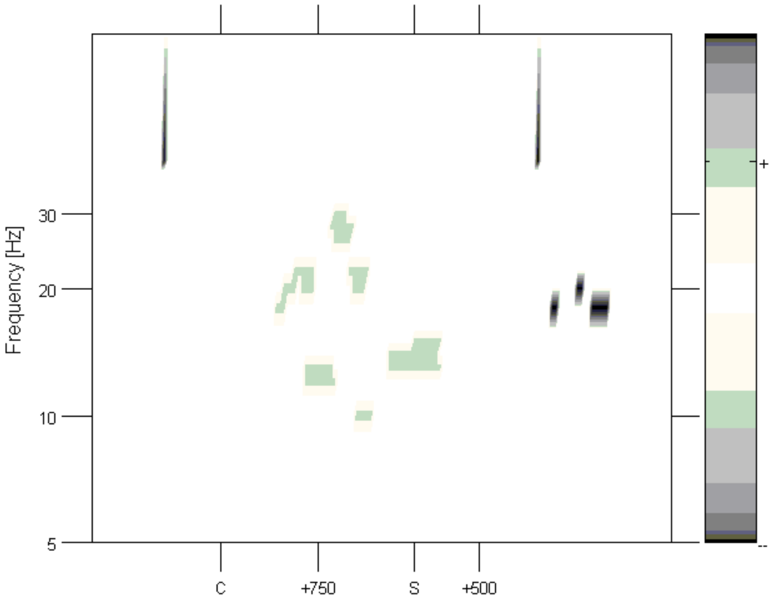


Figure 2.42: Mu-band (8 - 10 Hz, top) and beta-band (18 - 24 Hz, bottom) time course

The time-frequency domain lateralization of the left and right EMG in the preparation interval was also calculated, using the LRP approach. The only cue to show preparation-interval EMG-LRP activity was all-information, repeated-elements sequences (figure 2.45). Increased amplitude was found from about 500 ms post-cue, over the whole frequency range with the exception of the beta band.

Figure 2.43: MRAA, full information cue, same responses



PLV's

To reduce the number of tests, only the electrodes F3, Fz, F4, C3, Cz, C4, P3, Pz and P4 were used. Testing all frequencies simultaneously for the full sample range gave no FDR-significant results on contrasts between informative and non-informative cues. Significant beta-band preparatory lateralization due to left- versus right-hand cueing (relative to the first response for all, different cues) was found for all, same and first-element cues. Visual inspection showed similar patterns non-significant for all informative cue types (figure 2.46). The plots show increased beta-band phase-locking for the hemisphere contralateral to the hand being prepared. No preparatory hand-related effects or clear modulation over time of the PLV between EEG and EMG channels were found.

2.5.5 Discussion

Behavioral data and event-related, oscillatory and phase-locking measures of EEG and EMG patterns were studied in relation to cueing elements of a two-element response sequence. The improvement of first-response reaction times due to information in the cue shows that subjects are using the cues to prepare in some way, even if the immediate movement is unknown. Physiological data (see below) further suggests that preparation is at least partly motor-related, and not only due to preparing for the visual stimuli. The most important influence on the inter-response time seems likely to be whether the same finger had to be used, in which case the mechanics of retracting the finger and re-pressing the key would take more time than a key press with a different finger. Within the different-elements sequences, it can be seen that the first and second responses occur in quicker succession when either or both elements are cued. This may indicate the ability to prepare the necessary coordination needed for a fast right - left or left - right response sequence. The efficacy of cueing the second element on the inter-response time provides further behavioral evidence that

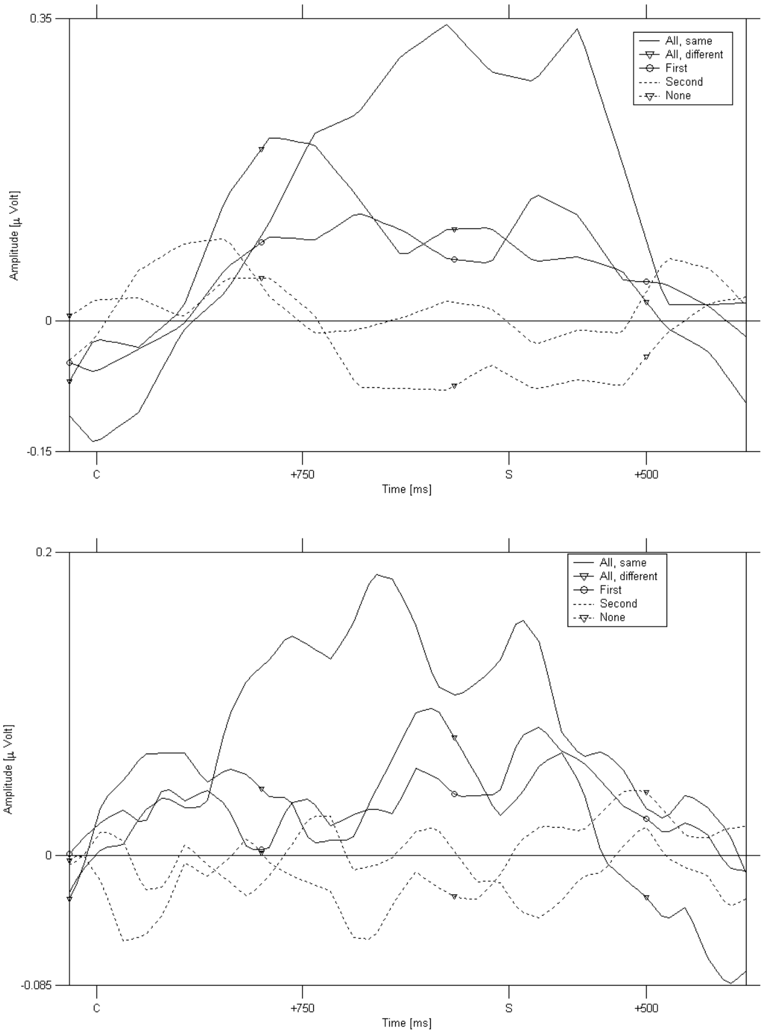
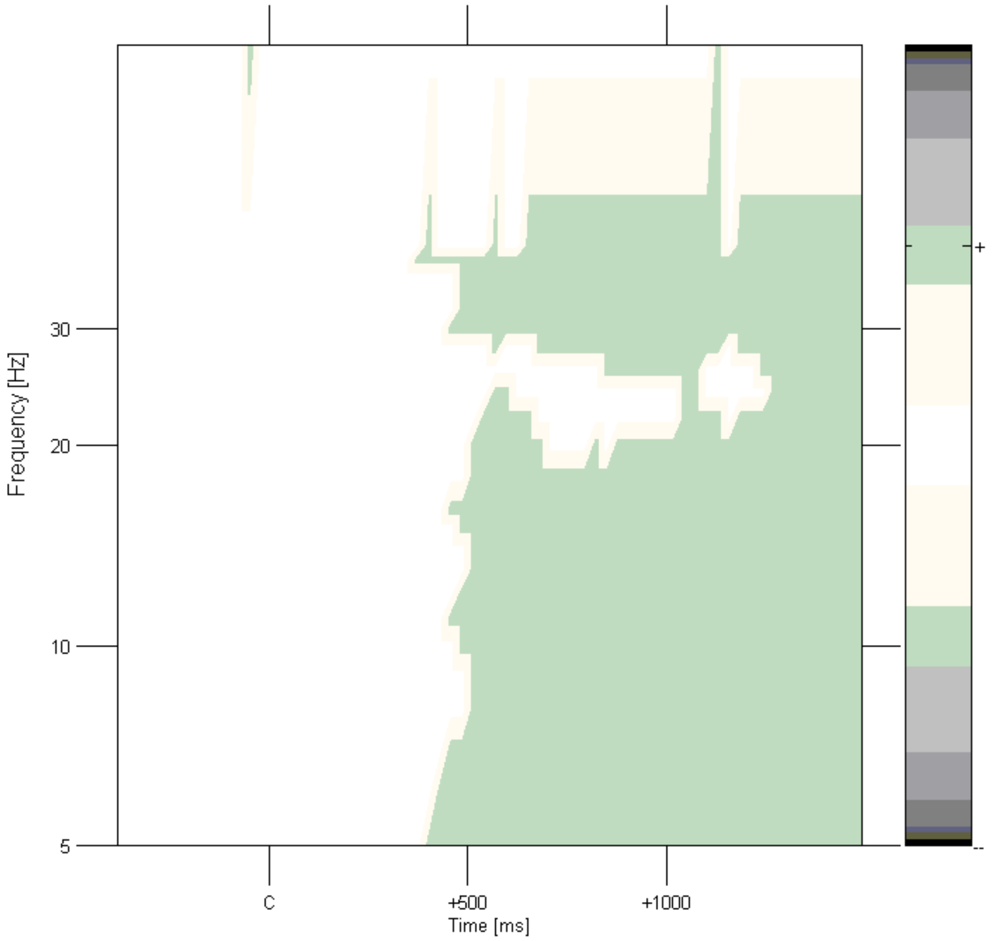


Figure 2.44: MRAA time courses, mu (top) and beta (bottom) band

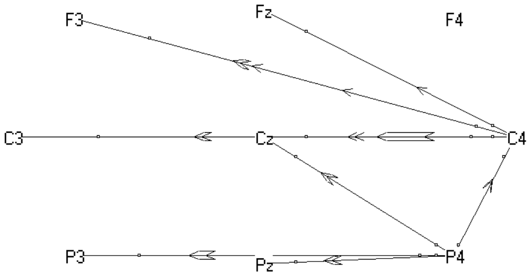
Figure 2.45: MRAA for EMG channels, full information cue, same responses



subjects are able to use such prior information in some way, even though the behavioral expression of the cue-information and the cue itself are separated by time and an interspersed action.

The accuracy data showed the pattern that cueing the first response decreases the accuracy of the second, for both same- and different-element sequences, and cueing the second response decreases the accuracy of the first, but only for repeated elements. One hypothetical explanation for the negative effect of cueing the second response on the accuracy of the first is that using information concerning a response that will come after the immediate response to be given involves inhibiting the space where the first response would be prepared, to avoid mis-mapping the response. The mechanisms of such inhibition may still interfere with setting up the correct response after stimulus presentation. An alternative hypothesis is that supplying the second element causes some kind of overconfidence, so that subjects tend to respond before all the necessary evidence for a correct response has been acquired.

These results were found for non-specific instructions to subjects, who were only told to respond as quickly as possible. With these non-specific instructions, subjects appeared to prefer to provide the sequence as a whole, and to generate that full movement as quickly as possible. Results would



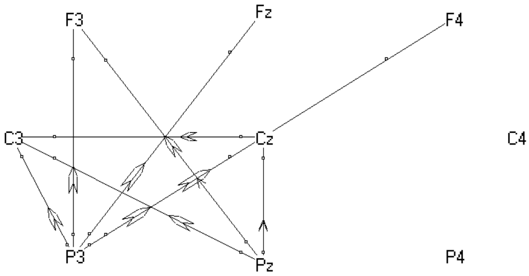


Figure 2.46: Significant beta-band positive (top) and negative (bottom) PLV differences, t-values for left- minus right-hand preparation. Values were based on the mean over all informative cue types. The plot should be read as follows. Periods of significant datapoints with a positive sign are represented by the arrows on the line drawn between the involved electrodes. The begin- and end-times of these periods are represented by the point and end of the arrow on the line. The arrow points in the direction of time, so if the arrow is close to the region it points to, the period of significance occurs near the end of the trial. Marks indicate cue and stimulus times.

presumably be different if subjects were instructed to respond specifically to the first stimulus as quickly as possible, in which case second-response cueing may be used to a lesser extent or in a different way. For the purposes of this study, however, the important point is that second-response cueing did have behavioral effects and preparatory activity related to second-response cues could be tentatively interpreted as motor-related preparation that is not directly concerned with movement generation.

In the ERP's, the most obvious effect was a lowered P300 when all information had been cued, as would be expected because in this condition only a color change occurred at "stimulus presentation". The post-cue positive peak was greatest when the cue contained most information, in broad agreement with the kind of effect found in the cued task switching (section 2.3) and cued response (section 2.6) studies. The CNV was more pronounced for the cues (first and second element only) in which mapping was partial, or when different responses had to be assigned to their correct position in the sequence (full-information, different-elements). For the single-element cues, this may be due to these conditions' combination of combining retrospective and prospective memory; in the other two conditions, either there was no retrospective information to maintained (no information cue) or no prospective information to be anticipated (full cue). For the different-element cue, temporal sequencing - which of course could also be described as a kind of prospective and retroactive memory - may be the underlying function reflected by the CNV. As described in section 1.3.2, prefrontal cortex seems likely to have played a role if preparation involved such broadly-tuned temporal encoding.

The LRP showed two effects, both for all-information cues: first, lateralization during the preparation interval for different-element sequences, and second, a quick triggering for repeated-element sequences that occurs just before the known time of stimulus presentation. The difference in preparation-interval lateralization may be due to a "balancing" problem. For a different-elements sequence, two areas of cortex are active, so the prepared responses might cancel each other out unless one is more strongly pre-activated. Hypothetically, a state of balanced mutual inhibition may be achieved until the first response is triggered by the stimulus. For repeated-elements sequences, no such balance would be automatically caused by the sequence composition. Prior activation might then be harder to maintain without initiating undesired movement. The lack of a preparatory LRP when the first response could, in principle, be prepared, may be related to the apparent tendency of subjects to wait for a fully-specified sequence before generating responses.

All informative cues showed preparatory central-parietal beta-band desynchronization relative to non-informative cues, a pattern that is consistent with motor as opposed to perceptual preparation. However, only the all-information cues for repeated-elements sequences (that is, pure single-hand preparation) evoked significant beta-band lateralization; these cues were also followed by the clearest alpha-band preparatory desynchronization. Note the dissociation from the LRP here: of the two all-information cues, it was the different-element sequence that showed preparatory time-domain lateralization. The frequency-domain lateralization found for the repeated-element sequences precedes the quick post-stimulus lateralization.

Beta-band phase-locking showed lateralized patterns between cue and stimulus due to the cued hand, for all informative cue types. The hemisphere associated with hand being prepared showed increased phase-locking with other EEG channels. Note that this pattern occurred when oscillatory amplitude in the same frequency band decreased. It cannot be simply attributed to stronger or a larger area of oscillations. A hypothetical explanation is that the patterns reflect the activation of a small set of phase-locked action representations in the beta band, at the same time as the suppression of many more possible representations which, in the absence of motor control, fire in the same frequency band. The net result would be a reduction of beta amplitude, but since what is left of beta-band activity is a single representation, the phase-locking of that representation would dominate overall phase-locking.

In summary, three broad conclusions can be drawn from the data. First, the brain-behavior evoked by the various cues has at least partially to do with neuronal phase relations. Second, the preparation of both the first and second elements is at least partially motor and not just based on foreknowledge of the stimuli. Finally, it seems possible that a distinction may exist between neuronal activity for movement activation and that for movement representation that runs roughly along the line between firing rate and phase-locking. That is, the location and overall intensity of brain activity may not be the only factor determining its effect on behavior.

The results of this experiment suggest that further research using sequence-element cueing and oscillatory EEG measures would be fruitful. More variations of sequence schemes could be used to explore what kinds of movement-to-sequence element mappings show similar physiological effects. Perhaps one of the most interesting questions to be explored is to what extent the idea of movement exists in phase-relations in such a way that the execution of movements can be postponed. It would seem that the ability to simulate consequences of actions in some safe internal world must have strongly influenced the adaptability and hence evolutionary path of humans. The biological changes associated with that ability would then be of interest for understanding both the evolution of the species and the development of the individual. The possible role of dynamic coding, flexibly distributed both within and outside the cortex, and how the brain has evolved to make use of such coding to achieve adaptability, is another question that could profit from measures of neuronal phase-locking, especially if combined with detailed anatomical studies and mathematical modeling. Redefining representations of motor programs as organizational principles of motor-related neural activity may help in formulating hypotheses on the conditions for the running of motor programs, that is, how complex actions are embedded in memory.

2.6 Cued information and response probability

2.6.1 Introduction

In previous experiments, motor preparation involved task sets with responses assigned to one or the other hand (sections 2.1 and 2.4) or sequences of responses (section 2.5), In this experiment, the preparation of single movements was studied. Further, response probability was manipulated to test a suggested dissociation between time- and frequency-domain measures of lateralization, based on the hand - modality switching study (section 2.1). In that study, effects on preparatory activity due to the hand to be used in the upcoming task set and of the response speed were found. The effects of interest to the present study were based on measures of lateralization: the lateralized readiness potential (LRP), the motor-related amplitude asymmetry (MRAA), and lateralized patterns of phase locking. The LRP, as discussed in section 1.3.4, reflects both the production and preparation of responses. The global time course of the LRP around the response - stimulus interval reflected, as would be expected, the sequence of response hands. On repetition trials, the LRP appeared to reflect a persistent lateralization, while no evidence for a pre-stimulus LRP in the direction of the upcoming hand could be found for switch trials. A fast - slow difference was found for the switch trials, but not the repetition trials, in which the LRP moved more in the direction of the upcoming response on fast trials. However, even on fast switch trials, the pre-stimulus LRP only appeared to reflect a greater decay to equilibrium, as opposed to a reversal of lateralization. In contrast, the MRAA, in the mu and beta band, showed clear pre-stimulus lateralization, reflecting greater ERD of the contralateral hand, for both repetition and alternation trials. Mu- and beta-band ERD would be expected around response and during response preparation (section 1.6), but the dissociation of the LRP and MRAA concerning pre-stimulation lateralization and sensitivity to response-speed was not expected. Beta-band phase-locking also showed pre-stimulus lateralization, with increased phase-locking over the contralateral hemisphere, especially frontal - central electrode pairs. Neither frequency-domain measure showed fast - slow differences in the hand - modality switching task.

The results led to the hypothesis that the motor-related lateralization of oscillatory brain activity, reflected in the MRAA and phase locking, is involved with what - that is, which hand - is being prepared, while the lateralization of time-domain activity, reflected in the LRP, encodes how effectively, in terms of subsequent performance, the hand is being prepared. In the present study, it was attempted to manipulate the "how effectively" part of preparation. The "how" in this case was manipulated by presenting subjects with either a response-choice task, or the same task with an added go - nogo dimension, in which on half of the trials no response was to be given. It was expected that more effort would be invested in preparation when it was certain that a response would have to be given, than when the nogo probability was 50 %. In both conditions, the "what" of preparation - which hand - was equally known, so that by hypothesis effects on the LRP but not on frequency-domain measures should be found of go probability.

2.6.2 Method

Subjects

Sixteen right-handed subjects, of college age (mean 25 years old), were tested. Seven of the subjects were male. All subjects were informed of the experimental procedures and gave written consent. Subjects received a fee for participation.

Task

The task was to respond with one of four fingers (left and right hand, index and middle finger) to a visually presented stimulus. Responses were given using the keys z, x, '.'and '/' no a standard keyboard. The stimulus consisted of two letters, one directly above the other. Each letter subtended around 1 degree visual angle. The top and bottom letter indicated the hand (L or R) and finger (M or I), respectively. Stimuli were preceded, by one second, by a cue. The cue was either neutral or filled in the hand part of the stimulus. Uncued parameters were shown as an asterisk, at the same locations as the imperative stimuli. The size of stimuli was around one degree visual angle. Cues remained onscreen until they were replaced by the stimulus, which remained onscreen until response, or 750 ms post-stimulus on no-go trials. The inter-trial interval was 750 ms. Cue types were blocked.

A further manipulation was a between-blocks factor of go-probability. Stimuli could be presented in gray or red, red being a command not to respond. In 100 % blocks, all stimuli were gray; in 50 % blocks, stimuli were equally likely to be go or no-go.

Subjects performed six blocks of 100 trials: one neutral-cue block for each go probability, and two hand-cue blocks for each go probability.

Procedure

Subjects were trained on this and two other tasks for around 45 to 60 minutes. The other tasks are described in sections 2.4 and 2.5. Training for this task involved performing one of each block type, each block containing 15 trials. Errors were indicated by a beep during training. Training ended when at most three errors were made, and the mean reaction time was under 600 ms. Training was followed by electrode placement. Subjects were instructed to take as much time as they needed to rest between blocks.

EEG and EMG measurement

Ag-AgCl electrodes were used for both EEG and EMG recordings. The following EEG electrode positions were measured: Fp1, Fpz, Fp2, AFz, F3, Fz, F4, FC3, FC1, FCz, FC2, FC4, C3, Cz, C4, CP3, CP4, P3, Pz and P4. EEG impedance was kept below 5 kΩ. The sampling frequency was 250 Hz. The voltage range was 500 μV sampled using 4096 bits, providing an EEG resolution of 0.12 μV. EMG was recorded from electrodes positioned lengthwise along the lower arm, at around one and two thirds of the length of the left and right flexor digitalis superficialis. The difference between the two channels was taken, per arm, and this signal was rectified to produce the EMG signal. EMG impedance was kept below 10 kΩ.

2.6.3 Data analysis

Statistical analyses were done using Matlab [141] and SPSS [219]. Brain Vision [26] was used for visual inspection and artefact rejection, segmentation and ocular correction. A wavelet analysis approach [124] was used to further analyze the EEG data, using the program Gamma [66]. For further details, see section 2.1. The frequencies from 5 to 35 Hz were chosen as mean frequencies, with a 1 Hz uncertainty parameter (standard deviation in frequency, σ_f) up to 16 Hz, and 2 Hz for higher frequecies. The distance between frequencies was equal to the standard deviation.

For time-frequency analyses, t-scores were computed for all electrodes, combinations of frequencies (for phase measures), frequencies and time points, and these multiple tests were analyzed using the false discovery rate (FDR) procedure [22]. This procedure controls the proportion of rejected null hypotheses which are rejected falsely when multiple differences are being tested. A false discovery rate with a two-sided error rate of 5 % was chosen.

Lateralization measures were calculated as described in section 2.1: (left - right hemisphere activity, given left-hand responses) - (Left - right hemisphere activity, given right-hand responses).

2.6.4 Results

Reaction time

Only accurate trials with reaction times between 100 and 2000 ms were included. Tests were performed using repeated measures MANOVA. Reaction time differed significantly between go probabilities (F(1, 15) = 15, p = .001) and cue type (F(1, 15) = 108, p = .000), and the factors interacted (F(1, 15) = 16, p = .001). Reaction times for hand cues were 450 ms (50 % go) and 407 ms (100 % go), and 591 ms (50 % go) and 578 ms (100 % go) for neutral cues. Accuracy for hand and neutral cues was, respectively, 95 % (for both 50 and 100 % go) and 92 % (50 % go) and 95 % (100 % go).

Time-domain measures

Figure 2.47, top, shows the cue-locked ERP's for the four conditions. The two main features are a post-cue positive peak and a late CNV, both of which are larger for the hand than the neutral cue. The ERP at the plotted midline electrodes (Fz, FCz, Cz, Pz) was tested at 400 - 600 ms and 800 - 1000 ms post-cue using repeated measures MANOVA. At the positive peak, effects were found of hand cueing (F(1, 15) = 23, p = .000), electrode (F(3, 45) = 4.5, p = .027), go probability by electrode (F(3, 13) = 14, p = .000) and hand cueing by electrode (F(3, 13) = 13, p = .000). At Pz, the positive peak was greater for the 50 % probability condition. On the late CNV, effects were found of hand cueing (F(1, 15) = 8, p = .013), electrode (F(3, 45) = 14, p = .000), probability by electrode (F(3, 45) = 5.5, p = .011), hand cueing by electrode (F(3, 45) = 5.8, p = .005) and the three-way interaction (F(3, 45) = 5.5, p = .014). The 50 % go probability was associated with a greater CNV, the difference being greater at frontal sites.

LRP's are shown in figure 2.47, bottom. The LRP was significantly greater when the go probability was 100%, tested over 800 - 1000 ms post-cue (t(15) = 2.9, p = .011). Note that in the 50 % go condition, the post-stimulus LRP is low due to the no-go trials.

Instantaneous amplitude

First, the effect of hand preparation will be considered. Hand cueing had different effects on instantaneous amplitude in the 100 % and 50 % go probability conditions. For 50 % go blocks, no significant effects were found using the FDR procedure, while effects in the theta and beta band were found for 100 % go blocks (figure 2.48). In the theta band, amplitude increased, most clearly frontally, from 500 ms post-cue up to stimulus presentation. Fronto-central beta-band ERD also started, mainly, around 500 ms post-cue, with earlier significant ERD during the first half second of the cue-stimulus interval at Fz. Theta (5 - 7 Hz) and beta (18 - 24 Hz) amplitude time courses are shown in figure 2.49, showing that similar effects were also present in the 50 % go blocks. No

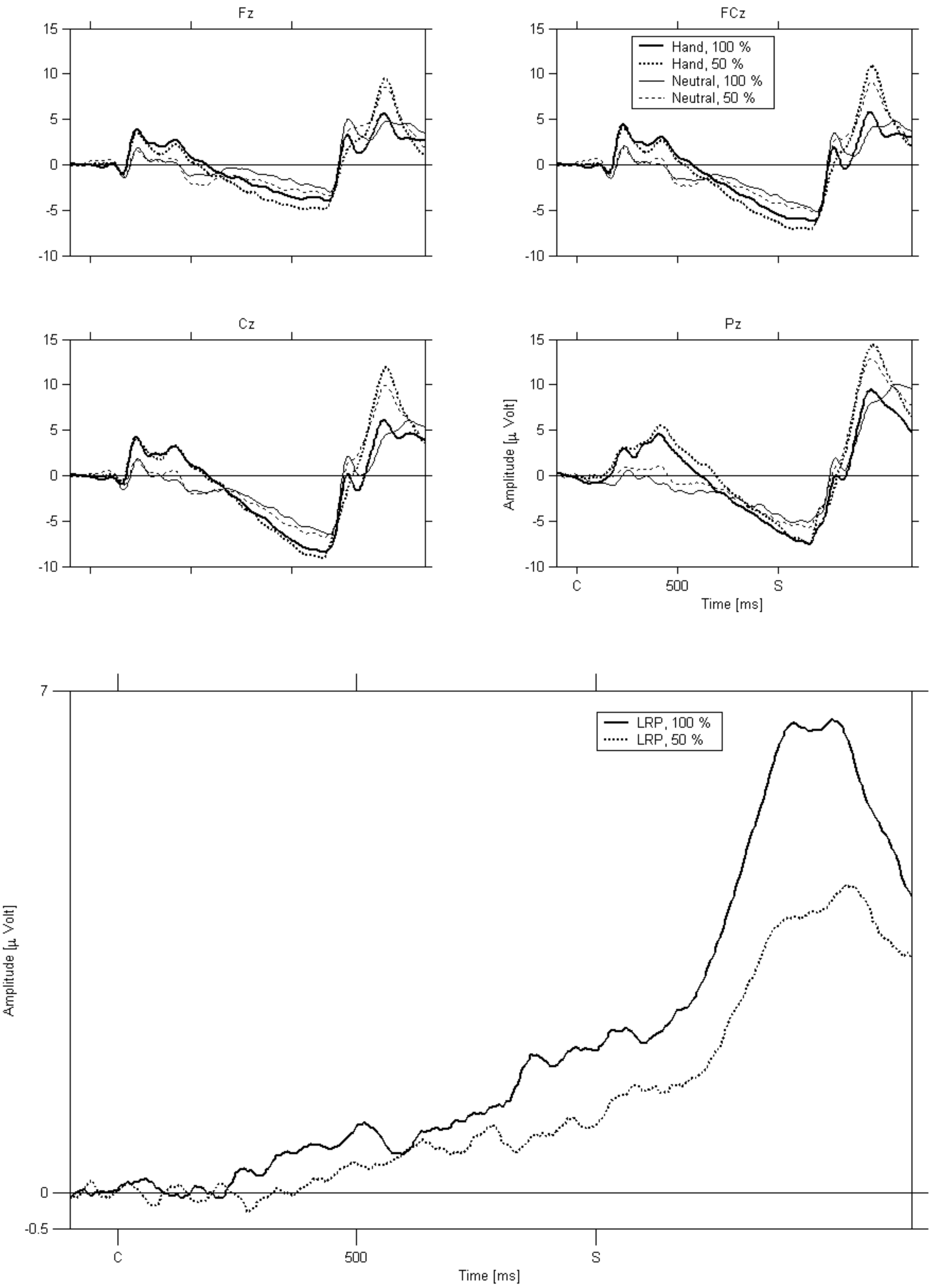


Figure 2.47: Cue-locked ERP's (top) and LRP's (bottom)

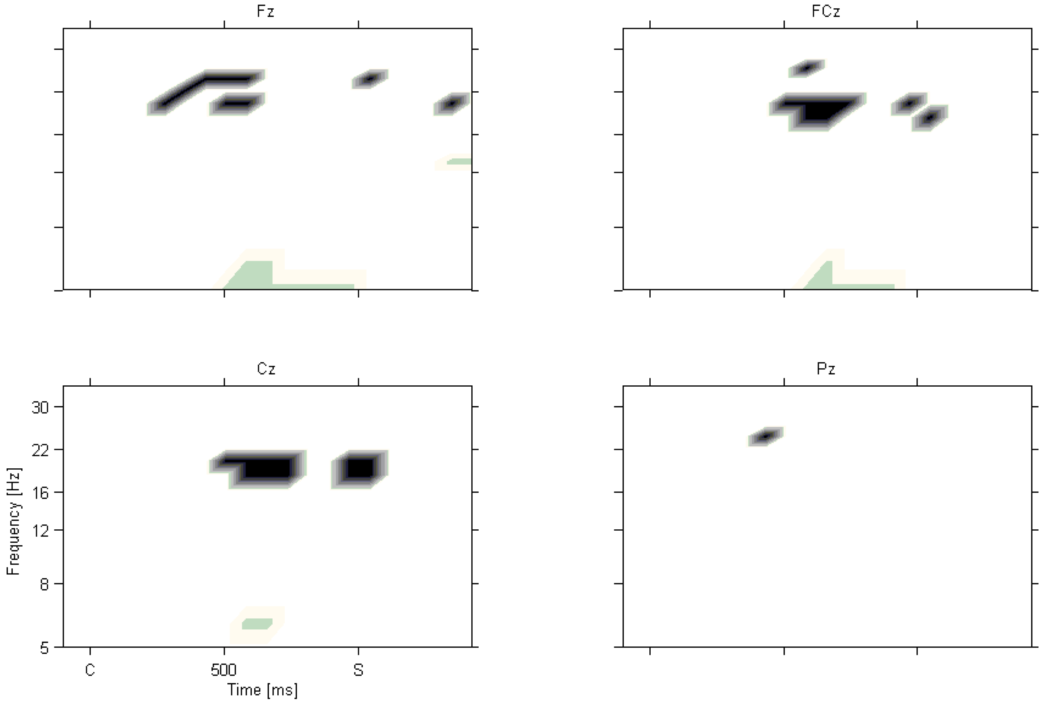


Figure 2.48: Significant differences for the hand cueing - neutral cue contrast, for 100 % go blocks. Gray and black regions are significantly positive and negative, respectively.

significant effects were found for go probability or the interaction between go probability and hand cueing.

For the 100 % go condition, a positive motor-related amplitude asymmetry (MRAA) arose in the mu and beta bands, in the first and second half of the cue - stimulus interval respectively (figure 2.50, top). When go probability was 50 %, a positive beta-band asymmetry arose at the end of cue - stimulus interval, and a 16 Hz negative asymmetry arose at 500 ms post-cue (figure 2.50, bottom). MRAA time courses are shown in figure 2.51, showing similar time courses for the 50 % and 100 % go probabilities. Using FDR, two differences MRAA's of the go probabilities were found to be significant. Both differences are reflected in the time courses of figure 2.51: an early increase in MRAA for 100 % trials at 8 Hz, around 400 - 500 ms post-cue, and a late increase at 22 Hz MRAA for 100 % trials around 700 to 800 ms post-cue.

Phase locking

Testing all pairs of EEG channels, no significant differences were found in the cue - stimulus interval between hand cue - neutral cue conditions or for left versus right hand cueing, for either go probability. Visual inspection of the data showed some trends. There was an increase in posterior beta band coherence for hand cues in the 100 % go condition, but not for the 50 % go condition. For the left - right contrasts, for both go probabilities, some mu- and beta-band lateralization was visible, most apparently for the beta band and right hemisphere, with increased PLV values between sensorimotor and central regions following left-hand cues.

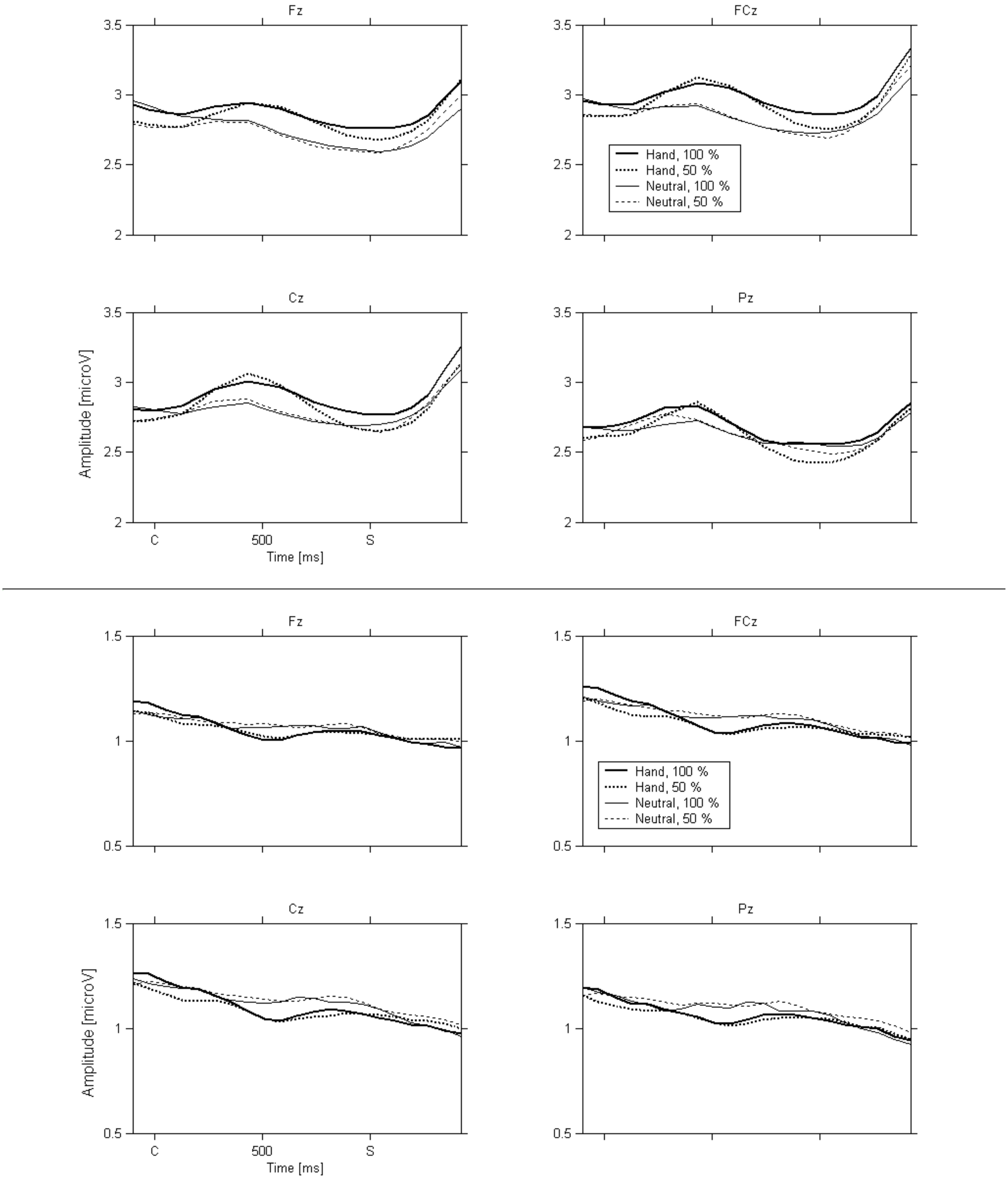


Figure 2.49: Theta- (top) and beta- (bottom) band amplitude time course

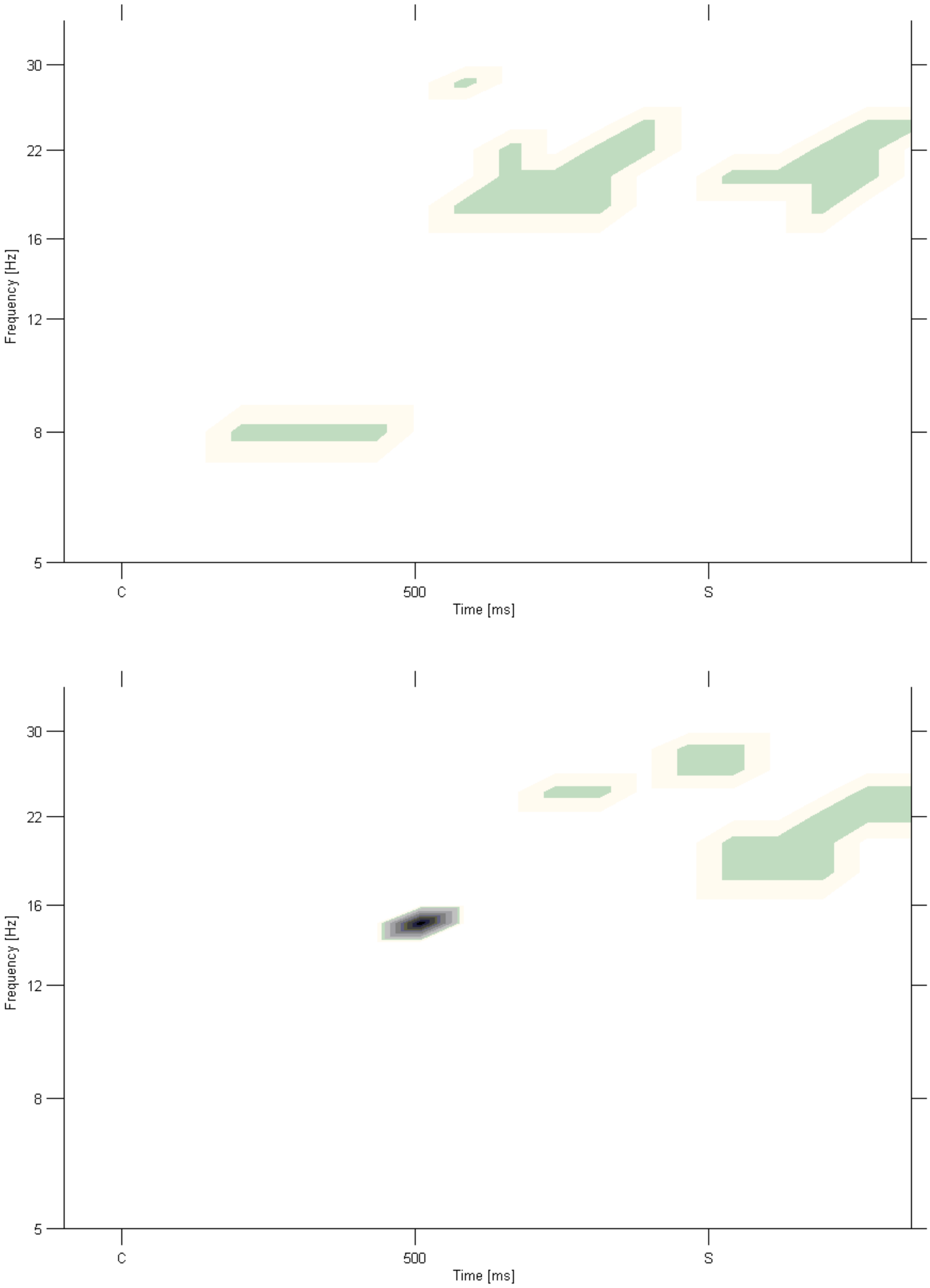


Figure 2.50: Amplitude lateralization for 100 % go (top) and 50 % (bottom) blocks. Gray and black regions are significantly positive and negative, respectively, based on the FDR procedure.

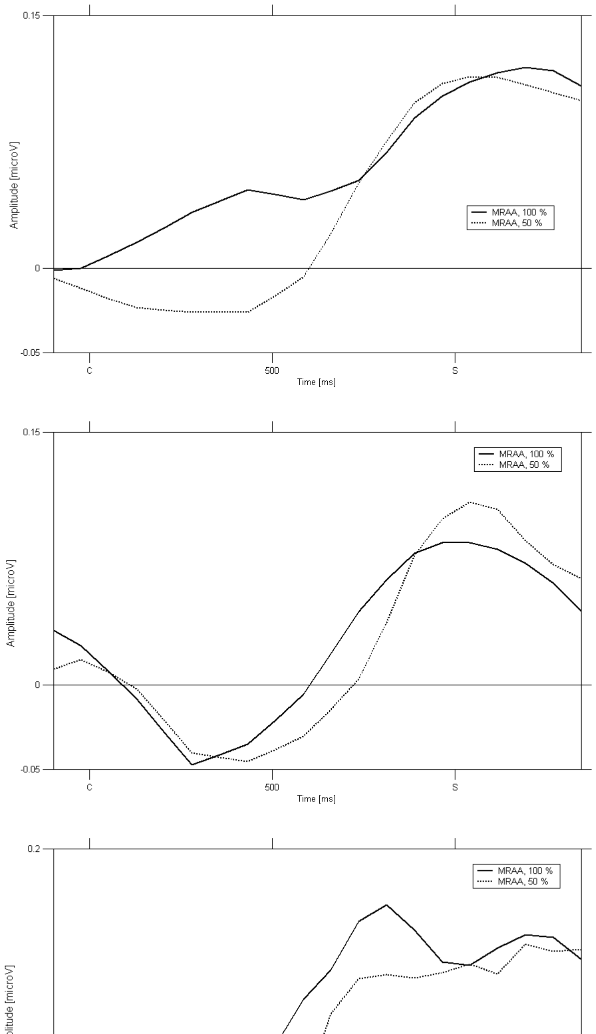


Figure 2.51: MRAA time course. From top to bottom: mu band (8 - 10 Hz), 16 Hz, beta band (18 - 24 Hz)

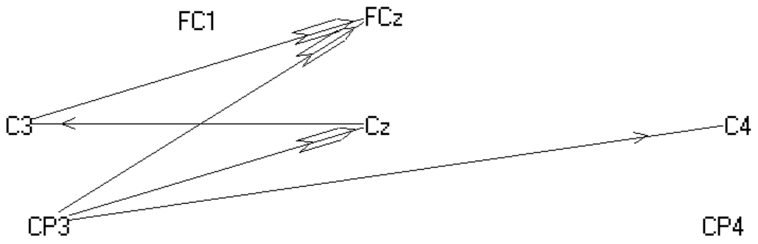
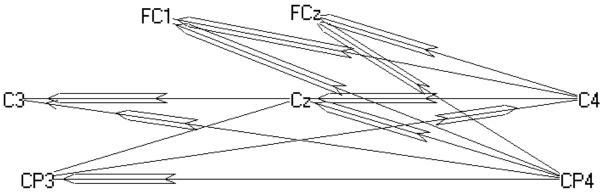


Figure 2.52: Beta-band phase locking, hand - neutral cue, pseudo-significant positive differences.

In an attempt to better visualize the lateralization trends during the cue - stimulus interval, a selection of electrodes was made based on the observed patterns and FDR was repeated for the time courses for the mu (8 - 12 Hz) and beta (18 - 24 Hz) bands separately. The data points selected in thus way are pseudo-significant, based on data fishing, but could nevertheless be used to guide replication attempts. See section 2.1, figure 2.11 for details on the method of plotting. In the mu band, positive differences were found for the 100 % go, hand - neutral cue contrast (figure 2.52), for the left hemisphere at the end of the preparation interval. In the beta band, lateralization was found for the left - right contrast, for the main effect of hand and for both go probabilities. As neither the interaction contrast nor visual inspection showed significant differences, the results of the left - right contrast are plotted for the main effect (figure 2.53.

2.6.5 Discussion

The following results were found for non-lateralization measures. A post-cue positive peak was found following hand cues, similar to that found in the sequence-element cueing and cued task switching tasks. The peak was followed by a CNV, again greater for the informative than neutral cue types. Effects of probability found on the ERP were a smaller parietal peak, but a greater frontal CNV. The smaller positive peak may be due the fact that, less information was provided in the 50 % go condition - it is unknown whether the stimulus will be go or no-go. In contrast, more non-hand-specific preparation may be done in that condition, in the sense of perhaps preparing



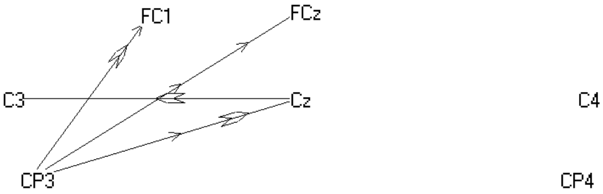


Figure 2.53: Beta-band phase locking, left - right hand preparation, positive (top) and negative (bottom).

to inhibit the response. Hand cueing resulted in an increase of frontal theta-band amplitude from around 500 ms post-cue, as well as central beta ERD. Significant beta ERD for hand cues was present at Fz in the first, and centrally in the second half of the cue - stimulus interval. Hand cues also resulted in increased phase-locking over the left hemisphere, at the end of the preparation interval. No significant effects of go probability were found on frequency-domain measures.

Lateralization for left- versus right-hand cueing was found for all measures. For the LRP, lateralization was higher for the 100 % go condition. In mu- and beta-band amplitude, lateralization was found, arising in the second half of the preparation interval for both conditions. In the 100 % go condition, an additional early low-alpha lateralization was found, and late-interval beta-band lateralization was greater. In the 50 % go condition, roughly the same beta-band lateralization was seen at the end of the pre-stimulus interval, as well as post-stimulus. Around 500 ms, a period of 16 Hz reversed lateralization (ERS over the hemisphere contralateral to the cued hand) was found, that only reached significance for the 50 % go condition but was also clearly present for the 100 % go condition. This may reflect inhibition of responding, to avoid false-positive responses evoked by cue presentation. In phase-locking, during the second half of the preparation interval, electrodes near the relevant motor hemisphere showed increased phase-locking with, especially, frontal areas.

The lateralization results thus do not completely follow the hypothesis of a time - frequency distinction between "what" and "how" preparation, as some differences between go probabilities were found in the MRAA as well as the LRP. Phase-locking, however, remained sensitive only to which hand was cued. Further, no significant differences were found in the mu band during the second half of the preparation interval. This may be the period most related to movement preparation, as opposed to the earlier post-cue period which may be more related to encoding the cue than to controlling the state of motor areas. Further, the late difference found for the beta-band may be due to variation in the time between cue presentation and the rise of an effective preparatory state. So, the hypothesis of a "what" - " how" LRP - MRAA distinction would seem to require further study before being rejected.

Chapter 3

Discussion

3.1 Discussion of results

As summarized below, the various contrasts, fast - slow, switch - hold, left - right hand, as well as cue types, were associated with differences in the time course of the LRP, instantaneous amplitude and phase locking, and lateralization in those measures.

3.1.1 ERP's

In the ERP's, an increased post-cue positive peak, lasting from around 300 to 600 ms post-cue, was found for the following cue conditions. First, in the cued chiastic switching study (section 2.3), when the cue was different than the previous cue, the peak was greater. This effect determined the grouping of conditions at frontal - central channels, e.g. the switch - hold and hold - switch sequences grouping together. At parietal - occipital channels, there was a further effect of switching, switch cues being followed by a more positive peak than hold cues. Given a cue- and task-switch, a greater peak preceded fast than slow responses. Second, in the sequence cueing task (section 2.5), cues providing both elements of the sequence had a greater parietal - occipital peak. Third, when cueing response hand in the choice / go - no go task (section 2.6), hand cues showed a greater peak than neutral cues. Taking the results together, the post-cue peak appears to reflect what is done with information contained in the cue. Note that a switch and a hold cue contain the same amount of information - one bit, reducing the uncertainty in a set of two equally probable events. So, the peak does not reflect how much information is in the cue, but how much or what kind of activity is caused by that information within the first half second post-cue. This seems consistent with ERP studies showing task-related effects, e.g. of the task-relevance of stimuli, on the P3 component, as described in section 1.3.4, although the frontal distribution of long-lasting positivity does not seem to be described by either the P3a or P3b.

Later in preparation intervals, slow negative potentials were found to reflect various kinds of preparation. These potenitals had the general characteristics of preparatory CNV-like components described in section 1.3.4. In the hand - modality task switching study, such potentials at frontal channels were greatest for fast alternation trials (section 2.1). In the hand-switch only study (2.4), but not significantly in the modality-switch study (2.2), alternation trials were again preceded by greater frontal negativity than repetition trials. In the cued switching task the main effects were a conspicuously weak frontal - central - parietal potential for slow hold - hold sequences, in which the least preparation would be expected and a fast - slow grouping occipitally, for the cue repetition conditions. In the sequence cueing study, single-element cues were followed by the greatest negative potential, centrally. In comparison with neutral and full-information cues, single-element cues allow only a half-finished kind of preparation: a motor program is being written, but cannot be completed. Perhaps this results in a stronger anticipation of the missing element, that is reflected in the negative potential, than the wait for the "go" signal that stimulus presentation provides when the full motor program can be specified. In the choice / go - no go task, hand cues resulted in negative potentials than neutral cues. So in these studies, negative pre-imperative stimulus potentials, with varying scalp distributions, covaried with a manipulation (e.g. cue information) or measure (reaction time) of preparation.

The LRP showed a response speed by task switching interaction in the hand-modality switching task. In the choice / go - nogo task, cueing the hand to be used for an upcoming imperative stimulus resulted in a pre-stimulus LRP, that was larger when the probability of response was higher. In the sequence cueing task, a pre-stimulus LRP was found only for fully specified sequences with different elements. When the sequence was fully specified but consisted of repeated responses, the LRP did not develop during the cue - stimulus interval until just before stimulus presentation, but then rose sharply.

3.1.2 Theta-band amplitude and phase locking

Pre-stimulus theta band activity was found to predict subsequent reaction times in the hand - modality alternating runs task, for both alternation and repetition trials, and the chiastic switching task, but only in the switch - switch sequence. The lack of an effect for hold - switch sequences in the cued chiastic switching task is an inconsistency that may be worth further study, as in the alternating runs task, the alternation trails were always part of a hold - switch sequence. The reaction-time effect for hand - modality switching consisted of higher amplitude during the response-stimulus interval for fast trials, from 500 ms post-response to stimulus presentation, as well as increased amplitude immediately after the response. The effect from 500 ms decreased from frontal to occipital sites, while the earlier effect was found only at frontal and central sites.

For both fast and slow trials in the hand - modality switching task, the overall time course was qualitatively similar, consisting of peaks around the external events (response and stimulus). In the switch - switch sequence for chiastic switching, fast and slow trials showed a different time course, with the slow condition showing a later post-cue peak in amplitude, most clearly in the parietal - occipital region. In the fast switch - switch condition, central - parietal regions showed increased theta-band phase-locking from around 750 ms post-cue, relative to the other trial sequences, and a decrease in frontal phase locking. This phase-locking pattern is perhaps one of the most interesting results in terms of possible transient large-scale cortical states implementing task sets. Although the result needs to be replicated, some speculative hypotheses can be formulated. Since prefrontal neurons can encode past and future events (section 1.3), the low frontal phase locking may reflect the weakness of the memory of both the most recent and upcoming task set. Alternatively, the decrease in phase locking may be a form of large-scale theta-band ERD in which only a small subset of activity is allowed in some form of noise reduction. The posterior increase in phase locking may reflect the effect of memory retrieval on the cortex, as discussed in sections 1.3.1 and 1.4.3; perhaps this retrieval requires a longer period or intensity of activity to recall the correct task-set memory in the relatively unstable context of switch - switch sequences.

Modality-specific switch - hold effects in theta-band amplitude were found at occipital - parietal sites in the modality switching task. Both switch-to-visual and switch-to-auditory trials showed a pre-stimulus relative increase (or delay of post-response decay) in amplitude, but this increase persisted longer, over around 500 to 1000 ms in the response - stimulus interval, preceding visual alternation trials. The pattern over conditions and time suggested that the oscillatory activity may be part of a process of selection, as discussed further in section 3.2.2. Theta-band amplitude was found to lateralize along with hand preparation, but only in the hand-switching task and only for repetition trials. In these trials, amplitude increased over the hemisphere controlling the prepared / just used hand, during the response and for around 500 ms post-response. As this effect was the only motor-related lateralization effect outside the expected mu and beta bands, it is both interesting and in need of replication. Since the transience and timing of the effect are similar to the occipital visual-switch theta burst, the same kind of speculative interpretation may be applied. That is, perhaps multiple regions of neurons in the hand or motor area are activated, followed by competition until a relevant subset remains (see section 3.2.2). Finally, in the hand-cueing task, hand cues were followed, from 500 ms up to stimulus presentation, by an increase in frontal theta-band amplitude, relative to neutral cues. This and the fast - slow effect in the hand - modality alternating runs task are the only theta-band effects that persisted over the whole preparation interval, and so may reflect either a preparatory state or a repeating preparatory process, e.g. noise reduction through convergence, as opposed to a transient preparatory "toggling" process.

3.1.3 Alpha band amplitude and phase locking

Pre-stimulus alpha-, or mu-band motor-related lateralization was found in all relevant tasks. A modality-related effect was found in the response-stimulus interval of the modality-switching task. When an auditory trial was repeated, occipital amplitude increased from response to around 800 ms into the interval. What precisely the underlying neural activity is and what it achieves are uncertain, but would seem likely to involve thalamocortical interactions decreasing the effect of visual information on the state of associative cortex (section 1.5). A further question the effect raises is why it did not occur preceding switch trials. If the effect reflects effective preparatory activity, its absence would seem to be due to an inability or difficulty to perform that activity in the alternation context. This could be due either to just having performed a visual task, or to not yet having performed an auditory task. It seems possible that, especially because visual input was constant during the whole of the modality-switching task, that the switch away from the visual task cannot be completed pre-stimulus. In that case, the effect may reveal a mechanism by which task-set inertia (section 1.2) occurs.

In the cued chiastic switching task, high central - parietal alpha-band phase locking was found during the second half of the cue - stimulus interval for the fast hold - hold condition. It may be important in interpreting this activity that this sequence involved a lack of change that is perhaps analogous to postural stability (section 1.6). Finally, in the sequence cueing task, full - information cues resulted in central - parietal alpha-band ERD relative to neutral cues, around 600 - 900 ms post-cue. As this was the only condition in which the full response sequence could be imaged before the imperative stimulus, the effect could reflect motor imagery, perhaps as a method to keep the motor program in mind by rehearsal.

3.1.4 Beta band amplitude and phase locking

Lateralized motor-related beta-band ERD and phase-locking, especially between frontal and motor regions, were found when switching between hands, in the hand-modality and hand-only switching tasks. So, the activity that survives ERD is phase-locked to other areas, although it is not clear when that subset of activity becomes phase-locked: does phase-locking increase concurrently with ERD, or was the activity already phase locked while ERD perhaps pruned the non-phase-locked activity away? Lateralization in phase-locking and ERD do not seem to be two measures of the same process, at least not in the context of the choice - go/nogo experiment. Cueing the response hand resulted in some differences in lateralized ERD, i.e. an early low-alpha and late beta-band increase in MRAA for 100 % go blocks, while no probability effect was found on phase-locking. However, this dissociation is based on differences in statistical significance and so may be an artefact of differences in noise in the two measures. Further study is needed to better determine relationship between lateralization in phase locking and, especially, the beta band. Low beta-band (16 Hz) ERS was found around 500 ms post-cue, significantly for the 50 % but also as a trend for the 100 % go probabilities. Given the post-cue temporal context, this burst may reflect a way of the inhibition of overt responses in the face of motor-related "internal" processes. In the sequence-cueing task, increased pre-stimulus contralateral ERD was found for fully specified, repeated-element sequences, while lateralized phase-locking was found for the left- versus right-hand cues, for all cue types. Finally, in the hand-switching task, EEG-EMG phase locking increased between the EMG channel of the hand being switched away from, and contralateral central sites. This suggests that part of switching involves "freezing" the inappropriate hand and in that way inhibiting the irrelevant task set.

Non-lateralized effects were also found in the beta band. Fast trials were preceded by beta-band ERD, over central and parietal regions, in the hand - modality switching task. In the chiastic switching task, an increase of pre-stimulus beta-band amplitude was found preceding slow switch trials, in a switch - switch sequence. The effect is similar to the lateralized ERS in the choice / go-nogo task. In both cases, responses were not given quickly (post imperative stimulus), or at all (post-cue). Possibly, subjects were confused on some switch - switch trials, and the peak reflected preparing not to respond too quickly, when an error was likely.

Finally, beta-band ERD was found in situations in which a response could be prepared. All cues in the sequence cueing task were followed by, primarily frontal - central, beta-band ERD in the cue-stimulus interval. When cueing response hand in the 100 % go blocks, beta-band phase locking increased at the end of the preparation interval relative to neutral cues. It remains to be determined exactly what relation this ERD has with preparation. For instance, is the ERD only a consequence of changes in the brain's information processing, or does ERD itself change how information is processed? In either case, the role of motor-related cortical activity seems likely to have to be understood both in terms of effects on the subcortical feedback systems for movement (described in section 1.6) and from the point of view of the question: what neural computations result in a mapping from motor-related goals to the patterns of activity such as the various lateralization measures?

3.2 Conclusions

A number of conclusions can be drawn from the studies, concerning the following questions. Can preparatory effects be found on time - frequency domain measures? Do such measures provide important extra information over ERP's? Under what conditions in task switching does oscillatory activity occur in the theta, alpha and beta bands? Can EEG data be used to study questions on task switching, e.g. is there evidence for a fallible preparatory switching process [47] (section 1.2)? What kind of brain activity is involved in motor preparation outside of the task switching context? The following sections discuss the conclusions that can be drawn from the studies, and the studies' limitations.

3.2.1 EEG measures

The studies explored preparatory brain activity, using a number of EEG measures. The measures - ERP's, LRP's, instantaneous amplitude and phase-locking - were sensitive to the various experimental manipulations. Further, the measures were dissociable from each other. Some contrasts affected time-domain measures but not frequency-domain measures of lateralization, such as the fast - slow by switch - hold interaction in the hand - modality switching study. So including these measures in EEG studies seems to be worthwhile, both because they do capture some aspect of brain activity and because they may provide additional physiological information from which to draw (psychological) conclusions. A very general conclusion is that brain activity in the studied contexts does indeed involve changes in large-scale frequency-domain behavior. Further, the data emphasized the importance of measures aimed at non-stationary signals: effects often involved transient increases, decreases, peaks and troughs in frequency-domain measures.

There are two important limitations in the analyses of the present studies. First, many more measures of EEG activity exist than oscillatory amplitude and the PLV. Non-linear couplings, for instance where an increase in the level of activity in one channel is associated with an increase of the frequency of oscillations in another, would not be detected using the PLV; neither would consistently coupled changes in amplitude in different frequency bands. Further, the PLV is sensitive only to consistent phase differences at equivalent time points over trials. It could be that phase-locking occurs over a certain period on each trial, but with arbitrary phase differences [124], and such phase locking, which is perhaps closer to what would intuitively be understood by the term, would require other methods [125] than the PLV to be detected. Finally, the gamma band may well contain an important part of brain activity [228]. Unfortunately, it also contains much activity due to muscle artefacts (visible in the response-speed contrast in the hand-modality switching task, section 2.1) and the development of reliable artefact removal seems to be required or at least desirable for EEG data to be analyzed in this band (see below).

Also, in the current analyses no attempt was made to determine directionality between channels, i.e. whether activity in channel A could be said to cause that in channel B more than vice versa. Directionality must be defined in terms of some model that is then fitted to the data, e.g. Granger causality is a definition of causality, and directionality, that defines the statement "A causes B" as "the present of B is predicted by the past of A". Techniques such as structural equation modelling and the directed transfer function [9] have been used to search for such relations between time series with high temporal resolution, such as the EEG. Such studies may reveal more details of the mechanisms of hierarchies of control, such as the dependence in the prefrontal cortex of stimulus on context on episodic information [119] (section 1.3.2). Note, however, that control and causality are not synonymous: all the steps in the controlled process are causal, as are automatic processes. Measuring control would seem to require correlating activity and error reduction, not past and present.

A general problem that remains with measures in explorative studies is that the number of possible analysis techniques is infinite. More detailed hypotheses on brain processes could provide more specific predictions in terms of relations in the data. This would also reduce the statistical problems of testing ”everything by everything”.

The second type of limitation is that of spatial resolution. Analyses in the present studies concerned individual channels or clusters of channels, not underlying sources, as could be looked for using source localization [236] [81], or statistically well-defined components such as provided by independent component analysis [96] (ICA). ICA may also provide a solution to the problem of muscle artefacts, if such activity can be cleanly separated from that from neural sources. Building on the characteristics of and experimental effects on the measures that were found in the present studies, further research could introduce more sophisticated analyses to improve spatial resolution. For instance, coherence data between scalp electrodes can be used to estimate underlying coherence between points on a grid of locations in the brain and a given reference, using Dynamic Imaging of Coherent Sources (DICS [81]). Source localization may also provide information on the relation between lateralized beta-band ERD and phase locking: are the locked underlying sources, if phase locking between sources is in fact the cause of the phase locking between channels, the same as the sources undergoing ERD? Describing the data using sources or components would further reduce statistical problems, given reliable sources. Integration with anatomical, in vivo and other neuroimaging results would of course be improved with measures related to brain regions as opposed to scalp positions.

3.2.2 Preparatory activity and processes

Although further study is clearly needed before confident generalizations can be made, the data provide some suggestions on processes underlying behavior, and vice versa, the behavioral contexts in which activity was found provide suggestions on the function of that activity. In the switching studies, the most important result is that preparing to switch tasks is associated with a different pattern of brain activity than preparing for a repeated task. Further, interactions on the ERP and LRP were found between response speed and trial type (alternation versus repetition). This would appear to support the general idea that preparing for switch trials is ”special”, although not what the precise nature of this preparation is or whether the difference should be described as some kind of additional ”switch” process (i.e. endogenous reconfiguration [197]) that is absent for hold trials. It is possible for instance that at some level of description, for both switch and hold trials, a goal must be retrieved from memory, but that the consequence of retrieval (e.g. some form of internal conflict) is different in the switch and hold contexts. Some speculations on what preparatory processes might underlie the measures pre-stimulus activity are given below.

In the hand-modality switching task, pre-stimulus theta-band amplitude was higher for fast trials, regardless of whether a switch was necessary. Other pre-stimulus activity - lateralized phase locking - was related to whether a switch was necessary, but not to response speed. The CNV showed an interaction between response speed and switching. Such results illustrate the complex nature of preparation. Preparation, defined as that which improves subsequent performance, may constitute recalling what must be prepared; overcoming the effects of a no-longer correct task set; changing the sensitivity of responses to different modalities; preventing a set of responses from being given; or reducing noise in a goal-directed state that would cause slowness or errors. The present studies suggest, as would be expected from the literature discussed in the introduction, that the physical events that result in prepared behavior involve both rate and phase coding. Although clearly more research is needed, some speculative and badly specified assignments can be made, that may be useful in generating more specific hypotheses. Extrapolating from the present data, large-scale phase locking may be part of the way goals are encoded, or equivalently, of how the error signal for cognitive control is defined neurally. The reduction of that error signal appears to involve local oscillatory behavior, e.g. bursts of theta or periods of mu- and beta-band ERD. Elevated firing rates may be the bottom line behavior, encoding specific responses or codes in associative cortex. Pre-stimulus theta-band activity could be hypothesized to provide an autoassociative form of noise reduction, every burst of activity providing an iteration analagous to the behavior of a Hopfield network. Such a process could be one aspect of preparation: error reduction in the context of a task set implementation, nested in other processes that define what constitutes "error".

The theta-band bursts found preceding switch trials in the modality- and chiastic-switching tasks appeared to reflect a preparatory switching process. It was hypothesized that such bursts reflect periods in which different patterns of activity compete, so that the cessation of increased EEG amplitude would indicate the resolution of competition between task sets. An association between a switch in activity and a burst of oscillatory activity occurs in the simplified model of switching illustrated in figure 3.1. In this model, a switch is made from one to another population of neurons. The mechanism is based on the most active population receiving most recurrent inhibition when the switch is triggered. The switch "command" consists only of indiscriminate excitatory input, of which the concrete effect depends on this lower-level toggling mechanism (a similar mechanism was used to allow gating in a model of prefrontal context-sensitivity, in which a network learned to perform a continuous performance ("AX") task [27]).

Only preliminary modelling work, based on the integrate-and-fire neurons used in Wang [237], was done using the described architecture. However, in a simulation of the effect of common inhibition on competition, a short period of input did evoke a period of simultaneous oscillations in a set of sub-populations (figure 3.2). The dual oscillation continued for a certain period after the command had been given, i.e., after the excitation stopped. After a number of cycles of recurrent inhibition, one population evoked recurrent inhibition before enough neurons in the other population fired to ensure its survival into the next cycle, so that in the end only one population remained active. So, as in the hypothesis concerning what association bursts of oscillatory activity could have with task switching, the resolution of the period of competition was marked by a reduction in the summed oscillatory activity.

The model illustrates a number of points. First, an unspecified switch command can be transformed into a shift of patterns of activity that is more complex than the command itself. This could be termed a "blind switch", or "abstract switch command": the population responsible for the reorganization of activity, from population A to population B, does not need to "know" about A or B; it simply says "switch" and what happens in terms of A and B is determined locally. This is only intended to illustrate the feasability of the existence of a blind switching mechanism, but the general idea does agree with the WwM hypothesis and associated literature described in section 1.3. Second, the model provides an example of a hypothetical switching criterion in neural terms: the relative activity, or stability, of a subset of activity is the measure used to determine what gets switched. Third, the model illustrates a separation between the initiation of a switch - in this case the firing of the switch population - and subsequent processes needed for the switch com-

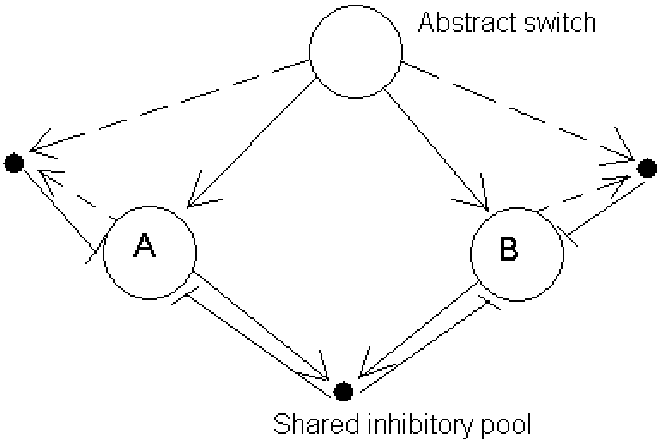


Figure 3.1: A simplified switching model. Arrows and "T"-connections represent excitatory and inhibitory connections, respectively. Strong and weak connections are plotted as continuous and dashed lines, respectively. Circles represent uniform populations of excitatory or inhibitory neurons. Connections between and within populations include both fast (AMPA) and slow (NMDA) synaptic dynamics, as in Wang [237]. With slow-dynamic synapses, recurrent inhibition results in an ongoing oscillation (section 1.1.4. Due to the lateral inhibition, if sufficient neurons in population, e.g., A fire to evokes an inhibitory pulse back to itself and B, before sufficient neurons within B fire to excite itself so that firing occurs after inhibition stops, only A will continue to fire. The unshared inhibitory pools require excitation from both the connected excitatory population and the abstract "switch-command" population to fire. So, only the currently active population will undergo inhibition when the command pulse is given. This serves as a toggling, weak-to-strong mechanism.

mand to have an effect - the competition during the period of simultaneous oscillation. Finally, the model illustrates, in an embryonic way, how behavioral patterns could be explained via relatively large-scale neural structures and processes.

Some points are also illustrated by absences in the model. How for instance are the populations being switched between defined flexibly? What triggers the switch command? How is that trigger set from instructions? Modelling work seems necessary to provide satisfactory answers to such questions in computational terms, as well as explicit causal processes that can be mapped to the anatomy and physiology of the nervous system [27]. As discussed in section 1.2, models of task switching can be used to challenge assumptions and conclusions thought to be implied by data [70]. Models that specify functions for oscillatory activity [237] [101] and phase coding [94] are especially relevant to time - frequency domain data, and by extension, to the behavioral contexts in which effects in such data are found.

A limitation of the current task switching studies is that not all combinations of manipulations were tested. Ideally, different types of cueing (alternating runs, explicit task cues, explicit switch - hold cues) would be crossed with different types of switch (modality, effector, chiastic, combinations). Further, many questions on task switching remain unanswered. For instance, if it exists, how is the command to switch embedded in memory? How are instructions transformed into task

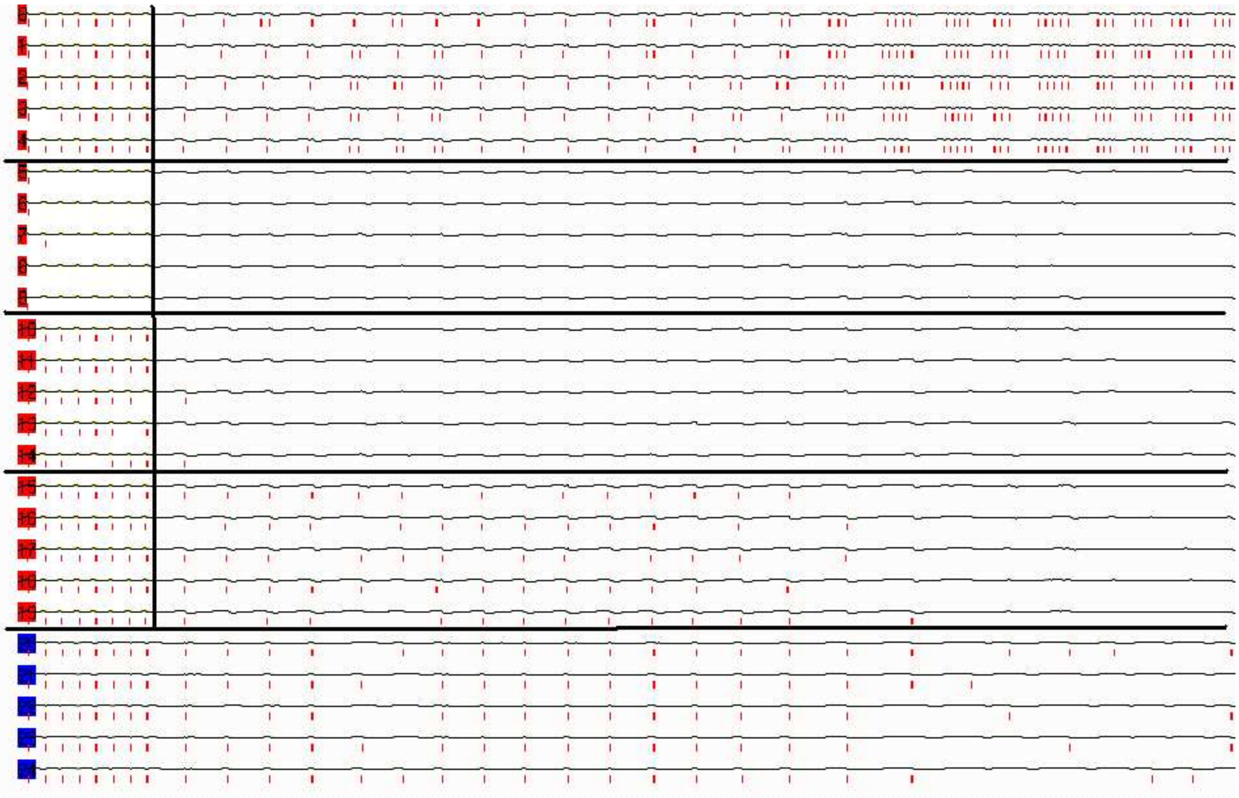


Figure 3.2: An example of the behavior of the implemented common-inhibition competition. In this model, four groups of five excitatory neurons were made, which were all-to-all connected internally, via both AMPA and NMDA synapses, but had no between-group connections. The top twenty lines show the time course (2000 ms) of the membrane potentials of the four clusters, separated by thick lines. Vertical dash marks indicate spikes. All neurons in the four excitatory groups excited the same inhibitory population (the bottom five lines), which projected back onto all the excitatory neurons. Excitatory input (as in the "switch command") was applied to the excitatory groups from the start of the plotted period up to the vertical thick line. Three of the four groups fire due to the input, which results in an oscillation due to recurrent inhibition. After the input is removed, the competition phase starts. One population loses immediately, while two populations remain active until finally only one remains, locked in the recurrent inhibition oscillation and so periodically causing the losing populations to continue to be inhibited.

sets and switching? How is long-term memory used to perform a novel task? Such questions may also benefit from combined biological - computational thinking, as computational work forces concepts to be explicitly defined and can propose causal mechanisms, while biological results provide an evolutionary grounding and possibly highly relevant fields of anatomical and physiological data (as was disussed in, e.g., sections 1.3.2 and 1.4.3).

The data concerning motor preparation suggest that different kinds of, especially beta band, activity are involved in levels of some kind of motor hierarchy. Lateralized phase locking was found when subjects knew that they would have to use the left or right hand. This occurred without significant modulation by whether responses would be fast or slow, whether a task switch was necessary, what kind of response sequence was cued or whether there was a chance no response would be necessary at all. Lateralized ERD was also insensitive to response speed, but was dependent on task switching, response sequence and, although relatively subtly, to go probability. The LRP, finally, was most sensitive to conditions, depending on response speed, task switching, response sequence and go probability. This "nestedness", of local time domain in local frequency domain in relational frequency domain activity, could be described as following a hierarchy from knowing to doing. The further from rate coding the type of activity, the more indirect the relation to specific, overt movements seems to be. This would suggest that "higher" cognition (e.g. working memory functions as opposed to low-level visual processing) in the brain is not mapped to certain locations, but to certain distributed states, as would be expected from the literature reviewed in section 1.3. In that case, part of the function of organizational regions would appear to be setting up widespread states, in terms of types of activity, under certain learned circumstances.

In conclusion, more work is needed to construct better hypothetical models, from which observed patterns of behavior to be explained emerge, and in which computational principles are shown to be implemented in biologically based structures and mechanisms. Such models should provide testable predictions about brain activity, which would hopefully progress to become more and more explicit and detailed. An important class of models would seem to be those that relate changes in information processing to goals. Goals may coexist at different time scales, and as illustrated by the tower of hanoi, or missionary and cannibal type of problems, conflicts may occur between goals at different time scales. Understanding how such goals may conflict may provide insight in psychologically or clinically relevant behavior, for instance when people are unable to put aside short-term profits to achieve long-term goals. The neuroscientific component of the study of such goals would seem to be likely to involve the temporal gradient in the prefrontal cortex described in section 1.3.2. A further possible conflict between types of goals would be between explicit and implicit goals, for instance as seems to be the case in task switching: there is an explicit, or conscious, verbalizable goal concerning stimulus - response mappings, but an implicit, unconscious goal of the brain to achieve stability. The assumption that the brain is always attempting to achieve some goal, even if it fails to achieve goal-directed behavior, may help understand insanity [126]. Two main questions appear to lie at the basis of studying goal-directed behavior and processes. First, what is the error signal, i.e. what is being controlled - pleasant perceptual input? Maximal behavioral rest, as in Freud's secondary process? Can we consciously control internal states implementing stimulus - response mappings, as opposed to their perceived consequences, directly? Perhaps through symbolic thought, e.g. language [154]? Second, what are the automatic processes being controlled? It seems likely that understanding control, that is always "control of X", can never be understood better than the controlled processes. This bottom-up consideration also seems important from an evolutionary perspective, as presumably control could only evolve after less flexible and conditional patterns of behavior. Work on evolutionary explanations of the nervous system's development seems likely to help work on understanding what the mind is now, as well as the converse.

The present studies show that time - frequency domain analyses of preparatory activity reveal a potentially important part of brain activity involved in such goal implementation and goal conflicts. So, however the brain organizes itself to achieve cognitive control, complete hypotheses on this organization should include large-scale patterns of oscillatory neural behavior and its functional roles. The existence of organizational principles on relatively large scales may be a necessary and sufficient condition for the reliable construction of a "mid-level" language of brain activity, in which objects consist of patterns of neural activity, emerging from many neuronal interactions between brain structures and resulting in behavior aimed at interacting with the world. Such a language would provide a link between the behavior of individual or small groups of neurons and psychological constructs aimed at explaining overt behavior. Discovering / constructing this language, as is being done in e.g. modelling work discussed in previous sections [237] [27] [54], would seem to require a close partnership between empirical (especially psychological and biological) and theoretical (especially mathematical) study.

Samenvatting (Dutch summary)

Dit proefschrift gaat over hoe mensen een keuze maken uit meerdere mogelijke handelwijzen. Het resultaat van deze keuze wordt beschreven als een taakset: een tijdelijke verzameling stimulus-responskoppelingen. Mensen kunnen wisselen van taakset, wanneer dat nodig is om een bepaald doel te bereiken. Zo is het doel de oorzaak van de taakset, maar tegelijk geldt dat het doel ontstaat uit deterministische, biologische processen die niet psychologisch te duiden zijn als bewuste keuzes. Keuzevrijheid is dus betrekkelijk en kan zowel doelgericht als deterministisch genoemd worden.

Het veranderen van taakset wordt een taakswitch genoemd. Na een taakswitch is de reactietijd vertraagd. De reden hiervoor is nog onbekend. Meer inzicht in de onderliggende hersenprocessen zou kunnen bijdragen aan een beter begrip van zowel het verschijnsel taakswitchen op zich, als de negatieve effecten ervan op de taakprestatie. Om verbanden te kunnen leggen tussen fysieke hersenprocessen enerzijds en het gedragsmatig en psychologisch gedefinieerde taakswitchen anderzijds, is het nodig bepaalde psychologische concepten, zoals cognitieve controle, te reduceren tot algemene begrippen die een duidelijke betekenis hebben in fysieke systemen. In het bijzonder gaat het hier natuurlijk om het brein. Begrippen die hier gebruikt kunnen worden, zijn informatie en communicatie, controle en stabiele toestanden. Een taakswitch is dan te beschrijven als het gevolg van een verandering in een doeltoestand in een controlesysteem dat de communicatie tussen perceptie en actie regelt.

Taakswitchen is een voorbeeld van flexibel, doelgericht gedrag, waarbij informatie tijdelijk op één van verschillende mogelijke manieren moet worden verwerkt. Dit soort gedrag is afhankelijk van het functioneren van met name prefrontale cortex, maar ook van samenwerking tussen hersengebieden. Er zijn binnen betrokken gebieden verschillende soorten neurale activiteit mogelijk: bijvoorbeeld het optreden van oscillaties van verschillende frequenties. Bij de ene frequentie lijkt een andere psychologische interpretatie te passen dan bij een andere. Voor dit proefschrift zijn drie frequentiebanden van belang: de thêta- (5 - 7 Hz), alpha- (8 - 12 Hz) en bêta- (18-24 Hz) banden. In de thêtaband is activiteit gevonden die voor het werkgeheugen van belang lijkt te zijn. Alfaband-activiteit lijkt tijdelijk informatieverwerking in specifieke neurale gebieden te inhiberen. De bêtaband tenslotte, lijkt motorische stabiliteit te versterken.

In de hier beschreven experimenten is gekeken naar de relatie tussen hersenactiviteit in de genoemde frequentiebanden en het voorbereiden van een taakset. Het ging daarbij soms specifiek om het taakswitchen, en soms meer algemeen om het voorbereiden van handelingen. Hersenactiviteit werd gemeten met het elektro-encefalogram (EEG), dat een beeld geeft van synchrone postsynaptische potentialen over delen van de cortex. Naast de activiteit in verschillende frequentiebanden - het tijdsverloop van amplitude en fasekoppeling - werden event-related potentials (ERP's) gemeten. De belangrijkste componenten van de ERP's waren de CNV (contingent negative variation, een maat voor voorbereiding op een toekomstige gebeurtenis) en de LRP (lateralized readiness potential, een maat voor het voorbereiden en uitvoeren van een actie met of de linker-, of de rechterhand). Hieronder worden zes experimenten besproken waarin vooral naar het EEG tijdens de voorbereiding op stimuli is gekeken.

1. *Een taakswitch experiment, waarbij tussen zowel handen als modaliteiten gewisseld moest worden.* De taaksets in deze taak bevatten stimuli uit óf de visuele óf de auditieve modaliteit, en responsen die met óf de linker- óf de rechterhand gegeven moesten worden. Aan de hand van reactietijden is een schatting gemaakt van de kans dat iemand wel of niet van taakset heeft gewisseld, zodat de condities wel- en niet succesvol-switchen vergeleken konden worden. Een

vergelijkbaar snel - langzaam onderscheid werd gemaakt voor de taak-herhaal situatie, zodat gezocht kon worden naar mogelijke patronen die uniek in de succesvolle (snelle) switchconditie voorkwamen. Het succesvol taakswitchen was van de andere condities te onderscheiden in het pre-stimulus EEG: de CNV en LRP waren dan groter. De amplitude in de thêta band was niet gevoelig voor het switchen maar voorspelde wel de reactietijd voor zowel de switch- als de herhaalcondities. De lateralisatie van alpha en bêta amplitude boven de motorcortices van de voor-te-bereiden hand nam toe voor stimulusaanbieding. Het effect in de bêtaband trad specifiek op wanneer van taakset veranderd moest worden. Tenslotte nam de bêtabandfasekoppeling rondom de motorcortex van de te gebruiken hand toe. Dit gelateraliseerde patroon van fasekoppelingen was sterker wanneer van taakset (dus hand) gewisseld moest worden.

2. *Taakswitchen: wisselen tussen modaliteiten.* In de voorgaande taak werden wel hand- maar geen modaliteit-gerelateerde effecten gevonden. Het zou kunnen dat proefpersonen in die taak alleen motorische voorbereiding gebruikten. Door de responsen gelijk te houden en de stimuli in de taaksets te wisselen kon met meer zekerheid bepaald worden of switchen tussen modaliteiten een meetbaar effect op het EEG heeft. Dat bleek het geval te zijn: het switchen naar de visuele taak ging gepaard met een korte periode van verhoogde pre-stimulus thêtabandamplitude over visuele gebieden. Ook werd in de alphaband een interactie tussen switchen - herhalen en modaliteit gevonden: bij het herhalen van een auditieve taakset werd een periode van verhoogde alphabandamplitude gevonden.

3. *Taakswitchen: wisselen binnen hand en modaliteit.* In deze taak werden de elementen van de taakset kruislings verwisseld. Er moesten nu andere relaties gelegd worden tussen specifieke stimuli en responsen. In tegenstelling tot eerdere taken kon nu dus niet meer volstaan worden met het globaal veranderen van hand of modaliteit om een taakswitch te bereiken. Een cue gaf aan of proefpersonen moesten veranderen van taakset, of hun oude taakset moesten hanteren. In deze taak werden complexe patronen in gedrag en EEG gevonden die niet alleen van switchen versus herhalen afhingen, maar ook van tweede-orde condities. Het maakte verschil of er twee keer achterelkaar een switch kwam, of eerst een switch en dan een herhaling, enzovoort. Met andere woorden, of er een switch van taak optrad, maar ook of de cue veranderde. Een opvallend resultaat was een positieve piek in de ERP zowel na een verandering van cue, als na een taakswitch. Maar gegeven een cueswitch, ging ook een taakswitch gepaard met een verhoogde positieve piek na de cue. Een switch na een switch bleek vergezeld te gaan van een uniek patroon in pre-stimulus thêtabandfasekoppeling. De fasekoppeling van rechts-frontale electrodes was laag, terwijl links posterieur de fasekoppeling hoog was.

4. *Taakswitchen: wisselen tussen handen.* In deze taak bleef de modaliteit visueel. De proefpersonen wisselden alleen van hand. De motorgerelateerde effecten van de eerste taak werden gerepliceerd en uitgebreid met resultaten op relaties tussen hersen- en spieractiviteit. Wanneer van hand gewisseld moest worden, was de btabandfasekoppeling tussen de irrelevante handcortex en de spieren in de bijbehorende arm verhoogd. Dit werd geïnterpreteerd als een manier om de responsen van de oude taakset te inhiberen.

5. *Motorpreparatie: het voorbereiden van motorsequenties.* Hierbij werden imperatieve stimuli aangeboden die een sequentie van twee responsen aangaven. Deze stimuli werden voorafgegaan door een cue die geheel of gedeeltelijk de imperatieve stimulus bekend kon maken. Er

waren twee responsen: links of rechts. De vraag was wat er zou gebeuren als de tweede respons bekend was: zou dit tot motorgerelateerde lateralisatie leiden, ondanks dat er eerst een ander respons gegeven moest worden? Zouden de verschillende soorten lateralisatie - LRP, gelateraliseerde amplitude, fasekoppelingpatronen - onder verschillende omstandigheden optreden tijdens preparatie? Dit bleek het geval te zijn. De pre-stimulus LRP week alleen duidelijk van nul af wanneer de hele sequentie bekend was, en alleen dan als die sequentie bestond uit één linker- en één rechterhand respons. De bêtabandamplitude lateraliseerde ook alleen voor volledig bekende sequenties, maar nu alleen wanneer de sequentie tweemaal dezelfde respons bevatte. Fasekoppeling in de bêtaband liet een gelateraliseerd patroon zien voor beide volledig bekende sequenties, maar ook wanneer slechts de eerste respons bekend was; en wanneer slechts de tweede respons bekend was, bleek, hoewel zwakker, ook lateralisatie zichtbaar te zijn. In ongelateraliseerde bêtaamplitude gingen alle soorten voorbereiding, ook wanneer alleen de tweede respons bekend was, gepaard met een korte periode van amplitudeverlaging na de cue.

6. *Motorpreparatie: go - no go* In deze taak moesten proefpersonen op een stimulus reageren met de eerste of tweede vinger van de linker- of rechterhand. Voor de stimulus werd een cue gegeven, die óf neutraal was (geen informatie gaf), óf aangaf of de rechter- of linkerhand gebruikt zou moeten worden. Verder probeerden wij de inzet, de mate van voorbereiding, te beïnvloeden door de kans te manipuleren dat er een respons gegeven moest worden na sommige stimuli (de "go" kans: dit was in sommige blokken 50 % en in andere 100 %). Het geven van handinformatie bleek een positieve piek na de cue te geven, zoals ook gevonden werd in experiment 3. De pre-stimulus LRP was groter wanneer zéker een respons gegeven moest worden. Thêtabandamplitude was hoger na een informatieve dan na een neutrale cue. Pre-stimulus gelateraliseerde alpha- en bêtaamplitude, na een informatieve cue, werd alleen gevonden wanneer een respons zeker was.

Deze resultaten laten zien dat bij het voorbereiden van een taakset, in het bijzonder bij taakswitchen, en bij aspecten van het voorbereiden van handelingen, veranderingen in ritmische hersenactiviteit optreden die in het EEG meetbaar zijn. Statistische toetsing liet zien dat het patroon van veranderingen bij de meeste proefpersonen vergelijkbaar was. Dit suggereert dat de manier waarop de hersenen doelgericht gedrag mogelijk maken niet wezenlijk verschilt bij verschillende mensen. Verder zijn *1)* componenten van het ERP, *2)* de amplitude in verschillende frequentiebanden en *3)* patronen van fasekoppeling gevoelig voor verschillende experimentele manipulaties. De methode en resultaten leveren veel aanknopingspunten voor verder empirisch onderzoek, maar ook mogelijkheden voor toetsbare computationele modellen.

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