

## 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 analogous 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 characteristic regions of the imagined stimulus became dependent on prefrontal regions. A specific 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; its "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 decoupled 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 color was 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 caudal 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 measurable 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 summing 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). ERPs 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 desynchronization, 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 responds 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-lock 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, or 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.

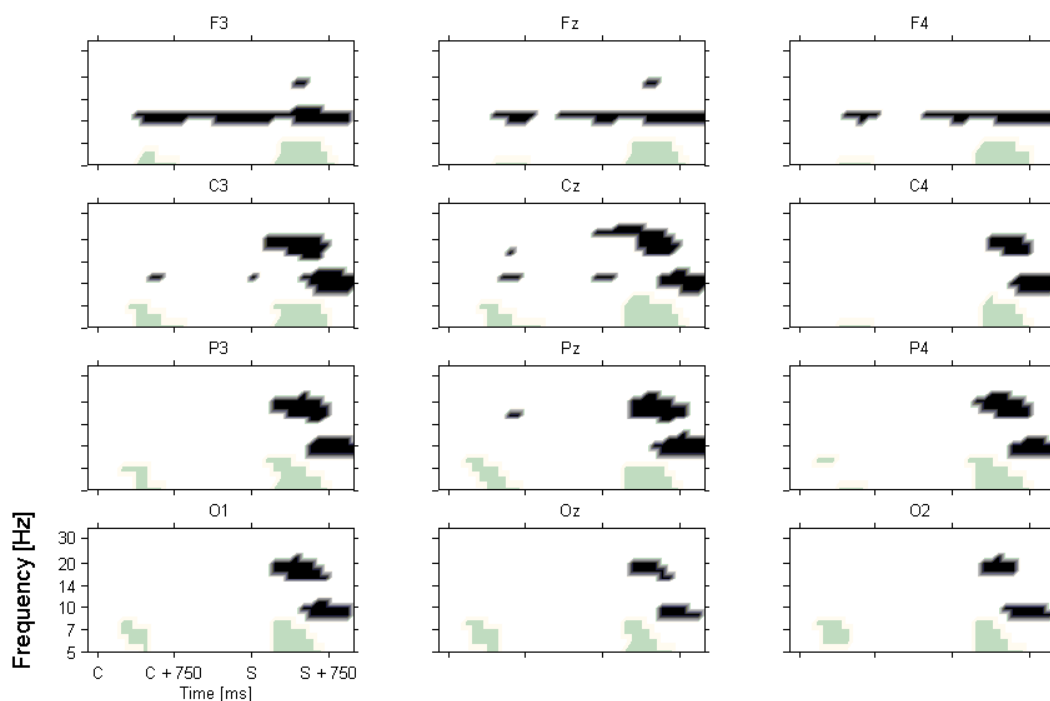


Figure 1.1: An empirical example of event-related instantaneous amplitude. The time period covers a cue (C) - stimulus (S) interval of 1500 ms. The vertical axis shows frequency. At each time - frequency point, the proportion change from the pre-cue baseline was calculated for the associated frequency 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.