

The role of theta oscillations in memory and decision making

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Introduction

Oscillatory brain activity in the theta (4-8Hz) frequency range is believed to play a role in many different cognitive functions, including memory and decision making. Both memory performance and decision making have been found to cause changes in the amplitude of theta oscillations within many different brain regions (e.g. Sederberg et al, 2003), and the coherence between them (e.g. Benchenane et al, 2010). Performance in these tasks has also been associated with phase-locking of higher-frequency (beta, gamma) oscillations to theta oscillations (e.g. Sauseng et al, 2010).

It is clear that decision making tasks can require the retrieval of relevant information from memory, and vice versa, memory tasks also involve decisions. To some extent, these two tasks rely on the same underlying cognitive processes. Yet, although the role of theta oscillations in both of these cognitive functions has been studied extensively, these studies and review articles typically focus on only one type of task and do not compare the topography of oscillations to those found in other tasks to see if they overlap.

There are some articles that address the role of theta oscillations in both memory retrieval and decision making. For example, a study done by Jacobs et al (2006) directly addresses this question, and a review by Womelsdorf et al (2010a) on the role of theta in decision making also discusses some findings on memory processes, but only to the extent that they are needed for decision making (which is limited to the retrieval of relevant information). There is not yet a comprehensive review of the involvement of theta in both memory and decision making, and the degree to which the theta activity that is found is the same for both processes.

This review sets out to investigate to what extent the theta activity involved in memory and decision making is similar. This similarity can be defined on several different levels, such as the brain areas where theta activity is found, the change in amplitude and coherence of theta oscillations that is associated with improved task performance, and even the phase of the theta oscillation in which other signals like higher-frequency oscillations are placed. An overview of the similarity between findings in both lines of research may shed light on the relation between these different cognitive functions. If we know to what extent theta activity is similar during these two kinds of tasks, this may also help us determine to what extent these and other broad cognitive functions rely on the same cognitive sub-processes and neural mechanisms.

In the first two chapters, we will outline the changes in theta activity that are associated with memory and decision making tasks separately. We will describe how theta activity in different brain areas changes as a function of successful task performance, where these changes take place and which cognitive sub-processes they are believed to reflect. In both of these chapters, it is striking that many different sub-processes of both types of cognitive tasks are associated with increases in theta power and coherence in frontal cortex. Moreover, authors in both fields have suggested that this frontal theta activity may reflect a form of cognitive control that is not limited to any particular sub-process, or even any particular type of task. Therefore, the third and final chapter will discuss evidence for such a process that is needed across different forms of cognitive functioning, and evidence that it may be reflected by frontal theta.

In addition to changes in theta activity in one brain area, we aim to identify changes in theta synchronization between different areas that are associated with successful task performance in both fields. An increase of theta power by itself does not explain how different brain areas work together to perform a task. The synchronization of oscillations across different brain regions and frequencies could be a general mechanism by which the different sub-processes needed to accomplish a complex cognitive function are coordinated (Nyhus & Curran, 2010). Given the shared patterns of theta activity for these tasks and the fact that many authors believe this activity to reflect a common process, we will investigate if these shared oscillations synchronize with different brain regions depending on which task is being performed. This could reflect the recruitment of task-specific sub-processes by a more general cognitive control system.

Chapter 1:

Theta activity and decision making

Many studies have been done that look at the role of theta oscillations in decision making tasks, and particularly with regard to action regulation. Luu et al (2003) define this as “a process that involves learning which behavior is relevant in a given context, monitoring the outcome of an action, and switching to a different behavior when expected outcomes are violated.” There seems to be a consensus that this process takes place in medial (pre)frontal cortex (mPFC), most likely in the anterior cingulate cortex (ACC), in cooperation with other brain regions. Cohen et al (2007) show that ACC is responsible for signaling errors and feedback, and using this to improve performance. Many other studies also support the involvement of medial frontal cortex in reward processing and adaptation of behavior (e.g. Marco-Pallares et al, 2008; Cohen et al, 2009).

In this chapter, we will look at the role of theta activity at several different stages of the decision making process. First we will discuss theta activity that is present before and while a decision is made. This will be followed by discussions of neural responses to errors and negative feedback. Finally, we will look at theta activity during the adjustment of behavior in response to the outcomes of previous decisions. All of these stages of the decision making process seem to have an effect on theta activity in a network of brain structures that includes medial and lateral (pre)frontal cortex and parts of the striatum and limbic system. This has led to the proposal of several “decision making networks” in which these structures play a role. These will be discussed at the end of this chapter.

Decision points

An important part of a decision making task is, of course, the decision itself. There are several studies that have looked at theta activity at so-called decision points, the moment when all the necessary information is accumulated so that a decision can be made.

Womelsdorf et al (2010b) have looked at the representation of task rules, or stimulus-response mappings, and whether neural activity can be used to predict which mapping will be applied on a given trial. There is evidence that these task rules are represented by groups of neurons in prefrontal cortex (PFC) and anterior cingulate cortex (Womelsdorf et al, 2010a). In a task where macaques needed to switch between making pro-saccades and anti-saccades to a peripheral stimulus, theta activity in ACC predicted which SR mapping the monkey was going to apply. The latency of this theta activity was earliest (0.4s before probe onset) right after a switch, but declined after more trials with the same rule. Theta activity in prefrontal cortex showed the opposite pattern, only reaching the same latency of 0.4s after several trials with the same rule. The authors conclude that ACC responds to changing task demands and tracks these demands in order to initiate selective cognitive control signals to correct errors. The early theta activity in ACC was found on the trials immediately following errors, when task rules needed to be re-established (Womelsdorf et al, 2010b).

Womelsdorf et al (2010a) believe that ACC can only perform its action monitoring function when it has information about which behavior is adequate within the relevant task rules, and suggest that this information is retrieved by interacting with hippocampus and reward circuitry in orbitofrontal cortex and striatum. Reward anticipation, or the associations of reward with different possible actions, depends on the evaluation of rewards. Signatures of this process have been found in ACC itself and dorsolateral PFC (dlPFC), dorsomedial and ventral striatum and orbitofrontal cortex (Womelsdorf et al, 2010a).

DeCoteau et al (2007) looked at local field potentials in the striatum and hippocampus of rats while they learned to perform conditional T-maze task. They found that theta rhythms in these two areas synchronized at decision points, adopting opposite phases, in a way that reflected the amount of learning that occurred. Van der Meer & Redish (2009) recorded the spiking activity of neuronal ensembles in rat ventral striatum and found reward representations, not only when a reward was delivered, but also at decision points. The authors suggest this may be needed for the evaluation of different options during decision making. Benchenane et al (2010) also recorded single neuron activity in rats, and found phase locking of prefrontal neurons to hippocampal theta activity as the animal

traversed the decision point in a maze task. The strength of this theta coherence was correlated with the amount of learning that had occurred. Combined with other studies showing that theta influences spike timing, Womelsdorf et al (2010a) believe that these findings indicate that theta synchronization is involved in the link between reward prediction and a decision.

In another study in rodents, Van Wingerden et al (2010) show evidence that theta activity in orbitofrontal cortex represents both the predictability of reward, and whether a positive or a negative reward is expected. This information is needed to inform other structures, like ACC, about the expected value of different possible choices.

Jacobs et al (2006) have also looked at theta activity at decision points, but in the context of a working memory task. They used a Sternberg task, where subjects need to remember a set of items and are then shown a probe item, after which they need to decide whether this probe was part of the memory set or not. In this paradigm, task difficulty can be manipulated by varying the number of items that need to be held in memory. Jacobs et al (2006) found that post-probe theta power was inversely related to memory load at widespread electrode locations. During the delay phase of the task, the relation of theta power to memory load was reversed, so that theta was positively correlated with memory load. Gevins et al (1997) have also shown that frontal midline theta is increased as a result of greater task difficulty. Luu et al (2003) interpret this to reflect the greater demand for monitoring performance outcome that comes with increased memory load. Jacobs et al (2006) suggest that central theta power, as well as an error-related ERP component called the error-related negativity (ERN; see below), in fact reflect decision difficulty. In their study, electrodes over ACC show an increase in theta power that starts after probe onset and lasts until the time when the subject makes a response (Jacobs et al, 2006). Of several different variables, the one that best correlated with this pattern was reaction time quartile, a measure that reflects a subject's confidence as lower confidence tends to lead to longer reaction times. According to Jacobs et al (2006), incorrect responses are characterized by decreased confidence, and it is possible that this is what causes the error-related negativity (ERN). In support of this, even on correct trials (where the ERN itself cannot occur because no error is made) the ERP voltage was most negative for slow responses. This indicates a relation between ERP negativity and decision confidence that is not restricted to error trials.

After a discussion of many different brain areas that play a role in decision making and evidence that theta activity is found in each of them, Womelsdorf et al (2010a) suggest that the critical role for theta-synchronized activity is the retrieval of choice-relevant information around decision points. They propose a model in which choice selection ultimately depends on a build-up of sufficient coherence within a network of areas that represent different kinds of information needed for a decision.

Errors and negative feedback

Sometimes, a decision is made that is not correct. Several studies have looked at brain activity during erroneous decisions, before any feedback is given, and compared this to brain activity during correct trials. It is important to distinguish this from the brain's response to negative or positive feedback, which will be discussed separately. At the same time, several studies find similar neural responses to errors and to negative feedback. As a result, some authors believe that they reflect the activity of the same action monitoring system and formulated theories of action monitoring that are based on the neural responses to both errors and negative feedback. Some of such theories will be discussed further in this section, but we will start by discussing these two lines of evidence separately.

Brain activity associated with errors

There do not seem to be many studies that have looked at oscillatory brain activity during erroneous decisions. However, Cavanagh et al (2009) have looked at activity in medial and lateral PFC during error trials, comparing them to the trials directly before and after. They found that medial PFC responds to errors with increases of power (from response onset to at least until 400ms post-response) and phase synchrony in the theta band, consistent with a view that the ACC encodes prediction error following feedback in order to update predictions. Lateral PFC does not show this response, but theta phase synchrony between mPFC and lPFC is increased on error trials and this synchrony is predictive

of the degree of later behavioral adjustment. The authors suggest that these changes in activity during errors can be used to establish an interaction between action monitoring systems in ACC and cognitive control systems in IPFC to adjust behavior.

Many of the EEG studies involving decision making tasks look at event-related potentials (ERPs) rather than oscillatory brain activity. In these ERP studies, one component is often found during error trials. The error-related negativity (ERN) is a negative voltage deflection that accompanies an erroneous response. It shares functional and topographic characteristics with a component called the medial frontal negativity (MFN; Cohen et al, 2007; Marco-Pallares et al, 2008). Both are negative potentials found in mid-frontal electrode locations during errors on a task, and are thought to reflect the activity of a system that evaluates outcomes of decisions to guide behavior (Cohen et al, 2007). In addition, both components are believed to be related to theta activity, although there is evidence that they are driven by slightly distinct neural generators (Marco-Pallares et al, 2008).

Neural responses to feedback

Both erroneous and correct responses on decision making tasks are usually followed by feedback, which can then be used by the subject to improve their performance on future trials.

This feedback is often found to be associated with increases in theta power and coherence in areas associated with decision making. For example, Cohen et al (2007) find that like erroneous responses (Cavanagh et al, 2009), negative feedback (losses compared to wins) is followed by an increase of medial frontal theta power (at electrode Fz). In addition, phase coherence in the theta band is also increased, and this effect lasts up to 600ms post-feedback. Cohen et al (2009) obtained similar findings in nucleus accumbens, another brain region that is believed to be involved in reward processing and goal-directed behavior (see below for more details about this study).

In a very different study, Oya et al (2005) measured activity in medial prefrontal cortex of a single patient using depth electrodes. In this study, feedback also elicited both increased theta power (200-600ms post-feedback) and significant phase-locking across trials in the theta band within mPFC.

Similar to the response to errors, the processing of feedback has often been studied using event-related potentials. An ERP component that is often found in these studies is the feedback-related negativity (FRN). Like the ERN/MFN, the FRN is also found in fronto-central electrodes, and is believed to reflect the activity of an action-monitoring system that is most likely located in ACC (Luu et al, 2003; Cohen et al, 2007; Cavanagh et al, 2010) The FRN typically peaks around 300ms post-feedback (Cohen et al, 2007). Despite their similarities, some authors stress the fundamental difference between these components: whereas the ERN is elicited by incorrect compared to correct responses, the FRN is modulated by good or bad feedback (Luu et al, 2003). Nevertheless, the two components are believed to have similar underlying mechanisms (Cohen et al, 2007; Cavanagh et al, 2010).

The question whether FRN is more related to negative or positive prediction error has yielded conflicting results. This may in part be due to the fact that there was no reliable measure of prediction error, so that calculations of expected rewards may have been based on untested assumptions (Cavanagh et al, 2010). However, studies of oscillatory responses to feedback have been able to shed more light on this issue, and this will be discussed below.

Considering the evidence discussed so far, what stands out is that both the oscillatory activity and the ERP components found seem to be qualitatively similar during errors and feedback. Although less is known about the oscillatory correlates of errors and feedback processing than about ERPs, there is converging evidence that the ERP components that are found in relation to errors and negative feedback in fact reflect changes in ongoing oscillations, rather than sudden bursts of activity. More specifically, there seems to be a consensus that these ERP components originate from changes in mediofrontal theta activity (Luu et al, 2003; Cohen et al, 2007; Marco-Pallares et al, 2008; Cavanagh et al, 2010).

In addition to the ERN/MFN and FRN, both errors and negative feedback are often associated with an increase in theta power (e.g. Cohen et al, 2007; Cavanagh et al, 2009). As a result, the ERP negativity is believed to result from a general increase in theta power and a phase-locking of ongoing theta

activity in response to errors. In relation to this, Hyman et al (2011) believe that phase-locking of mPFC neurons to hippocampal theta activity reflects directing attention to task-relevant stimuli. In addition, the authors observed a reset of theta activity following errors, which they believe serves as a signal that the relations between cues and reward expectations have changed. Several authors believe that ERP components are generated by a phase resetting of ongoing oscillations (Sauseng et al, 2007). Other evidence for the theta origin of ERP components comes from a study by Luu and Tucker (2001), who bandpass-filtered their signal between 4 and 12Hz before doing an ERP analysis. Despite this filter, the FRN component was largely intact. This supports the view that the FRN, too, is driven for a large part by activity in the theta band.

As the previous paragraphs illustrate, several different oscillatory phenomena in different parts of the brain are associated with errors and/or negative feedback. Several authors have proposed theories about the roles of these different forms of brain activity, and used task manipulations to tease apart the neural correlates of different sub-processes related to errors and feedback. In the next paragraphs, we will discuss some of these theories and the evidence supporting them.

Magnitude of prediction error

Although ideas about prediction error are often inferred from the outcomes of certain trials, prediction error does not depend only on the outcome of a choice, but on the difference between that outcome and the outcome that was expected. Therefore, Cohen et al (2007) postulate that the brain's response to feedback should also be modulated by the probability of good versus bad feedback. However, the authors state that previous studies about the relation between FRN magnitude and outcome probability have yielded conflicting findings. Their findings support the view that the response to feedback is modulated by reward expectation: more unexpected wins elicited more theta power and phase coherence (300-600ms post-feedback), as well as a larger ERP response. In line with this, Cavanagh et al (2010) used computational models of reinforcement learning to estimate reward expectation on a single-trial level. Consistent with the ideas of Cohen et al (2007), this study also found that medial frontal theta, as well as theta-band coherence between mPFC and IPFC, reflects the magnitude of prediction error.

However, in the study by Oya et al (2005), the increases in theta power and phase-locking in mPFC were not linearly correlated with prediction error (PE). In fact, the magnitude of prediction error, unlike the magnitude of punishment itself, mainly seemed to influence mPFC alpha rather than theta power. This led the authors to conclude that although mPFC processes both feedback magnitude and (positive) prediction error, the effect of expectations during feedback is not reflected in theta activity, making it fundamentally different from the ERN, which they believe is driven by oscillations in the theta band. Future research may shed light on this discrepancy regarding the relation between theta activity and prediction error.

Different responses to negative and positive feedback

Although studies of feedback tend to look at both positive and negative feedback, studies on activity before feedback seem to place much more emphasis on error signals than on responses to correct trials. Not many studies seem to have investigated whether activity found in relation to errors also has some counterpart corresponding to correct task performance. Marco-Pallares et al (2008) state that for error responses in prefrontal and cingulate cortex, it is unclear whether neurons only exhibit a unidirectional error signal, or if they also respond to successful trials. With regard to MFC, Marco-Pallares et al (2008) conclude that their findings are consistent with a unidirectional error signal in ACC, possibly conveyed by the midbrain dopamine system. In one study of activity that takes place before a decision is even made, Van Wingerden et al (2010) show that orbitofrontal theta activity represents whether a positive or a negative reward is expected.

With regard to feedback, more attention is given to positively rewarded trials. In fact, Womelsdorf (2010a) discuss that one of the functions of the decision making network is to distinguish between positive (reward) and negative (punishment) feedback. Still, it is not always clear whether the regions

involved in reward processing exhibit a qualitatively different response to different reward valences (i.e. positive versus negative feedback).

Marco-Pallares et al (2008) discuss evidence that midbrain dopaminergic neurons projecting to ventral striatum increase their activity following better-than-expected feedback, as well as decreasing their activity after worse-than-predicted feedback, while activity does not change for well-predicted rewards. These authors also report increased theta power at midline electrode sites after losses, and increased beta oscillations following wins. In other words, positive and negative feedback are reflected by oscillations in two different frequency bands, both of which are likely to accommodate functional coupling of different brain regions. As a result, the authors suggest that gains and losses may be processed by two distinct neural networks, where the former involves ventral striatum and midbrain neurons, and the latter involves activation of the amygdala. They further cite evidence that higher theta/beta ratios are associated with poor decisions in the Iowa gambling task (Schutter & van Honk, 2005), again suggesting that errors and negative feedback are processed by the same neural structures. Cohen et al (2007) state that previous research has yielded conflicting results about whether the FRN is only related to losses or wins, or to both, and did a study to compare ERP and oscillatory responses at Fz to both wins and losses. They find that all feedback-related ERPs showed phase-locking in the theta band and enhanced gamma power, but only responses to losses are also driven by increased power in the theta band (300-600ms post-feedback) and theta phase coherence (300-400ms). Wins, on the other hand, show increased power (300-400ms) in a band that the authors refer to as lower gamma, but which is in fact part of the frequency range that Marco-Pallares et al (2008) refer to as beta. This means that the findings of Cohen et al (2007) are entirely consistent with the result of Marco-Pallares et al (2008) that theta activity in medial frontal cortex represents losses while wins are reflected by higher frequency oscillations.

Cavanagh et al (2010), on the other hand, found that medial frontal theta changes following both positive and negative feedback, as it relates to the magnitude of prediction error. They suggest that positive feedback may elicit ERP components with a positive deflection, which obscure the FRN. However, the current study does not show evidence of ERP components that were larger on correct than incorrect trials. Furthermore, although the ACC seems to reflect both positive and negative mismatch, the authors believe it may be particularly sensitive to punishment, which they say may or may not be related to mesolimbic dopamine-driven reward prediction computations.

This study by Cavanagh et al (2010) built on their earlier study of medial and lateral PFC responses to errors. Here, the authors investigated theta synchronization between mPFC and IPFC following feedback and found that in addition to being increased on error trials, it was also greater following negative than positive feedback.

With regard to lateral PFC, there is a lot of evidence that this region is involved in working memory. Cavanagh et al (2010) suggest that the working memory system in this area responds to both losses, with delayed behavioral adjustment, and wins, by storing positive stimulus-response associations that lead to faster reaction times when the same stimulus is presented again. In line with this, IPFC activity correlated with prediction error for both positive and negative feedback. The authors suggest that the IPFC does not compute reward prediction error as such, as it does not discriminate between positive and negative feedback, but rather reflects the salience of prediction violation or mismatch in general, or the absolute size of prediction error.

As the last few paragraphs illustrate, there is some conflicting evidence on the different neural responses to positive and negative feedback and more research is needed to find the exact neural activity responsible for processing these forms of feedback. The same is true for the relation between frontal theta activity and prediction error. What we can conclude at this point, is that both errors and (negative) feedback are associated with increases in the power and phase coherence of frontal theta activity and similar ERP components in frontal electrodes. To what extent this activity can be interpreted to reflect the activity of the same action monitoring network during both these stages of decision making tasks, is discussed in more detail below.

Behavioral adaptation

Aside from signaling errors and processing feedback, the action monitoring system which many believe is based in ACC should be capable of using this information to improve future performance. In fact, another purpose of the study by Cavanagh et al (2010) was to find out whether changes in theta power following errors or feedback are related to subsequent behavioral adaptation.

For the increase in theta synchronization between mPFC and IPFC after negative feedback, Cavanagh et al (2010) conclude that it is not related to behavioral adjustment, meaning that there is no difference between negative and positive feedback with regard to changing behavior. Instead, the authors conclude that theta synchronization between mPFC and IPFC for both kinds of feedback represents the degree of prediction error in service of behavioral adaptation. Furthermore, theta power in mPFC itself covaried not only with prediction error, but also with immediate reaction time (RT) slowing, a behavioral response to errors. In line with this, the magnitude of the feedback-related negativity (FRN) is also modulated by the degree to which behavioral adaptation is possible, and whether feedback can be used for this purpose. Combining these results and previous findings on error processing (Cavanagh et al, 2009), the authors propose a system in which mPFC processes both errors and violations of expectations, and responds to them by interacting with cognitive control systems in IPFC via theta phase synchrony. Their findings support the idea that the same ACC-based system that processes errors and feedback is also involved in subsequent behavioral adaptation.

Reaction time slowing following errors is believed to be a manifestation of increased cognitive control (Cavanagh et al, 2009). Notably, in the study by Cavanagh et al (2010), this adaptation of behavior after errors was specific to trials in which the same stimulus was presented again, suggesting that working memory processes are involved. Conversely, trials with a correct response were followed by reaction time speeding. The authors suggest that this reflects the encoding of a positive association between stimulus and response in working memory. Theta activity in lateral prefrontal cortex was found to be related to delayed behavioral adaptations, consistent with a role for this structure in working memory. These changes in reaction time were not directly related to prediction error, but both were associated with theta power increases in right IPFC.

In addition to their own findings, Cavanagh et al (2010) discuss evidence that a lose-switch strategy (changing one's strategy after negative feedback) reflects the activity of ACC in response to punishment, as negative feedback indicates a need to adapt behavior. This is believed to occur in parallel with incremental reinforcement learning processes in the basal ganglia (Cavanagh et al, 2010). Reversal learning tasks make it possible to assess whether changes in brain activity are directly related to this behavioral adaptation, by comparing trials with the same feedback after which the participant did or did not switch their strategy. Cohen et al (2009) examined activity in nucleus accumbens during such a task. Nucleus accumbens is part of the basal ganglia, and is believed to interact with midbrain dopamine structures and medial frontal cortex for the adaptation of goal-directed behavior. It has been found to be involved in a variety of processes related to decision making and reinforcement learning (Cohen et al, 2009). Specifically, oscillatory activity in nucleus accumbens has been linked to reward processing and adaptation of behavior in pursuit of a goal (Cohen et al, 2007; Marco-Pallares et al, 2008).

In their study, Cohen et al (2009) compared ERPs and oscillatory activity in nucleus accumbens between win/stay, loss/stay and loss/switch trials. In addition to a general increase in power for all task conditions, theta oscillations show enhanced power and inter-trial phase coherence (200-600ms post-feedback) for losses compared to wins. The ERP also shows a maximally negative potential for losses, similar to what is found in medial frontal cortex following negative feedback. However, none of these effects were significantly different between loss-stay and loss-switch trials, indicating that they are more related to the processing of negative feedback than to the adaptation of behavior.

In contrast, inter-site synchrony of theta oscillations between the left and right nucleus accumbens was significantly greater for loss/switch than for loss/stay or win trials. On loss-switch trials, this inter-accumbens phase coherence at 6Hz correlated with subsequent RT slowing on a trial-to-trial basis. These results indicate that behavioral adjustment causes an increased connectivity between the two nuclei accumbens, that cannot be explained by a general increase in theta power as this did not differ significantly between loss/stay and loss/switch trials. This means that phase coupling between regions

carries information beyond oscillations within either of the regions alone. The study also looked at synchrony between each side of nucleus accumbens and Fz (the electrode overlying MFC). This synchrony was greater than baseline in all conditions, but did not differ significantly between any of the three task conditions. This suggests that behavioral adjustment does not require greater interaction between nucleus accumbens and MFC than the rest of the task.

In addition to inter-site phase coupling, this study also investigated inter-frequency phase coupling. Even though the task elicited strong theta oscillations in nucleus accumbens, the only significant phase coupling that was found there was between gamma and alpha oscillations. This coupling breaks down during loss-switch trials, which the authors suggest reflects a remapping of the relations between actions and rewards. Taking all these findings together, the authors conclude that nucleus accumbens responds to the need to adjust behavior following errors by shifting from a local oscillatory organization (reflected by the local alpha-gamma coupling) to a more global oscillatory organization (reflected by theta phase coupling between the two nuclei accumbens).

Theta networks

In addition to nucleus accumbens and medial frontal cortex, several other brain areas have been proposed to be part of a decision making network. For example, Oya et al (2005) suggest that in addition to mPFC, basal ganglia and other regions of PFC (consistent with Cohen et al (2009) and Cavanagh et al (2009, 2010)), amygdala and insula are also involved in evaluation of reward expectation. As discussed before, Womelsdorf et al (2010a) believe that the action monitoring function of ACC relies on reward evaluation and reward prediction processes in hippocampus, dlPFC, orbitofrontal cortex and striatum.

Luu et al (2003) also believe action regulation depends on several different cortical and limbic structures in addition to ACC, and that their activities are linked through theta oscillations. As a candidate system, they propose the Papez circuit (Papez, 1937) that includes the cingulate cortex, hippocampus, and thalamus. In this view, the anterior cingulate cortex is involved in early stages of discrimination learning, getting input from the amygdala and dorsal striatum. At a later stage, the posterior cingulate cortex is involved in novelty/familiarity judgements and action selection based on context, possibly with hippocampal input (Luu et al, 2003). Other evidence for the involvement of the hippocampus in action regulation is cited from studies with non-human primates, where withholding an expected reward elicits hippocampal theta oscillations (Luu et al, 2003) and in rodents, where reward-predictive signals in frontal cortex disappear following disconnection from hippocampus (Ramus et al, 2007).

In line with the fact that so many different areas show signatures of sub-processes needed in decision making tasks, and the hypothesis that these different areas coordinate their activity through theta synchronization, Womelsdorf et al (2010a) discuss evidence that independent theta rhythmicity has been found in most of the areas discussed above, including thalamus, rhinal cortex, amygdala, cingulate cortex, dorsal striatum, nucleus accumbens and VTA. There is also evidence for theta synchronization between many of these regions: e.g. orbitofrontal-prefrontal-cingulate cortex, striatum to neocortex and between hippocampus and all of these areas.

Different sub-processes, same theta?

As we have seen before, several different sub-processes of decision making tasks seem to elicit very similar patterns of theta activity. For example, feedback elicits frontal theta activity that is very similar to the activity observed during error trials. Some authors have interpreted this as evidence that different stages of decision making tasks are all performed by the same action monitoring network. However, the finding of similar theta activity in scalp EEG does not necessarily mean that the exact same neural structures are involved. In fact, there is some evidence for subtle differences between the neural correlates of the different sub-processes of decision making tasks.

As the findings of Cohen et al (2009) demonstrate, there are also similarities between the neural correlates of negative feedback and the subsequent adjustment of behavior, but again, there are

differences between them as well. At least in nucleus accumbens, local theta power seems to represent losses versus wins, while inter-site synchrony is specific to trials where behavior is changed. With regard to medial frontal cortex, this region may be subdivided into smaller functional areas that are involved in slightly different stages of the decision making process. Luu et al (2003) have investigated whether the different ERP components that are believed to originate from anterior cingulate cortex, come from different areas within ACC. They found that the ERN involved both rostral and dorsal regions of the ACC, whereas the FRN only engaged the dorsal region. Both regions showed theta oscillations, but activation of the dorsal region leads the ventral region with a phase difference of 60°. The authors conclude that action regulation involves two different, cooperating regions of ACC. The fact that ERN and FRN, to some extent, seem to come from different regions, suggests that error processing and feedback processing at least partly rely on different neuronal ensembles. However, the spatial resolution of scalp EEG makes it difficult to determine this with certainty. It would be interesting for future studies to investigate whether more differences can be found between the neural responses to errors, feedback and behavioral adaptation. The studies described here provide a lot of evidence that medial frontal cortex is involved in action monitoring, but there is also evidence that it is involved in other cognitive processes. Cohen et al (2007) cite evidence that medial frontal regions, including ACC, exhibit large theta oscillations during rest, sleep and cognitive tasks, and that these oscillations are modulated by cognitive demands like working memory and attention. The same is true for some of the other brain areas mentioned above. Once we know more about the exact sub-processes that certain neural activity patterns in MFC and other areas represent, we may be able to see if the same sub-processes are involved in different cognitive functions.

Relation between power and phase coherence

In both medial frontal cortex and nucleus accumbens, several studies find that theta power and local phase coherence behave very similarly (e.g. Oya et al, 2005; Cohen et al, 2009; Cavanagh et al, 2009, 2010). On the other hand, Cohen et al (2007) report that phase locking in the theta band is seen following both wins and losses, whereas an increase in theta power only occurs after losses. An interesting direction for future research would be to investigate which manipulations can elicit different responses in power and phase coherence, to shed light on the different contributions of these two oscillatory phenomena, and possibly their relation to the ERP components observed in these tasks.

In conclusion, this chapter has shown that increased theta power and phase coherence are found at every different stage of decision making tasks, indicating that theta activity plays an important role in this cognitive function. Moreover, much of this theta activity during different sub-processes is found in the same brain areas, notably frontal cortex and nucleus accumbens. This makes it difficult to determine the precise neural correlates of each separate sub-process, something which would be helpful in determining whether the same sub-process with the same underlying mechanism also occurs during other cognitive tasks.

On the other hand, it is striking that different sub-processes seem to elicit similar patterns of theta activity in frontal cortex. While there are still some conflicting results that raise questions for future research, this fundamental finding suggests that frontal theta activity plays a role in decision making that transcends any particular sub-process. What this role could be, and whether it is a process that is involved in other cognitive functions as well, is discussed in chapter 3.

There is also some evidence for theta synchronization between different areas, or phase-locking between theta and higher frequency oscillations. However, these phenomena do not seem to have been studied in the context of decision making nearly as much as local theta activity in separate brain areas. In order to learn more about how all the different sub-processes involved in decision making tasks are performed and coordinated by the brain, it would be useful to do more research into synchronization phenomena in the context of these tasks. This may also tell us more about whether similar mechanisms are involved in the performance of decision making and memory, or even other cognitive tasks.

Chapter 2: Theta activity and memory

There is a lot of evidence that theta activity plays an important role in memory processes. According to Sauseng et al (2010), theta activity is mostly reported in episodic long-term memory and working memory (WM) tasks. For example, there is evidence of increased theta activity in human cortex during both encoding and retrieval (Kahana, 2006; Sauseng et al, 2010). In addition to theta amplitude, (working) memory demands also cause theta phase synchronization between many different brain areas (Womelsdorf et al, 2010; Düzel et al, 2010) and phase synchronization between theta and higher frequency oscillations (e.g. Canolty et al, 2006; Axmacher et al, 2010). In this chapter, I will try to outline which role theta plays in different brain areas, different types of memory (short- versus long-term, different stimulus modalities) and different stages of the memory process.

First, we will look at evidence for the role of theta activity in the different stages of memory performance: encoding, retention and retrieval. Then, a model that distinguishes these different stages will be discussed. Finally, there will be a summary of theories suggesting that the function of theta is not restricted to memory, but that it is also important for other cognitive processes and the coordination of these different subprocesses in cognitive functioning.

Encoding in working memory and long-term episodic memory

As stated before, there is extensive evidence for the role of theta activity in working memory (Sauseng et al, 2010). For example, in an intracranial EEG study, Raghavachari et al (2001) found that theta activity in several different brain regions increased at the start of the encoding period of a Sternberg working memory task, and did not decrease until the end of a trial. The authors believe this pattern reflects the “gating” of oscillatory activity by the task, and propose that this gating is related to the organization of working memory (see below).

In the type of study done by Raghavachari et al (2001), it may be difficult to distinguish the separate contributions of encoding and maintenance. However, there are many studies that specifically look at the encoding of items in longer-term memory, and the role of oscillatory activity in this. The storing of items beyond the time span of transient storage in working memory relies, among other things, on synaptic plasticity. There is evidence that synaptic plasticity, in the form of long-term potentiation (LTP), is best induced in dentate gyrus and CA1 hippocampal neurons by stimulation at theta frequency, specifically at the peak of the theta oscillation (Nyhus & Curran, 2010). This finding also suggests a possible function of the often observed phase reset of theta activity upon stimulus presentation (Jutras and Buffalo, 2010). Such a reset could ensure that theta activity is at the optimal phase to facilitate the induction of LTP when a stimulus is presented.

In addition to the effect of theta on LTP, Nyhus and Curran (2010) cite several sources that show that frontal and posterior theta amplitude at encoding is positively correlated with subsequent recall. One of these sources on longer-term memory is an intracranial EEG study of free recall by Sederberg et al (2003), who performed a subsequent memory analysis. In this type of analysis, brain activity during encoding is differentiated based on the later recall of the items being studied. In this study, Sederberg et al (2003) find a positive subsequent memory effect (SME), or a positive correlation between oscillatory power and later recall, in the theta band in right temporal and frontal electrodes. This effect is highly significant between 600-1300 ms after stimulus onset. This study also found a positive gamma SME, but only a small degree of overlap between the electrodes that show these two effects.

In a later iEEG study, Sederberg et al (2007) also observed a positive frontal SME (restricted to left frontal eye field, BA 8) in the theta band during the first second of a two second encoding period. However, they also find a negative posterior SME in the theta band and other low frequencies during the early encoding period, which spreads to widespread electrodes during the second half of the encoding period. This negative theta SME is also present in hippocampus during the entire encoding period.

Very similar results were obtained by Sederberg et al (2006) in a scalp EEG study. This study shows a widespread negative theta SME which is most prominent in the second half of the 2000 ms encoding period. This effect was driven by items in the middle, rather than the start, of a study list. Although the analysis across the entire 2s encoding period only found a negative theta SME, the authors say there is some evidence for a small frontal positive theta SME within the first second of encoding, which may be linked to a concurrent increase in delta (2-4 Hz) activity (Sederberg et al, 2006).

Düzel et al (2010) describe how different studies show opposite effects of successful encoding on theta amplitude. Just like Sederberg et al (2007), Guderian et al (2009) also find a decrease in theta for later recalled words in a verbal free recall study. On the other hand, Osipova et al (2006) find an increase in theta power during the successful encoding of pictures in a recognition memory task. The difference between these effects may be due to the different tasks and stimuli used, but Düzel et al (2010) suggest that decreases in theta (and gamma) amplitude during successful encoding may also reflect increased neuronal response specificity, facilitated by preparatory tuning before stimulus onset. Indeed, there is evidence that theta amplitude before stimulus onset also influences later encoding. Guderian et al (2009) show that the amplitude of baseline theta in the human medial temporal lobe positively predicts subsequent recall, and that this is correlated with the later decrease in theta for successful encoding. Düzel et al (2010) suggest that contextual factors like novelty may in turn influence baseline theta activity and indirectly promote encoding. Jutras and Buffalo (2010) see this effect of baseline theta as evidence that oscillatory activity plays a role in generating a cognitive state that is beneficial for memory formation. What such a cognitive state could look like, is discussed in more detail in the next chapter.

As described, several different brain areas show local increases in theta power during successful encoding. Weiss and Rappelsberger (2000) investigated whether these regions also show evidence of increased interaction, and found that synchronization between frontal and posterior regions is increased in the theta band (and other frequency bands) during successful encoding.

An influential model of the ordering of multiple items in working memory was proposed by Lisman & Idiart (1995), who suggested that items are represented by successive gamma cycles within one theta cycle. The phase relation between each gamma cycle and the theta cycle in which it is nested, is believed to represent the temporal sequence in which the items were presented. Indeed, there is evidence for phase coupling between theta and gamma in human working memory (Canolty et al, 2006), as well as various other tasks. According to Sauseng et al (2010), in the case of multiple simultaneously presented items, the order of gamma cycles represents their spatial, rather than temporal, sequence.

Jensen and Lisman (1998) extended this model with the idea that the length of a theta cycle is influenced by the number of items that are stored in working memory. Their model predicts that the number of items that can be held in working memory is limited by the number of gamma cycles within one theta cycle. This number can be changed by a slowing of theta activity, or a phase reset of ongoing theta oscillations. Sauseng et al (2010) show that there is evidence for both mechanisms. They describe a study by Axmacher and others, who find a slowing of hippocampal theta frequency as a function of working memory load in a Sternberg-like task with faces as stimuli. On the other hand, findings by Jacobs et al (2006) do not support this idea. Instead, they find that the amplitude of the lowest frequency (4Hz) theta oscillations is negatively correlated with memory load at widespread electrode locations, which goes against the idea that these oscillations would replace faster theta oscillations for longer lists.

In addition to its function in working memory, Jensen and Lisman (2005) suggest that this theta-gamma interaction can serve as a cortical WM buffer for the encoding of item sequences in episodic memory by hippocampus. In line with this, Nyhus and Curran (2010) describe evidence from animal studies that theta modulation of MTL gamma oscillations supports episodic memory encoding.

Working memory retention

The relation between theta and memory load is not exactly clear. According to van Vugt et al (2010), the direction of this relation is different for different brain regions, stimulus materials and even participants. Both Sauseng et al (2010) and Womelsdorf et al (2010) cite evidence that theta in temporal cortex and frontal midline electrodes increases with memory load, while it decreases with load in early visual areas. One study of the relation between theta and memory load was done by Jensen and Tesche (2002), who found a parametric increase of frontal theta activity during the retention period with the number of digits to be remembered. Gevins et al (1997) also found an increase of frontal midline theta with memory load for both verbal and spatial stimuli, and further localized this signal to anterior cingulate cortex. Theta amplitude also increased with practice on the task, which the authors suggest reflects the increased effort involved in focusing attention after more time spent performing the task (Gevins et al, 1997).

Jacobs et al (2006) have studied the effect of memory load on theta activity in a Sternberg task with letters as stimuli, and find that theta activity after presentation of the probe stimulus is inversely related to memory load in widespread electrode locations. This suggests that the relation between theta and memory load is different at different times in a trial. It is possible that the positive correlation between theta power and memory load is specific for frontal cortex, where it is related to e.g. concentration while the opposite pattern found in more posterior electrodes is more related to memory processes themselves. However, Jacobs et al (2006) also found the inverse correlation in frontal electrodes, although it was less strong there than in more parietal locations.

In addition to changes in theta activity itself, the interaction between theta and higher frequency oscillations also plays a role in WM retention. Sauseng et al (2009) find phase coupling between theta and gamma during retention in a visuospatial WM task. More specifically, coupling of gamma phase (but not amplitude) to theta oscillations during the retention period of this task was stronger at posterior sites in the hemisphere where visual input was being processed, and increased with working memory load in a way that was predictive of individual working memory capacity (Sauseng et al, 2009). This is in line with a study by Axmacher et al (2010), who found increased theta-gamma coupling in human hippocampus during multi-item WM retention that is predictive of individual WM performance. It is striking that this effect was found in the hippocampus, because this region was long believed to be involved in long-term memory only, while working memory was believed to be the domain of frontal cortex. However, there is increasing evidence that the hippocampus also plays a role in working memory (e.g. van Vugt et al, 2010).

With regard to theta-band synchronization between different brain regions, Düzel et al (2010) cite evidence for increased theta-coupling of bilateral frontal and temporal regions, and regions in the visual ventral processing pathway, with increased memory load in a visual WM task.

Retrieval

There are different ways in which information can be retrieved from memory. Subjects can be asked to actively recall items from memory, with or without a cue, but memory can also be tested via recognition, where a test item is presented and subjects are asked to respond whether or not they have encountered this item before.

Recognition memory studies show different neural responses to targets (probe items that a subject has studied before) than to lures (previously unencountered probe items). Düzel et al (2005) found increased theta amplitude for targets compared to lures, in both left parietal and occipital electrodes. Jacobs et al (2006) also found that left-parietal theta activity 500 ms after probe onset was best predicted by whether this probe was a target or lure.

In addition to studies on oscillatory activity, the difference between targets and lures has been studied using ERP analysis. Düzel et al (2003) state that previously studied items in recognition memory tasks are typically associated with an increase in ERP positivity, which consists of an early, more frontal part that occurs 300-500ms after probe presentation, and a later more parietal part that occurs 500-800ms

post-probe. Düzel et al (2003) also conclude that the ERP components related to recognition memory mainly reflect oscillatory activity in the theta and alpha bands. Nevertheless, Jacobs et al (2006) believe that the known ERP target-lure effects are not directly related to the theta effect they find, although they cannot rule out the possibility that the two effects are related in a manner that is not captured by their analysis. Furthermore, the authors conclude that their effects are not specific to working memory, and that it is more likely that they result from a more general memory retrieval phenomenon. Alternatively, this theta activity could be part of a mechanism for comparing memory contents to sensory input. This possibility is explored in more detail later in this section. In addition to cortical areas, a study of human hippocampus by Ludowig et al (2008) also shows an ERP old-new effect during retrieval (as well as a subsequent memory effect during encoding).

Many studies of recognition memory distinguish between two kinds of responses: “remember”, where subjects correctly recognize the item and are able to recall the context in which they first encountered it, and “know”, when subjects rate the item as familiar but do not recall any details about seeing the item before. Sauseng et al (2010) cite evidence that theta is involved in the distinction between remember and know trials. Specifically, they describe two studies by Klimesch and others showing that remembered items elicit a longer theta response than items that were only familiar and that increased confidence about seeing an item before is associated with increased dorsolateral prefrontal and superior parietal theta activity.

Nyhus and Curran (2010) state there is evidence for greater hippocampal and posterior gamma and theta power for correctly remembered items, which the authors interpret as a hippocampal reinstatement of episodic memory representations in posterior cortex. Düzel et al (2010) also believe that recollection depends on the convergence of information from different brain regions in MTL, and that theta oscillations are involved in the coordination of interactions between these areas. A recognition memory study by Guderian and Düzel (2005) shows increased theta amplitude during remember versus know trials in prefrontal, mediotemporal and visual brain areas. The authors believe this reflects the binding of distributed cortical representations during the recollection of a study episode, via a link between cortical areas and hippocampus.

Among other variables, Jacobs et al (2006) have also studied theta effects of confidence in recognition memory. In a classic Sternberg task, they found that left-parietal theta was initially (300 ms post-probe) correlated with the degree of match between the probe item and a subject’s memory contents, as measured by a variable that incorporates both target/lure and relative reaction time. This effect is later replaced by the effect of target/lure status itself, that best predicted left-parietal theta 500 ms post-probe. The authors suggest that the early effect may be a graded familiarity signal, while the later target-lure effect reflects recollection. This would be consistent with the time course of ERP effects found by Curran (2000), where a familiarity-related component also occurred earlier in time than a component that reflected recollection.

In a review of the role of theta and memory retrieval in goal-directed behavior, Womelsdorf et al (2010) conclude that the previously described synchronization between brain areas via theta oscillations is important for the retrieval of information from both working memory and long-term memory in the service of decision making. This can also involve types of information that are not typically tested in memory tasks, like rules about the relationship between different stimuli, responses and rewards.

As in encoding and retention, the interaction between theta and gamma oscillations is also important at retrieval. Nyhus and Curran (2010) cite evidence that theta oscillations modulate gamma oscillations in anterior temporal scalp locations and hippocampus during successful retrieval. In support of Jensen and Lisman’s (1998) model, Sauseng et al (2010) cite evidence for theta phase resetting during WM retrieval in humans. Furthermore, they state that matching of sensory input with memory content in a recognition memory task involves transient synchronization of theta and gamma oscillations. In an earlier recognition memory study, Sauseng et al (2008) showed a theta phase reset in parietal and parieto-occipital locations shortly after probe onset, which led to increased theta-gamma phase coupling. The authors believe this reflects the integration of top-down and bottom-up information to facilitate matching (see below for more on top-down control of memory performance). This process is

believed to be initiated by frontal cortex, consistent with the findings of Düzel et al (2003), where targets are accompanied by an ERP response that starts in frontal cortex, and is only found in parietal cortex several hundred milliseconds later.

While the study by Sauseng et al (2008) involved longer-term episodic memory, a later study found similar results in a visuospatial Sternberg-like WM task, where stronger theta-gamma synchronization was observed in right parietal and occipital electrodes during match trials compared to non-match trials (Holz et al, 2010). This suggests that the process of matching memory contents with sensory input is the same for information maintained across different time scales. The involvement of gamma activity in such a general matching process is consistent with a model proposed by Herrmann et al (2004), in which early gamma oscillations in memory experiments reflect the comparison between top-down (memory) and bottom-up (sensory) information, while late gamma activity reflects the utilization of the outcome of this process.

The findings of Sauseng et al (2008) also suggest an alternative interpretation for the increased parietal theta activity found by Jacobs et al (2006) for increasing degrees of match between the probe items and memory contents, and later in the trial for targets compared to lures. Here, too, theta activity could be part of a mechanism where items in memory are compared to sensory input.

Encoding versus retrieval

Although there are many similarities between theta effects found during encoding and retrieval (e.g. increases in amplitude and coupling to gamma oscillations), there are also several studies that attempt to distinguish the neural mechanisms underlying these two stages of the memory process.

Hasselmo et al (2002) propose a model where hippocampal theta is involved in reversal learning, because encoding and retrieval occur at different phases of theta oscillations. According to this model, encoding is most effective during the trough of the theta cycle, when synaptic input from entorhinal cortex to CA3 and CA1 and the potential for LTP in synapses from CA3 are strong, but currents arising from CA3 are weak (Sauseng et al, 2010). Conversely, retrieval of existing stored associations is best when input from CA3 and CA1 to entorhinal cortex is strong, which is the case during theta peaks. To support this, there is evidence that synapses arising from CA3 show less synaptic transmission at the peak of local theta, while this is the optimal phase for the induction of LTP (Hasselmo et al, 2002). This model is supported by a iEEG study by Rizzuto et al (2006), who find a 180° phase difference in theta between encoding and retrieval in a verbal Sternberg task.

Colgin et al (2009) link this model to gamma oscillations. They show that gamma oscillations in CA1 can be divided into slow and fast components, that each interact with different brain areas at different phases of local theta oscillations. Fast gamma oscillations in CA1 synchronize with fast gamma in medial entorhinal cortex at the trough of the theta oscillation. Slow gamma oscillations, on the other hand, synchronize with slow gamma in CA3 during the descending phase of theta. Womelsdorf et al (2010) interpret these findings as reflecting the separation of encoding, which is externally triggered by incoming stimuli, from internally triggered retrieval.

Cognitive control

In relation to the previously described model of Hasselmo et al (2002), Jutras and Buffalo (2010) cite evidence that hippocampal theta influences activity in other brain areas, and Düzel et al (2010) suggest a master-slave relation between hippocampus and other brain areas. In fact, an important question in studies of cognitive functioning is whether the interaction between different brain areas is based on mutual entrainment, or whether one brain region controls the activity of the other areas involved in a task.

An important characteristic of working memory, and a reason why it is such a good model for the study of other complex cognitive functions, is the fact that WM tasks often require the use and coordination of many different cognitive sub-processes (Sauseng et al, 2010). A very influential model of working memory was originally proposed by Baddeley and Hitch in 1974 and later extended by

Baddeley (2000). In this model, the working memory system contains several modality-specific slave-components, which are controlled by one central executive. Combined, this system is able to integrate and manipulate information from different modalities and sources, including long-term memory. Although this model is conceptual, and not related to specific brain structures, many studies indicate that the central executive function is performed by neurons in prefrontal cortex.

According to Baddeley's model, verbal and visuospatial information rely on independent storage systems in different cortical networks. Sauseng et al (2010) cite evidence from Wu et al (2007) that when information from both modalities needs to be combined, there is stronger theta in bilateral dorsolateral prefrontal cortex, and stronger theta coherence between frontal sites and between left frontal and right temporal sites. This supports Sauseng et al's (2010) idea that interregional theta synchronization is important for the combined activation of cortical networks involved in different sub-processes of a complex WM task. In addition, the authors describe findings of Sarnthein et al (1998), who also find theta synchronization between prefrontal cortex and temporo-parietal sites during WM retention of verbal and visuospatial information, an effect which is most prominent in the left hemisphere for verbal information, and in the right hemisphere for spatial information. Sauseng et al (2010) describe similar findings in their own work for encoding and retrieval, and suggest that this reflects the activity of a prefrontal supervisory attention system which initiates an interaction with posterior, modality-specific storage systems via theta coherence.

In addition to encoding, retention and retrieval of information, the proposed central executive is also capable of manipulating information in the working memory store. In relation to this, Sauseng et al (2010) discuss mental arithmetical tasks, a class of WM tasks which require retention, frequent updating and manipulation of information in working memory. These tasks have also been found to rely on theta activity. Mizuhara and Yamaguchi (2007) found evidence for increased theta-coherence between bilateral prefrontal sites, and between left PFC and right parietal sites and vice versa. Sammer et al (2007) found an even larger EEG-theta network which included frontal and cingulate cortex, superior parietal and superior temporal areas, hippocampus and insular cortex. Furthermore, Sauseng et al (2010) describe evidence from their own studies for the involvement of a fronto-parietal theta network in a visual mental comparison task, which they believe also reflects the activity of a central executive mastering areas involved in sub-processes.

In addition to this evidence from mental arithmetical tasks, Griesmayr et al (2010) used a verbal delayed-match-to-sample task in which they compared a simple retention condition with a condition where information needed to be manipulated. They found that manipulation caused an increase in frontal midline theta, and in phase-coupling of frontal and left parietal gamma activity to this frontal theta activity in the negative slope before a theta peak. Sauseng et al (2010) interpret this as evidence that in addition to interregional theta synchronization, interregional coupling between theta and higher frequencies also plays a role in integrating different sub-processes required in a working memory task. This view may be combined with Jensen & Lisman's (1998) model of theta-gamma coupling in working memory by the possibility that task-specific content and sub-processes may be (partly) represented by gamma oscillations in task-specific brain areas, while these gamma oscillations are coordinated by frontal cortex via theta synchronization.

In line with Sauseng et al's (2010) views on working memory, Nyhus and Curran (2010) highlight the fact that episodic memory performance also relies on many different subprocesses, performed by widely distributed brain areas. They believe that it is important to identify the role of oscillatory activity in each different sub-process, something that may be done using multivariate analysis (Kahana, 2006; Jacobs et al, 2006). Nyhus and Curran (2010) suggest that top-down control in episodic memory is also established via frontal theta oscillations and synchronization between frontal and posterior brain areas. They show evidence that both during encoding (e.g. Weiss & Rappelsberger, 2000) and during retrieval (e.g. Düzel et al, 2005), increased frontal theta power and theta coherence between frontal and posterior (parietal and temporal) regions are associated with more successful memory performance. In addition, they view early theta power increases over frontal scalp locations as evidence of frontal top-down control at retrieval.

Combining extensive evidence for the role of theta activity and its interactions with higher frequencies during memory performance, Nyhus and Curran (2010) propose a model of episodic memory in which gamma serves to bind modality-specific perceptual representations in cortex and episodic representations in hippocampus and, in line with Lisman and Idiart's (1995) model, theta oscillations serve to temporally order these separate item representations. Consequently, the authors predict that tasks where the temporal order of items is important should elicit stronger theta/gamma coupling. The model also states that theta/gamma patterns present at encoding are reinstated in cortex at retrieval via feedback projections from hippocampus. Finally, frontal-hippocampal theta oscillations provide top-down control for selective encoding and retrieval of episodic memories.

Based on Lisman and Idiart's model, Sauseng et al (2010) also believe that the phase relation of gamma and theta that is involved in encoding is also important during retrieval. As described before, there is evidence that matching between sensory input and memory content relies on transient synchronization of theta and gamma oscillations (Sauseng et al, 2008). The same study also provides evidence for top-down signals from prefrontal cortex. Shortly before and after target presentation, preceding the previously described theta-gamma coupling, Sauseng et al (2008) show interregional theta synchronization in a large network, which they interpret as prefrontal areas providing a template to visual areas. In their view, local gamma activity in these visual areas represents bottom-up sensory input, which needs to be matched to the memory content provided by prefrontal cortex. This view is very similar to the model proposed by Nyhus and Curran (2010).

Nyhus and Curran (2010) conclude that their model is an example of how neural oscillations facilitate transient interactions between different brain regions to perform complex cognitive tasks, and that a better understanding of the role of oscillations during episodic memory performance may inform our understanding of large-scale brain dynamics in general and their relation to other cognitive phenomena. In line with this view, Sauseng et al (2010) conclude that the involvement of theta activity is probably not restricted to working memory tasks, but instead underlies cognitive control in many different cognitive systems. Similarly, the interaction between theta and gamma oscillations is believed to reflect a general mechanism for the organization of cortical processing.

This chapter has shown that theta activity plays a role in many different memory-related sub-processes, similar to what was found for decision making in the previous chapter. In addition, there is evidence that successful memory performance also depends on theta synchronization between different brain areas and synchronization between theta and higher frequencies. These findings have led several authors to propose theories about the role of theta in cognitive functioning in general. In the next chapter, we will discuss whether these theories are also applicable outside the field of memory, by seeing if they are consistent with the theta activity found in decision making tasks.

Chapter 3:

The role of theta activity in memory and decision making: similarities and differences

When we compare the previous two chapters, it is clear that memory and decision making are performed by different networks of brain areas. However, there are several brain areas where activity is associated with improved performance on both types of tasks. Moreover, it is striking that the function ascribed to these areas is the same in both cases: executive functioning, or top-down control over the activity of other brain areas. This suggests that certain principles of network organization play a role in both memory and decision making, and that these may be important for cognitive processing in general. In this chapter, we will point out some of the similarities and discuss how they could fit into a broader view of cognitive functioning.

On the other hand, there are brain areas and patterns of activity that are only found in one of the two tasks. In some cases, it is unclear to what extent this is due to a real difference between the neural networks performing each task and to what extent certain things simply have only been looked at in one context. The second aim of this chapter will be to point out caveats in the literature, and possible directions for future research that could help determine where the real similarities and differences lie between the sets of brain areas involved in memory performance and decision making and the mechanisms they use to communicate.

Frontal cortex: central executive?

One of the things that stand out in the previous two chapters, is that many different studies show the involvement of frontal brain areas. Not only do they show task-related theta activity, many of these studies also suggest synchronization between frontal cortex and other brain areas, and several different theories of cognitive performance suggest a similar, executive role for frontal cortex. In the first part of this chapter, we will discuss evidence for frontal activity during both memory performance and decision making, and theories about the role of frontal cortex in cognitive functioning in general that would be consistent with findings in both of these fields.

Local theta activity

Many different studies report frontal theta activity during cognitive tasks. Due to the limited spatial resolution of EEG and MEG, it is often not possible to pinpoint the specific part of frontal cortex where activity is coming from. In many cases, authors report a general “frontal midline theta”, which is theta activity at electrode Fz, during the performance of cognitive tasks. For example, both Gevins et al (1997) and Jensen & Tesche (2002) find an increase of frontal midline theta with memory load. Jacobs et al (2006) find that central theta is best predicted by a subject’s confidence, while Marco-Pallares et al (2008) show an increase in medial frontal theta for negative feedback. Several different authors name anterior cingulate cortex (ACC) as a likely source of frontal midline activity (e.g. Gevins et al, 1997; Onton et al, 2005), although other parts of frontal cortex cannot be ruled out as generators at this point. In any case, this activity is reported in a wide range of cognitive tasks.

A signal that is often found in the same electrode locations as frontal midline theta, are the ERP components described in relation to errors and feedback: the ERN and FRN. There is discussion in the literature on the hypothesized relation between frontal oscillatory activity and ERP, which we will not describe in detail here (but see e.g. Yeung et al (2007) and Trujillo et al (2007) for two different views on the origin of the ERN, and Sauseng et al (2007) for a review), but many authors believe these particular components to originate in ACC. For example, Marco-Pallares et al (2008) cite evidence that the ERN is related to frontal theta activity. If this is the case, the large similarity between the ERP signal characterizing errors (the ERN) and the ERP response to feedback (the FRN) also suggests a similarity of theta activity in frontal brain areas, possibly ACC, across different stages of the decision making process.

In addition to effects on frontal midline theta, several studies have also found decision making related activity in PFC in particular. One example is the work of Cavanagh and colleagues (2009, 2010) who have found increased theta activity within and between medial and lateral PFC at several different stages of the decision making process. As for ACC, even if we cannot be certain if it is the source of frontal midline theta, it is widely believed that this area is crucial for decision making. Its involvement has been found at every different stage of these tasks, from the decision point to feedback processing and behavioral adaptation (reviewed in chapter 1).

Several different studies have also found effects of working memory load on frontal midline theta (Sauseng et al, 2010; Womelsdorf et al, 2010). As discussed in chapter 2, there is ample evidence for the involvement of (pre)frontal cortex in encoding and retrieval of information in working memory. However, there is some evidence this part of the brain is also involved in long-term memory. For example, Sederberg and colleagues (2003, 2007) found subsequent memory effects in frontal cortex during memory tasks that went beyond the short time span and limited number of items of working memory. There is also evidence for synchronization between frontal cortex and posterior brain areas during episodic memory tasks (e.g. Weiss & Rappelsberger, 2000). Nyhus and Curran (2010) formulated a model of episodic memory in which frontal cortex is involved in top-down control of selective encoding and retrieval. This is very similar to Sauseng et al's (2010) model of working memory performance, in which frontal cortex also provides top-down control over memory processes in other brain areas via synchronized theta oscillations. The similarity between these two models suggests that at least in these two forms of memory, frontal cortex plays a similar role.

Instead of simply interpreting frontal theta effects as strictly decision making or working memory-related, it is interesting to ask whether they reflect something that goes beyond memory functioning per se, possibly the neural correlate of a more general cognitive phenomenon such as task difficulty or increased concentration.

As a result of the poor spatial resolution of EEG, it is not possible to know whether the frontal midline theta observed during decision making and memory tasks originates from the same or different areas within frontal cortex. This also makes it difficult to determine whether frontal midline theta reflects the same cognitive process in different tasks or whether it reflects different mechanisms, occurring in nearby parts of frontal cortex. In addition to this problem, between studies that do look at smaller sub-sections of frontal cortex and assign specific roles to them separately, there are a lot of similarities in the activity patterns and proposed functions of these different parts of frontal cortex. All of this makes it difficult to determine whether there are systematic differences between the roles of different frontal areas. We will discuss the evidence that is available, but hopefully future research will shed more light on this issue.

Despite these limitations, it is clear that several different parts of frontal cortex show theta activity during both memory and decision making tasks, and that this activity is predictive of how well a task is performed. This suggests that theta activity in frontal cortex is crucial for successful performance, at least in these two domains. Moreover, the fact that frontal theta activity is seen in such a wide range of different tasks, and at different stages within tasks, suggests that its involvement is not restricted to memory and decision making alone, but is likely to be a characteristic of cognitive functioning in general. The next section will outline a number of cognitive sub-processes this frontal theta activity may reflect.

Theoretical views on the role of frontal cortex

An important candidate for a common sub-process that is required in many different cognitive tasks, is cognitive control. Indeed, this concept has been tied to frontal theta activity by several different authors. As described in chapter 2, Sauseng et al (2010) believe that frontal theta activity is not restricted to working memory, but is likely to play a role in cognitive control in many different cognitive tasks. Although the term "central executive" is most often found in models of working memory, the concept of cognitive control can also be found in decision making literature. In fact, the idea of an action monitoring system that evaluates and guides the performance of different brain areas

performing sub-processes of the decision making process is very similar to the proposed function of the central executive in working memory. Moreover, this function is also associated with frontal brain areas: the area most often named as the hub of action monitoring networks is ACC, but there is also evidence for a role for PFC in action monitoring (e.g. Cavanagh et al, 2009; 2010).

Womelsdorf et al (2010a) show evidence that both areas are involved in the retention of task rules in a reversal learning task. However, while PFC showed the fastest response after several trials with the same rules, ACC was quickest right after task rules were switched. This suggests that in this particular task, there may be subtle differences between the roles of different parts of frontal cortex, where ACC may be more involved in tracking changing task demands and re-establishing new task rules after a change. Interestingly, Onton et al (2005) offer a similar interpretation for activity observed during a working memory task. The authors suggest that variations in frontal midline theta, likely originating from ACC, reflect adjustments of medial frontal cortex to changing task demands. This study, using a working memory task, illustrates the idea that the tracking of task demands is required during many different cognitive tasks, and that the same neural network is likely to perform this function across different tasks.

In line with such a view, the response of ACC to changes in memory load can also be interpreted as a response to increased task difficulty. Jacobs et al (2006) found that central theta was best predicted by a subject's response confidence, which would be lower on more difficult trials. According to Jacobs et al (2006), the ERN that is observed during error trials may also reflect the fact that error trials tend to be more difficult and associated with decreased confidence, rather than errors per se.

An increase in task difficulty may in turn reflect a need for increased cognitive control, implemented by increased activity of executive brain areas. This is consistent with the increase in frontal theta that is found in more difficult trials, but also with many of the other cases in which such an increase is found. As discussed before, many different studies also find an increase in frontal theta activity in response to negative feedback and/or prediction error, and accompanying adaptations of behavior following feedback (reviewed in chapter 1). All of these could be interpreted as cases of an increased need for cognitive control.

Other authors also believe in a broad executive function for prefrontal cortex. For example, Miller and Cohen (2001) propose a general theory of PFC function in which PFC exerts top-down control over behavior by maintaining representations of goals and influencing activity in other brain areas in such a way that goals can be achieved. This view is not restricted to one type of cognitive task or one set of brain areas being manipulated by PFC.

Badre and Wagner (2004) performed an fMRI study to dissociate the different roles of dlPFC, frontopolar cortex and ACC during goal-directed behavior and conclude that each of these areas has a different function. However, with regard to ACC, they conclude that it shows a broad sensitivity to cognitive control demands, also suggesting a generalized control function for this area.

Again, there is some indication that there are differences between the exact roles of different frontal brain areas. As discussed in chapter 1, Cavanagh et al (2009, 2010) have looked at theta activity in medial and lateral PFC at different stages of a decision making task. Taking all their findings together, the authors proposed that mPFC is involved in the immediate signaling of and response to errors and prediction violations, while lPFC is more involved in control processes that require working memory, such as delayed behavioral adaptation (Cavanagh et al, 2010).

Theta: cognitive state?

Another way to phrase the idea that theta activity is not task-specific, in a way that is not restricted to frontal cortex, is the possibility that theta activity represents or facilitates a generalized "cognitive state" that enables successful memory encoding, but also other forms of cognitive functioning.

Evidence for such a view can be found particularly in the memory literature.

This proposed "cognitive state" may be translated to psychological terms like increased concentration, attention or mental effort. However, such a statement is difficult to verify because these concepts are

difficult to grasp in an experimental setting. In some of the tasks that have been discussed so far, one manipulation that would cause differences in this variable is task difficulty. As stated before, several different phenomena associated with increased difficulty, like higher working memory loads and decreased confidence, are associated with increased theta activity. This may indeed reflect the increased concentration that is required during such trials.

One example of theta activity that could be interpreted in such a way, is the activity found by Raghavachari et al (2001). During the Sternberg working memory task, this study found widespread theta activity that increased at the beginning of a trial, and did not decrease again until a decision had been made. The authors called this phenomenon the “cognitive gating” of theta oscillations. Rather than reflecting one particular sub-process, it is possible that such constantly increased theta activity represents some characteristic of cognitive tasks in general.

Another interesting finding that suggests that theta does not reflect task-specific processes themselves, but enables cognitive functioning in general, is the finding that encoding success is correlated with medial temporal lobe (MTL) theta activity before stimulus onset (Guderian et al, 2009). According to Jutras and Buffalo (2010), this suggests that theta activity is involved in “generating a cognitive state associated with successful memory formation”. However, the authors do not elaborate on how such a cognitive state would be defined. Düzel et al (2010) also cite the findings of Guderian et al (2009), and suggest that baseline theta may in turn be influenced by task context. This would provide a mechanism by which context, e.g. a challenging task environment, can influence the success of cognitive functioning.

A different interpretation of the sustained theta activity observed in these studies may be found in the temporal context model of Howard and Kahana (2002). In this model, temporal context is seen as a variable that slowly changes over time, allowing encoded memories to be linked to the moment in time when they were encoded by being stored with this context variable. According to the model, the activity associated with this context is reinstated when an item is recalled, providing an explanation for the well-known contiguity effect in free recall tasks. Theta activity could encode the representation of such a context variable. It would be conceivable that this representation is also active before stimulus onset, explaining the correlation between baseline theta and subsequent recall. However, this model does not explain the function of increased theta activity in tasks that do not involve episodic memory encoding.

As stated before, decision making tasks also seem to elicit theta activity during every stage of the task, suggesting again that this theta activity is not specific to one particular decision making-related sub-process, but reflects some process or state that is active during the entire task. Such activity can be seen in frontal cortex, but also in nucleus accumbens (e.g. Cohen et al 2009). However, the evidence for this kind of trial-wide involvement of theta activity outside frontal cortex is much less extensive in the decision making literature than in the field of memory. It is not clear at this point whether this is because such activity does not play a role, or because many researchers simply choose to focus on frontal midline theta and ERPs. This makes it difficult to determine whether sustained theta activity can really reflect a generalized cognitive state, rather than just a state of effective memory encoding.

Apart from the limited range of tasks in which widespread sustained theta activity has been found, it is also unclear where in the brain such a cognitive state would be generated. When we look at theta activity outside frontal cortex, there is conflicting evidence with regard to its relation with successful cognitive performance.

In addition to the increase in MTL theta before stimulus onset, Guderian et al (2009) also found a correlated decrease in MTL theta during the retention period that was also associated with better encoding. This is in line with Sederberg et al’s (2007) finding of a negative correlation between hippocampal theta power and subsequent recall. In light of these findings, it seems unlikely that MTL theta activity would contain a representation of context or represent some other kind of cognitive state which facilitates subsequent recall. Düzel et al (2010) offer a possible explanation for the discrepancy in MTL by suggesting that the decrease in theta may reflect increased response specificity, enabled by

preparatory tuning before stimulus presentation. However, Sederberg et al (2006, 2007) also find negative correlations between theta activity and successful encoding in many other electrode locations. In decision making tasks, increased theta is also found during error trials. These findings seem at odds with the idea that widespread theta activity strictly reflects a state of successful cognitive functioning, memory-related or otherwise.

In conclusion, the relation between theta activity and the success of cognitive functioning is not yet clear for many brain areas. This is in part due to conflicting findings, but also to the small number of studies that have been done into, for example, theta activity in posterior brain areas during decision making. With the evidence available now, we cannot conclude that sustained theta activity always facilitates cognitive performance.

What we can conclude from the literature presented in this section is that frontal theta activity seems to be involved in situations of increased cognitive control across a range of different tasks. This may be the oscillatory equivalent of concentration or mental effort, but that is difficult to conclude from the evidence that is currently available. Future studies may be able to shed more light on this by directly examining theta activity in a wider range of tasks that are specifically designed to look at the effect of concentration or mental effort per se, across more different cognitive sub-processes.

Another question is how frontal cortex, if it does indeed have an executive function, could use a sustained increase in theta activity to strengthen its control over other brain areas. The next section will describe possible mechanisms by which such control could be established.

Synchronisation with other brain areas and frequencies: top-down control?

Even if we assume that a sustained increase in frontal theta activity reflects a process like concentration or cognitive control, this does not explain how this activity affects the performance of other brain areas involved in a task. Also, if frontal theta activity is not involved in task-specific sub-processes like memory encoding or reward evaluation, it is unclear how the brain does perform these processes

A possible function of an increase in frontal theta activity could be to promote synchronization with other brain areas and with oscillations at higher frequencies, in order to coordinate and integrate the task-specific sub-processes performed by them. Indeed, many different authors have proposed models in which theta activity serves to connect different brain regions and/or order faster oscillations, some of which have been discussed here (e.g. Jensen & Lisman, 1998; Womelsdorf et al, 2010a; Nyhus & Curran, 2010; Sauseng et al, 2010).

Theta synchronization between brain areas

As described in the previous chapter, many studies show that successful (working) memory performance is associated with increased theta synchronization between different brain areas. For example, theta synchronization between frontal and posterior electrodes has been demonstrated during memory encoding (Weiss & Rappelsberger, 2001), working memory retention (Sarnthein et al, 1998) and retrieval (Sauseng et al, 2010) and manipulation of information in working memory (Griesmayr et al, 2010; but see chapter 2 for more examples of all of these). Düzel et al (2010) discuss evidence for increased theta synchronization between bilateral frontal and temporal cortex and parts of the visual pathway with increasing working memory load.

With regard to decision making, there is also some evidence for a role of theta synchronization between different brain areas, but it is much scarcer than in the memory literature. There is evidence for task-related synchronization between nearby areas like mPFC and IPFC (Cavanagh et al, 2009; 2010) or left and right nucleus accumbens (Cohen et al, 2009), but evidence for synchronization on a larger scale is difficult to find. Cohen et al (2009) also showed an increase in theta synchronization between bilateral nucleus accumbens and Fz during task performance compared to baseline, but this did not differ between different task conditions (e.g. losses versus wins). In a different kind of study,

Wang et al (2005) looked at the spike patterns of individual neurons in ACC and conclude that the activity of these neurons is modulated by prefrontal cortex in a way that is larger for more difficult tasks and errors. The authors believe this modulation gates output of ACC to neurons in temporal and frontal cortex via theta phase-locking in the service of dealing with the consequences of a response.

It is striking that in nearly all the cases where it was associated with more successful memory performance, theta synchronization involved frontal cortex in addition to more posterior areas. For example, Sarnthein et al (1998) found theta synchronization between PFC and temporo-parietal sites during WM retention, where the hemisphere in which this synchronization was strongest depended on the modality of the information being retained. If we consider frontal cortex as an area that is not specific to one particular cognitive task, given what was discussed in the previous paragraph, this suggests that more task-specific functions (such as memory operations) are performed by the more posterior areas that frontal areas synchronize with. Indeed, the difference in hemisphere in the study of Sarnthein et al (1998) suggests that while PFC is always involved, the other areas that are recruited depend on the exact requirements of the task at hand. Unfortunately, as discussed above, EEG cannot be used to determine exactly in which brain area synchronization occurs. As a result, it is difficult to say on a smaller spatial scale whether the areas that are synchronized with are different for different (parts of) tasks.

Another question of neuronal communication that arises when synchronization is found, concerns the *nature* of the cooperation between frontal and more posterior brain areas. Several authors have suggested a master-slave relation where frontal cortex controls the activity of other brain regions. In the context of working memory, such an organization would be consistent with the working memory model of Baddeley that was discussed in chapter 2, where the WM system is led by a central executive, believed to reside in frontal cortex, controlling several modality-specific slave components. Indeed, Sauseng et al (2010) propose a model of working memory that is very similar to this view. As discussed in chapter 2, they argue for the existence of a prefrontal supervisory attention system, which interacts with modality-specific storage systems via theta synchronization.

This model is very similar to the model that Nyhus and Curran (2010) propose for long-term memory, where synchronization of frontal theta with more posterior brain areas like hippocampus also reflects top-down control of frontal areas on encoding and retrieval. As discussed in chapter 2, Düzel et al (2010) also believe in the role of a master-slave interaction in long-term memory, rather than mutual entrainment between brain areas, although they believe that hippocampus or visual cortex may be responsible for controlling the flow of information instead of frontal cortex.

As the comparison at the beginning of this section makes clear, there have not been a lot of studies that looked at theta synchronization between brain areas in the context of decision making. As a result, it is unclear whether the findings and models presented here can be generalized to decision making, let alone cognitive functioning in general. However, there is some more theoretical evidence that theta synchronization may also play a role in the formation of a decision.

Guderian and Düzel (2005) looked at the difference in oscillatory activity between “remember” and “know” responses. They conclude that recollection (remember), compared to familiarity (know) is associated with synchronized theta activity in a network consisting of prefrontal, mediotemporal and visual brain areas. The authors suggest this finding may be related to the binding of distributed cortical representations of items during memory retrieval. This view is further elaborated on by Düzel et al (2010), who believe that remembering the presentation of an item instead of just knowing the item depends on the convergence in medial temporal lobe of information from different brain areas about the study episode. In their view, this information would be carried by synchronized theta oscillations between these different brain areas. Womelsdorf et al (2010a) propose a similar model for decision making tasks, where a decision is not made until sufficient information becomes available through the activation of different brain areas around a similar phase of theta activity.

Both of these views state that decisions are made following the convergence of evidence from different brain areas via synchronized theta oscillations. This suggests that despite the lack of experimental evidence for large-scale theta synchronization in decision making tasks, it could in fact play an important role in such tasks. Indeed, decision making tasks, like memory tasks, do require the

successful combination of information from different sources, and the mechanism by which this is achieved has not yet been identified. As a result, it would be a very interesting direction for future research to find out whether theta-band synchronization is involved in that as well. Such a finding would provide compelling support for the view that different forms of cognitive functioning are subserved by similar mechanisms of neuronal communication.

Interactions with higher frequency oscillations

In addition to synchronization with theta activity in other brain areas, there is also evidence for a role of synchronization between theta and other frequency bands in cognitive functioning. With regard to the functions of these different oscillations and their coordination, several authors discuss why frequencies in the theta band are particularly suited for the purpose of connecting distant brain areas, while higher frequencies, particularly those in the gamma band, would be more suited for task-specific processes and local operations.

Fries (2005) describes how synchronous oscillations are an ideal method to ensure effective implementation of top-down control on a neuronal level: by synchronizing its activity with that of the area to be controlled, a group of neurons can make sure that its signals arrive in the receiving neurons when they are most excitable, which means they are most sensitive to input. Why these oscillations are seen at different frequencies may partly be explained by the conduction delay, or distance, between the different areas whose activity needs to be synchronized. Jensen and Colgin (2007) describe the idea that due to these conduction delays, low-frequency oscillations like theta are particularly suited for synchronizing brain areas over large distances, while gamma is more suited for synchronization in local cell assemblies.

Another idea about the contributions of different frequencies comes from Fell et al (2003), who studied theta and gamma activity in hippocampus and rhinal cortex during the encoding phase of a free recall task. They found that theta-band coherence between these two structures was correlated with memory-related changes in gamma synchronization between the two, suggesting that the two forms of synchronization interact during memory encoding. The authors propose that theta reflects slowly modulated coupling between interacting brain areas, reflecting an “encoding state”, while gamma is more suited for the fast coupling and decoupling needed for memory processes themselves. This view, where theta activity is responsible for coupling different brain areas while task-specific content is carried by the faster gamma oscillations, is consistent with the interpretations of several authors who point out that the additional processing time of a single item in the Sternberg paradigm, between 20 and 80ms, is more consistent with one cycle of beta or gamma oscillations (up to 50Hz) per item (Schack et al, 2002; Jensen and Colgin, 2007). Interestingly, in cognitive architectures like ACT-R (Anderson et al, 2004), one cycle in which item representations are processed also corresponds to 50ms.

These are some examples of how the interaction between theta and gamma oscillations is believed to play a role in memory tasks. In fact, there is a lot of evidence suggesting that the interaction of theta and gamma oscillations is somehow involved in memory performance (see chapter 2). In decision making tasks, it is much less clear which role, if any, interactions between theta and higher frequency oscillations play in task performance. From most of the literature reviewed here, it is not clear whether they do not play a role at all, or whether this simply has not been looked at sufficiently. Some evidence for the role of gamma in decision making comes from a study by Berke (2009), who found high gamma oscillations in the rat ventral striatum that showed coherence with frontal cortex during a decision making task, and entrainment to theta rhythms following administration of amphetamine. Theta activity in the same area showed coherence with hippocampal theta. The author suggests that different frequencies of gamma activity may reflect different modes of information processing in service of decision making. Cohen et al (2009b) obtained similar results in humans, where gamma oscillations in nucleus accumbens (part of the ventral striatum) were phase-synchronized with oscillations between 8 and 12 Hz. The authors referred to these frequencies as alpha oscillations, but others consider oscillations up to 10 Hz to be part of the theta band. Although the evidence is scarce,

these findings offer some indication that decision making tasks also elicit gamma oscillations, and that these oscillations synchronize with theta activity.

As a general direction for further research, it would be interesting to see if the interaction between theta and gamma oscillations that is so prominent in the memory literature, can also be found in this other category of cognitive tasks. If so, this would further support the idea that similar mechanisms govern interactions between different sets of brain areas and, as a result, successful performance across a wider range of cognitive tasks.

The interaction between theta and gamma may reflect the activity of a system in which theta facilitates interaction between different brain areas while gamma carries the task-specific content, as suggested by some of the authors cited above. One such system has been proposed by Jensen and Lisman (1998), as discussed in chapter 1. In their view, items in memory are represented by separate gamma cycles, whose place in a theta cycle reflects the order in which the items were presented.

In addition to the function of frontal theta in top-down control of memory performance, the memory models proposed by Sauseng et al (2010) and Nyhus and Curran (2010) also include interactions between theta and higher frequencies. Like Jensen and Lisman (1998), Sauseng et al (2010) believe that the actual content of working memory is represented by gamma activity, while theta serves to order this gamma activity. One study that may provide evidence for such a view was done by Griesmayr et al (2010), who found synchronization between frontal midline theta and distributed gamma oscillations during a working memory task. This effect was stronger in a condition where the information in working memory needed to be manipulated, rather than simply maintained. The authors believe this difference reflects increased monitoring of the order of items, consistent with the model of Jensen and Lisman (1998).

Another memory study where an interaction between theta and gamma was found, was done by Mormann et al (2005). This study, using a recognition memory task, showed that gamma activity in rhinal cortex and hippocampus was modulated by theta oscillations. In addition, stimulus presentation was associated with a phase reset of low frequency oscillations, including theta, but this did not correlate with task performance. According to the authors, their results suggest that the resetting of theta activity upon stimulus presentation merely “sets the stage” for memory processing, possibly by producing optimal conditions for the induction of LTP. This too is consistent with the view that theta activity itself is not responsible for memory processes, but for guiding the higher frequency oscillations that are.

Of course, for this view to hold true, one would expect to find evidence for it in both the memory and the decision making literature. Unfortunately, we have not been able to find studies demonstrating an interaction between theta and gamma that is correlated with performance on a decision making task. The evidence available at this point does not allow us to conclude with certainty that all task-specific content is carried by oscillations outside the theta band or areas outside frontal cortex, as some authors have suggested. However, the evidence is consistent with a role for theta, especially in frontal cortex, that is not specific to any particular cognitive function but instead reflects a form of cognitive control that is needed regardless of the specific processes being performed. Whether this is the only function of frontal theta, or if it can still be involved in task-specific sub-processes, will hopefully become clear in the future.

Task-specific theta activity

So far, we have mainly discussed similarities between the brain regions where theta activity is found during memory and decision making tasks. The region that stands out most clearly in this comparison is frontal cortex, where many believe theta activity plays a role that is the same across a wide range of cognitive functions. However, as one would expect, there must also be differences between the brain areas involved in these two types of tasks. After all, there are cognitive sub-processes that are relevant only, or mostly, for one of the two cognitive functions discussed here. Frontal cortex may indeed control the activity of other brain areas where task-specific processes take place, but where are these areas, do they also work using theta activity, and which processes do they perform?

In EEG studies of memory, it is not uncommon that many different scalp electrodes show a similar effect of task performance. For example, Sederberg et al (2006) found a subsequent memory effect (SME) in the theta band across the entire scalp. This may in part be due to the poor spatial resolution of scalp EEG, but in an intracranial EEG study, Sederberg et al (2007) still found theta SMEs in many different brain areas. The same is true for working memory: Rachavachari et al (2001) found theta activity in many different electrodes that lasted for entire trials, and Jacobs et al (2006) report widespread effects of working memory load on theta activity. Despite the large number of different areas that seem to be needed for successful memory performance, quite a large proportion of those areas do not show activity during decision making, suggesting that they perform cognitive sub-processes that are specific to some cognitive tasks, rather than being needed for all cognitive functioning.

Due to the poor spatial resolution of EEG, it is difficult to determine exactly where task-related theta activity is produced. Nevertheless, some broad areas have been identified that consistently seem to participate in memory studies and that also show synchronization with frontal cortex during successful memory performance.

First of all, the area that is most often associated with memory is the medial temporal lobe: hippocampus and the surrounding structures. This area cannot be studied directly using EEG, but it is relatively well studied using depth electrodes in patients with temporal lobe epilepsy. As stated in chapter 2, this area is traditionally associated with episodic long-term memory, but there is evidence that it also plays a role in working memory. Guderian and Düzel (2005) showed increased theta activity in and between frontal cortex, temporal regions and brain areas processing visual input during “remember” compared to “know” trials. Düzel et al (2010) also find increased theta phase coupling between these areas with increased working memory load.

Parietal cortex is another part of the brain that is activated in many memory studies. Particularly, several authors report increased parietal theta activity for targets compared to lures (Düzel et al, 2005; Jacobs et al, 2006), and for “remember” compared to “know” responses (Sauseng et al, 2010). In addition, probe onset in a WM task was associated with a phase reset of parietal and parieto-occipital theta which facilitated phase coupling of local theta to gamma oscillations (Sauseng et al, 2008), and theta-gamma coherence in parietal cortex was found to be increased for match compared to non-match trials (Holz et al, 2010). There is also evidence that parietal cortex cooperates with frontal cortex during memory tasks. Sarnthein et al (1998) found increased frontal-parietal theta synchronization during WM retention, and Mizuhara and Yamaguchi (2007) found the same during manipulation of information in WM. Griesmayr et al (2010) found that such manipulation is also associated with increased coupling of parietal gamma activity to frontal midline theta.

All of these areas, temporal, parietal and visual cortex, seem to perform sub-processes needed in memory tasks. All of them also show evidence of synchronization with frontal cortex. This supports the view that frontal cortex controls overall task performance, and uses theta synchronization to connect to other brain areas as they are needed to perform a sub-process of a task to receive information or guide their activity. The fact that there is also evidence for synchronization between theta and local gamma activity in parietal cortex, could be interpreted as further support for the view that gamma oscillations carry task-related content, while theta is more involved in linking together different brain areas or ordering gamma cycles to facilitate the successful communication of this content.

With regard to the involvement of visual cortex in memory tasks, this may simply reflect the processing of sensory input like study items, or a probe item in a recognition memory task, rather than a memory-related process per se. It is possible that theta activity in the same area is needed for the processing of stimuli in other tasks, including decision making, but we have not been able to find evidence of this in the literature discussed here. The same is true for temporal and parietal cortex: their participation may be needed in other cognitive tasks as well, but of the two categories discussed here, their activity seems to be restricted to memory-related processes.

In the decision making literature, some of the areas that are often named as part of a decision making network are the basal ganglia. In particular, the ventral striatum with nucleus accumbens are widely believed to play a role in reward evaluation (Marco-Pallares et al, 2008; Womelsdorf et al, 2010a). As described in chapter 1, Cohen et al (2009) have studied nucleus accumbens activity using depth electrodes and found that theta power in this structure is stronger for negative than for positive feedback, but also that theta phase synchrony between left and right nucleus accumbens is increased for loss-switch compared to loss-stay trials, indicating a role in adaptation of behavior in addition to the evaluation of feedback.

Marco-Pallares et al (2008) state that changes in activity of the ventral striatum may be caused by projections from the midbrain dopamine system. In addition, the authors believe that the well-known frontal ERP responses to errors and feedback (ERN and FRN) reflect a negative prediction error signal from the midbrain dopamine system to ACC. Other authors also believe that neurons in this system interact with nucleus accumbens and medial frontal cortex (Cohen et al, 2009) and that they play a role in the computation of reward prediction (Cavanagh et al, 2010), which may drive the sensitivity of ACC to punishment (Cavanagh et al, 2010). Marco-Pallares et al (2008) on the other hand, believe that the midbrain dopamine system is involved in predicting gains, while losses are predicted by amygdala.

Although some authors have different opinions about the exact role of each structure, there seems to be agreement about the fact that these areas are involved in decision making processes. However, there is not a lot of information available on whether they interact with frontal cortex and whether theta activity plays a role in this. Part of this may be due to the fact that, like medial temporal lobe structures, the basal ganglia and midbrain dopamine system are located deep within the brain and cannot be studied using EEG. Unlike in the case of hippocampus, there are not many studies of these structures using depth electrodes that simultaneously looked at oscillatory activity in frontal cortex or other parts of the brain, to look for direct evidence of an interaction between these areas. Electrodes are only implanted for medical reasons, and this is less often the case in these structures than in the temporal lobe. Perhaps, more of such studies will be done in the future to shed more light on the possible interactions between frontal cortex areas that perform specific sub-processes of decision making tasks. This would help determine whether or not a model where frontal cortex monitors and controls the performance of other brain areas is also valid for this cognitive function.

For some of the areas described in this section, there is some indication that they may be involved in more than one different cognitive function. For example, some authors believe that hippocampus is involved in reward evaluation (Luu et al, 2003; Womelsdorf et al, 2010a). However, this may simply reflect cases where information from memory needs to be used, as neither of these authors offer evidence that the contribution of hippocampus to the decision making process is separate from its known memory function. There is also evidence that striatum is involved in procedural or reinforcement learning. However, as these tasks also involve rewards to promote learning, it is possible that the involvement of striatum is again limited to its known function: reward processing.

Conclusion

In this review, we have looked at the role of theta activity in the performance of memory and decision making tasks. It is clear from the literature discussed here that theta activity plays an important role in both tasks. Furthermore, our comparison of the two types of tasks shows that frontal theta activity, in particular, seems to be correlated with successful performance across a broad range of tasks. The fact that this activity is found in the same general location and that authors in both fields connect it to a similar cognitive process, makes it plausible that this frontal theta activity indeed reflects the activity of a common cognitive control system.

At the same time, both types of tasks also seem to elicit activity in more task-specific brain areas, and higher frequency bands. Although there is not as much evidence for these phenomena in decision making studies as there is in the memory literature, and more evidence would be needed to confirm the generalizability of the existing findings, the evidence that is available is consistent with a model where frontal cortex uses theta synchronization to recruit other brain areas and faster oscillations to perform more specific sub-processes as they are needed for the task at hand.

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