

Dissociation of sustained attention from central executive functions: local activity and interregional connectivity in the theta range

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Abstract

Human brain oscillatory activity was analysed in the electroencephalographic theta frequency range (4–7 Hz) while subjects executed complex sequential finger movements with varying task difficulty and memory load. Local frontal-midline theta activity was associated with the general level of cognitive demand, with the highest amplitudes in the most demanding condition. Using low-resolution electromagnetic tomography analysis (LORETA), this theta activity was localized in the anterior cingulate gyrus including the cingulate motor area. These results suggest that local theta activity in the anterior cingulate gyrus represents correlates of an attentional system that allocates cognitive resources. In addition, interregional connectivity in the theta frequency range was modulated by memory-related executive functions independently of task difficulty. Connectivity analyses revealed a more distributed long-range network including frontal and parietal cortices during execution of novel compared with well-trained finger movement sequences. Thus, these results are compatible with a model in which theta long-range coupling indicates integration of sensory information into executive control components of complex motor behaviour.

Introduction

It is well established that frontal-midline theta activity (i.e. rhythmic brain activity at about 5 Hz generated by medial frontal brain structures; see Ishii *et al.*, 1999) is increased during high levels of cognitive demand. Gevins *et al.* (1997) showed that in a working memory task with varying memory load theta power at frontal sites was most pronounced in conditions requiring the highest level of sustained attention. Similar results were reported by Pennekamp *et al.* (1994). In this context sustained attention does not represent simple alertness or arousal but the allocation of cortical resources for highly selective cognitive processes. There is evidence that not only attentional demands are related to increases in frontal-midline theta (e.g. Pennekamp *et al.*, 1994; Makeig *et al.*, 2004; Gomarús *et al.*, 2006), but also working memory load (e.g. Gevins *et al.*, 1997; Krause *et al.*, 2000; Jensen & Tesche, 2002; Onton *et al.*, 2005). However, it is difficult to discriminate these two factors as increasing memory load is usually paralleled by increased task demand. Therefore, it is not clear whether enhanced frontal-midline theta actually reflects memory processes or is solely modulated by sustained attention. This question was addressed recently by Gomarús *et al.* (2006) and Missonnier *et al.* (2006). Gomarús and co-workers ran in children a verbal memory task in which selective attention and memory load could be dissociated from each other. They reported that frontal-midline theta reactivity was only associated with attentional processes but not with memory load. The studies of Gomarús *et al.* and Missonnier *et al.* investigated these effects for verbal working memory, but until now this topic has not been addressed in the motor domain. One recent study reported a

dissociation between task complexity and memory load regarding electroencephalogram (EEG) power in a motor paradigm (Hummel *et al.*, 2003). However, Hummel and co-workers solely analysed power in the alpha and beta frequency bands, but not at the theta frequency range.

Independent of local frontal-midline theta power, interregional coherence at theta frequency was described to be related to memory load (Weiss *et al.*, 2000; Schack & Weiss, 2005; Schack *et al.*, 2005). In particular, coupling of long-range fronto-parietal networks was reported in experimental conditions with high memory load. In the present study, local frontal-midline power as well as interregional theta phase coherence was analysed in order to dissociate sustained attention from memory load during complex motor behaviour. While spectral power is used to detect changes in regional activation, phase coherence quantifies long-range functional connectivity. In the present study, subjects performed a motor memory task during which either memorized or novel finger movement sequences of different task complexity had to be executed. Based on the above-mentioned studies we hypothesized that more complex, and thus more demanding, experimental conditions would be associated with an enhanced local frontal-midline theta activity (Pennekamp *et al.*, 1994; Gevins *et al.*, 1997; Makeig *et al.*, 2004; Gomarús *et al.*, 2006), whereas interregional theta phase coherence should be associated with memory load (Weiss *et al.*, 2000; Schack & Weiss, 2005; Schack *et al.*, 2005).

Materials and methods

Twelve healthy volunteers participated in the study (seven female). The mean age was 26.6 ± 2.9 years (mean \pm SD). Only volunteers

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who did not regularly play the piano were included in this protocol, as musical (piano) education alters the way subjects learn complex finger movements. All subjects were right-handed according to the Edinburgh-Handedness-Scale and gave written informed consent according to the declaration of Helsinki (World Medical Association, 1996). The study protocol was approved by the review board of the University of Tuebingen Medical School.

The experiment consisted of two parts: an initial training session and a subsequent testing session the following day. During the training session motor sequences consisting of 16 consecutive finger movements (key presses on an electronic keyboard) had to be practiced until the subjects reached an overlearned level. The 'overlearned level' was accomplished as soon as the subjects were able to perform the motor sequences 10 times in a row without errors (Gerloff *et al.*, 1998; Hummel *et al.*, 2002, 2003, 2004). The fingers were labelled from 2 = index finger to 5 = little finger accordingly. Sequences of different complexity were used: (i) key presses in consecutive order up or down using four fingers (SCALE, e.g. 3-4-5-2-3-4-5-2-3-4-5-2-3-4-5-2); (ii) key presses in a complex non-consecutive order (COMPLEX, e.g. 5-5-4-2-3-4-3-5-3-5-4-4-2-4-2-3). No EEG was recorded during the training session.

During the testing session, subjects sat in front of a video screen with the right arm relaxed and resting on a pillow. The right hand was positioned palm down so that the response keys could be pressed easily and without any wrist movements. At the beginning and the end of the testing session EEG was acquired during unconstrained rest (REST) in which participants were asked to solely fixate on the centre of the monitor for 5 min.

During the experiment four tasks were performed: (i) execution of a previously trained scale-like sequence (SCALE_{MEM}); (ii) execution of a novel scale-like sequence (SCALE_{NOV}); (iii) execution of an overlearned complex sequence (COMPLEX_{MEM}); and (iv) execution of a novel complex sequence (COMPLEX_{NOV}). Visual cues presented on the video screen paced the rhythm at which the sequences had to be executed (one finger press/s). These visual cues were meaningless symbols for the previously trained sequences and numbers from 2 to 5 for the novel sequences. Trials of these four conditions were randomly intermixed.

EEG was recorded with a SynAmps 32-channel amplifier (NeuroScan, Herndon, VA, USA) at a sampling rate of 250 Hz from 28 Ag-AgCl scalp electrodes arranged according to the extended international 10-20-System and mounted in a flexible cap (Electro-Cap International, Eaton, OH, USA). As reference linked earlobes were used, impedance was kept below 5 kOhm, upper filter cutoff was 50 Hz and the time constant was set to DC.

Data were segmented into epochs of 1024 ms duration for each experimental condition separately. Using BESA 5.1 (MEGIS Software, Munich, Germany), complex demodulation of EEG signals was applied. For each condition and the resting condition power was calculated for single trials, averaged over the segments and collapsed over time. Power values were then averaged within the theta frequency range of 4–7 Hz (results on alpha and beta power have been reported elsewhere; Hummel *et al.*, 2003). Task-related power was calculated by relating the power difference between REST (POW_{rest}) and the four experimental conditions (POW_{activation}) to power in the resting condition. This was done according to the equation

$$\%TRPow = [(POW_{activation} - POW_{rest}) / POW_{rest}] * 100 \quad (1)$$

Complex demodulation was also used for calculation of phase coherence (phase-locking value or PLV as proposed by Lachaux *et al.*, 1999) as implemented in BESA 5.1 software. The PLV is a

measure of phase synchrony between a pair of electrodes. It can range between 0 and 1, with 0 meaning no phase coupling and 1 meaning absolute phase synchronization. PLV was used instead of conventional spectral coherence as pure phase coherence as measured by the PLV is less sensitive to task-related power modulations (Nunez *et al.*, 1997). Phase coupling was calculated for all 378 electrode pairs resulting from 28 scalp electrodes. As was done for task-related power, also phase coherence values were averaged over time and within the same frequency band. Then PLVs were Fisher-Z transformed to get a normal distribution of values. Thereafter, task-related phase coherence was calculated according to

$$\%TRPLV = [(PLV_{activation} - PLV_{rest}) / PLV_{rest}] * 100 \quad (2)$$

To statistically evaluate differences between the conditions in task-related power (%TRPow), we defined three regions of interest (ROI): left sensorimotor cortex (LSM) containing electrode sites FC3, C3 and CP3; right sensorimotor cortex (RSM) containing sites FC4, C4 and CP4; and fronto-mesial cortex (FM) composed of electrodes Fz, FCz and Cz (Homan *et al.*, 1987). A three-way repeated measures ANOVA was run with factors COMPLEXITY (scale vs. complex sequence), MEMORY (memorized sequences vs. novel sequences) and ROI (LSM, RSM, FM). The dependent variable was task-related theta power (%TRPow). The Greenhouse–Geisser correction was applied when necessary.

To determine the cortical sources of theta activity, low-resolution electromagnetic tomography analysis (LORETA; Pascual-Marqui *et al.*, 1994) was applied to the data. Single-trial theta power (4–7 Hz) was calculated in LORETA, and current source density was estimated for 2394 cortical voxels under the assumption that neighbouring voxels have similar activity. This was done for all four experimental conditions (SCALE_{MEM}, SCALE_{NOV}, COMPLEX_{MEM}, COMPLEX_{NOV}). Voxel-wise statistical non-parametrical mapping was run, and each experimental condition was compared with every other condition regarding current source density at theta frequency as the dependent variable. Voxel-wise comparisons were tested on the 5% significance level after correction for multiple comparisons (for details, see Nichols & Holmes, 2002).

As an exploratory analysis, one-sample *t*-tests with task-related phase coherence (%TRPLV) as the dependent measure were calculated for each electrode pair on the scalp level and each experimental condition. This was done to determine which electrode pairs showed significantly higher or smaller phase coherence during the respective experimental condition compared with REST. Deviances from REST were considered reliable if $P < 0.005$ (Sauseng *et al.*, 2005, 2006). The number of significant electrode pairs from this analysis was used to compare the four experimental conditions by means of Cochran's *Q*-tests (corrected for multiple comparisons).

Results

Task-related power analysis

The ANOVA revealed a significant interaction between factors COMPLEXITY, MEMORY and ROI on the theta power values ($F_{2/22} = 3.78$, $P < 0.05$). As demonstrated in Fig. 1 there was a prominent theta power increase at the frontal-midline ROI only in the condition where complex novel sequences (COMPLEX_{NOV}) had to be performed. *Post hoc t*-testing (corrected for multiple comparisons) showed that there were no significant differences between the three other conditions in frontal-midline theta power ($t_{11} < 3.13$; n.s.); however, there was a significantly larger theta power increase during

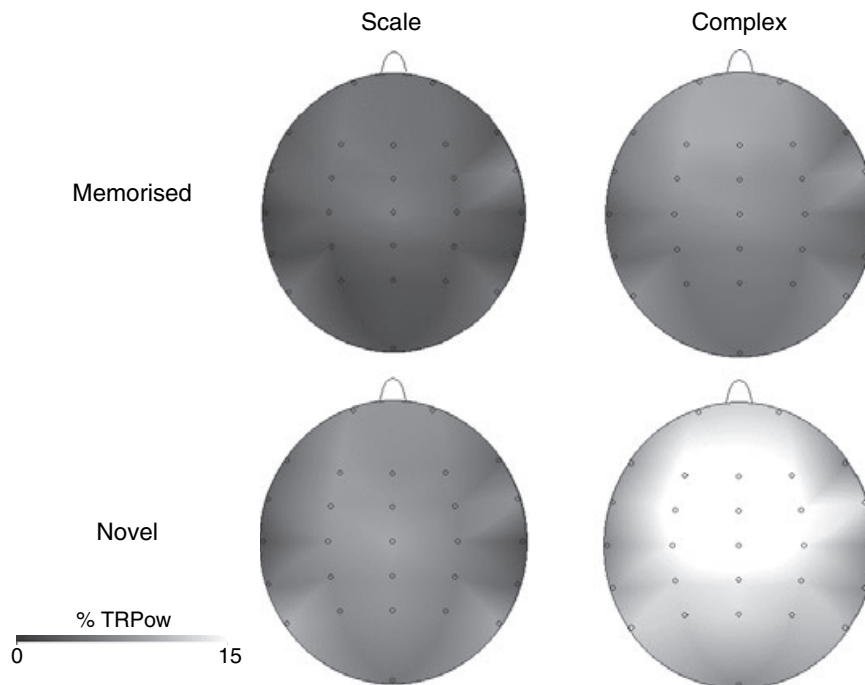


FIG. 1. Task-related theta (4–7 Hz) power increase. White indicates a strong task-related power increase compared with rest. Note that only during execution of novel and complex sequences is strong frontal-midline theta exhibited. This indicates that frontal theta activity reflects both memory load and sequence complexity.

COMPLEX_{NOV} than during the other three conditions ($t_{11} > 4.54$; $P < 0.05$). The interaction COMPLEXITY*MEMORY ($F_{1/11} = 9.85$, $P < 0.01$) and the main effects for factors COMPLEXITY ($F_{1/11} = 21.59$, $P < 0.01$), MEMORY ($F_{1/11} = 24.83$, $P < 0.01$) and ROI ($F_{1/11} = 4.79$, $P < 0.05$) were also significant.

LORETA

Results from LORETA are depicted in Fig. 2. During the execution of novel complex sequences (COMPLEX_{NOV}) significantly higher theta activity at the anterior cingulate gyrus including the cingulate motor area was found compared with all other conditions, the condition that also elicited pronounced frontal-midline theta increase at the scalp level. During COMPLEX_{NOV} significantly more theta activity at the left premotor and dorsolateral prefrontal areas and the right insula was exhibited compared with SCALE_{MEM}. The right insula showed additionally significant enhancement of power during COMPLEX_{NOV} compared with SCALE_{NOV}. Comparisons between SCALE_{NOV}, SCALE_{MEM} and COMPLEX_{MEM} did not show any significant effects at fronto-medial brain structures.

Task-related phase coherence analysis

Figure 3 depicts the results from task-related phase coherence analysis. In all four conditions, especially frontal and central, electrode pairs exhibited stronger phase coherence compared with rest. During performance of novel sequences a more distributed network, including fronto-parietal connections, was activated than during the execution of memorized sequences. Cochran's Q -tests revealed that the number of significant electrode pairs was larger during performance of novel sequences than during memorized sequences, independent of sequence complexity (SCALE_{MEM} vs. SCALE_{NOV}: $Q_{1/378} = 8.76$, $P < 0.05$; COMPLEX_{MEM} vs. COMPLEX_{NOV}: $Q_{1/378} = 18.25$, $P < 0.01$). For

memorized as well as for novel sequences complexity did not influence the number of significant pairs (SCALE_{MEM} vs. COMPLEX_{MEM}: $Q_{1/378} = 1.40$, n.s.; SCALE_{NOV} vs. COMPLEX_{NOV}: $Q_{1/378} = 2.32$, n.s.).

In order to directly compare task-related phase coherence between memorized and novel conditions, phase coherence estimates were averaged for complex and scale-like sequences for the memorized and novel condition, respectively. Paired sample t -tests between these two conditions with different memory load were run for each electrode pair. Figure 4 shows electrode pairs that differed significantly ($P < 0.005$) between memorized and novel conditions. Bold connections denote higher theta phase coherence during execution of novel compared with memorized sequences, in contrast dotted connections denote higher theta phase coherence during execution of memorized compared with novel sequences. A large number of long-range connections, in particular between frontal and posterior parietal electrode sites, showed greater phase coherence during the novel condition.

Discussion

The present study was designed to separate sustained attention from memory load during complex motor behaviour by analysis of human EEG theta activity. The main results were that local frontal-midline theta activity was increased in conditions requiring the highest level of task demand, and that interregional theta phase coherence dissociated between conditions of different memory load independently of task complexity.

Local frontal-midline theta and sustained attention

The most cognitively demanding condition, execution of complex novel sequences, was represented by the strongest frontal-midline

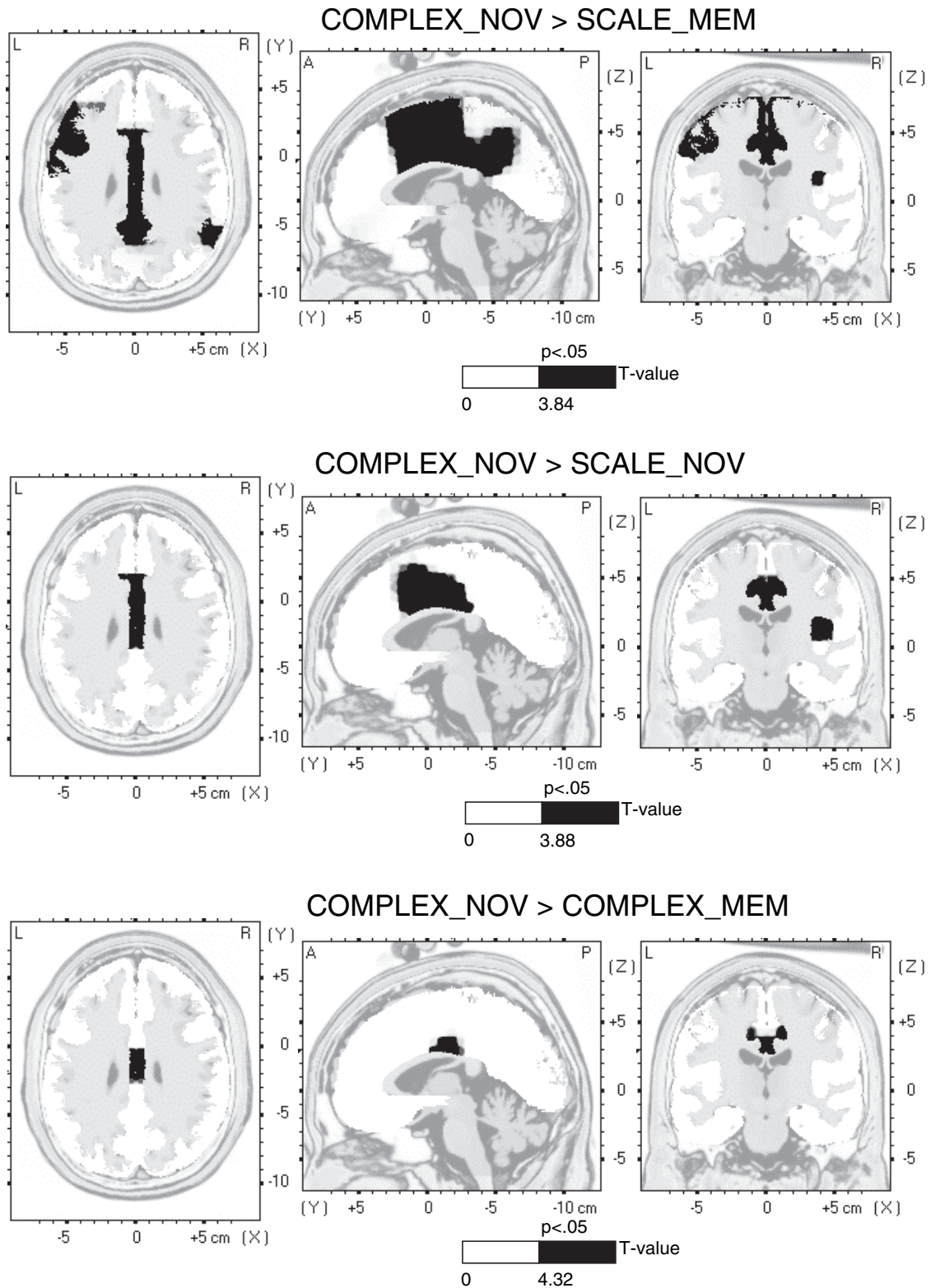


FIG. 2. LORETA source analysis of theta activity (4–7 Hz). The figure depicts comparisons of theta source activity between execution of novel complex sequences and the three other experimental conditions. For all three comparisons increased fronto-medial [$X, Y, Z = (-3, -18, 29)$] theta activity was found for COMPLEX_{NOV}, indicated in red colour ($P < 0.05$, corrected for multiple comparisons; linearity = 100).

theta power substantiated by a significant three-way interaction in the ANOVA run with theta power estimates from scalp derivations as expected. Frontal-midline theta depended on both kinematic complexity of the motor task and memory load. Hardly any increase of

theta activity at frontal-midline sites compared with rest was found when well-trained and memorized or scale-like novel sequences had been executed. These conditions required only a low level of cognitive demand and might have been performed without highly focused

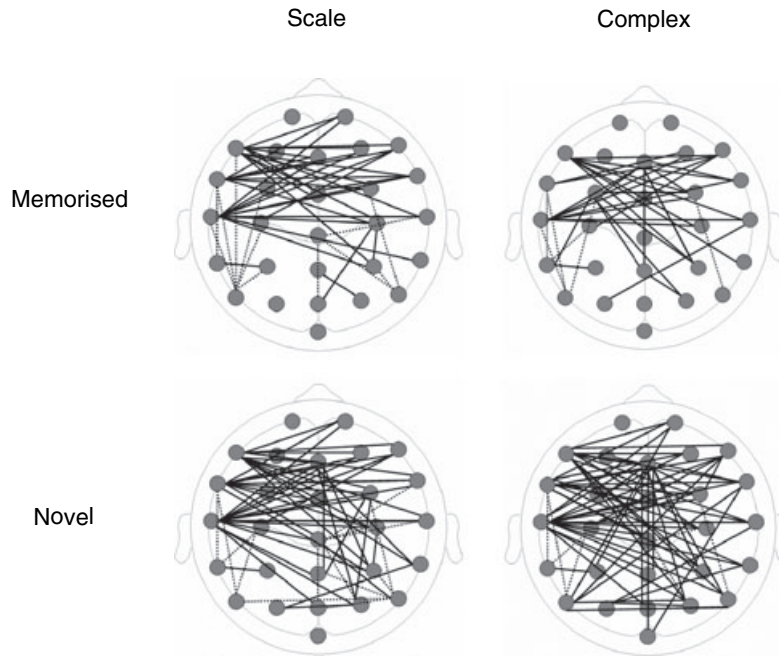


FIG. 3. Task-related theta phase coupling. Bold connections indicate a significant ($P < 0.005$) increase of theta phase coupling compared with rest, dotted lines indicate decrease of phase coupling. There are more significant electrode pairs during execution of novel sequences compared with performance of memorized ones. This effect is independent of task complexity. During both memorized and novel, there is no significant difference of the distributed theta network between scale and complex sequences.

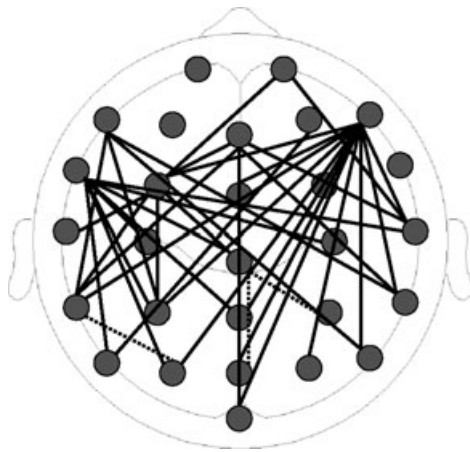


FIG. 4. Task-related theta phase coupling – comparison between memorized and novel condition. Dotted connections indicate significantly ($P < 0.005$) stronger phase coherence at theta frequency during execution of memorized sequences. Bold connections indicate stronger coupling in the novel sequence conditions. Note the fronto-parietal theta network that is activated during execution of novel sequences.

attention. During the experiment, participants were instructed to perform the key presses as correct as possible in all different experimental conditions. Thus, executing complex novel sequences, as the most difficult and cognitively demanding tasks, with comparable excellence as in the other conditions required to recruit and allocate more cognitive resources compared with the other conditions. This was reflected by pronounced frontal-midline theta activity during the complex novel condition. This is well in line with other studies reporting strong frontal-midline theta activity during focused attention (Pennekamp *et al.*, 1994; Gomarús *et al.*, 2006; Missonnier *et al.*,

2006) and in memory experiments with high cognitive demand (Gevins *et al.*, 1997; Onton *et al.*, 2005).

LORETA localized the anterior and motor cingulate gyrus as the source of this frontal-midline theta activity, which is well in line with previous findings (Gevins *et al.*, 1997; Ishii *et al.*, 1999; Makeig *et al.*, 2004; Onton *et al.*, 2005). Supporting the present results, in LORETA similarly the complex novel condition was the only condition showing pronounced theta activity at fronto-medial brain areas. The other conditions did not differ significantly from each other in terms of theta activity in the cingulate cortex. These data support the interpretation that frontal-midline theta power reflects the cognitive demand necessary to perform a complex task well.

Makeig *et al.* (2004) reported frontal-midline theta localized in the cingulate gyrus in a time window shortly after a manual response to a target stimulus in an attention paradigm. They interpreted their results in terms of frontal-midline theta reflecting context updating. This would be an alternative interpretation for the findings in the present study. No pronounced frontal theta activity was elicited by execution of memorized sequences. So, in contrast to novel sequences, during the memorized conditions no context updating was required. Thus, it is likely that context updating might be one relevant factor as it was possibly most pronounced in the experimental conditions that showed the highest frontal-midline theta activity. However, one would expect then that also in the scale-like novel condition (and not only in the complex novel condition) at least some frontal-midline theta should have been exhibited, which was not the case in the present study.

Interregional theta phase coupling and memory load

In contrast to local frontal theta activity, interregional phase coupling at theta frequency differentiated between conditions with high and low memory load independently of kinematic task complexity. Execution of novel sequences was reflected by more electrode pairs showing

significant task-related coherence than in the memorized conditions, whereas complex sequences did not differ from scale-like sequences neither in the memorized nor in the novel condition. This is in line with results from Sauseng *et al.* (2005, 2006) showing that theta long-range coupling does not reflect general (working memory) task demand.

However, based on previous studies (Weiss *et al.*, 2000; Schack & Weiss, 2005; Schack *et al.*, 2005) it was expected that higher memory load would have been associated with pronounced theta phase coherence. Surprisingly, stronger theta phase coherence was elicited by the novel sequence conditions. When phase coherence of the memorized and novel conditions were compared directly it was obvious that, in particular, long-range frontal to parietal connections showed stronger phase coherence during execution of novel sequences. Fronto-central phase coupling, however, was similar in all conditions indicating more basic mechanisms of response selection supported by results from Makeig *et al.* (2004).

Integration of visual and sensory-motor information has been demonstrated to be represented by long-range connectivity between posterior and fronto-central brain areas (Classen *et al.*, 1998; von Stein *et al.*, 2000; Hummel & Gerloff, 2005). Based on this, in the present study stronger fronto-parietal theta coupling might represent the integration of visual information with required motor response. In the memorized condition the visual cues provided only information about the rhythm (1 Hz) of the finger movements. In contrast, in the novel condition the visual cues provided information about the rhythm but, more importantly, also about which finger had to be used. This information had to be integrated into the respective motor response. Thus, in this condition proper visuo-motor integration was required for successful motor performance. During execution of memorized sequences integration of visual input was less important for successful motor performance as the required movements were retrieved from memory. Thus, it can be speculated that the amount of long-range interactions in the theta frequency represented the amount of visuo-motor integration necessary for proper performance. This suggestion is substantiated by the present results, with the largest amount of interregional coupling during the complex novel condition. Taking this interpretation into account the question remains open why the parietal electrode sites were mainly coupled to prefrontal electrode sites and not to central ones, such as electrode positions C3 and C4. Evidence to address this question comes from Sauseng *et al.* (2005, 2006) suggesting that fronto-parietal coupling at theta frequency is a marker for central executive functions of working memory. It was proposed by Baddeley (1992) that a central executive, which is settled within the prefrontal cortex, manages different working memory functions. It coordinates encoding and retrieval processes, and represents an interface between memory systems. Thus, in the present data prefrontal to parietal connectivity might not reflect integration of visual and motor information per se, but integration of visual information into a prefrontal control and executive system. This hypothesis is supported by the fact that there is more coupling in the novel sequence conditions because they require the coordination of a larger number of different cognitive processes, like analysis of visual cue, association of visual input and required response and memory encoding processes. This necessitates high activation of the central executive. On the other hand, during execution of memorized sequences less central executive functions were required and the system is tuned to more efficiency. Therefore, theta connectivity between prefrontal and parietal sites, in particular, was less pronounced.

The results of the present study revealed that local frontal-midline theta power, arising from the cingulate gyrus, is associated with

sustained attention. Long-range interregional theta coupling between prefrontal and parietal brain areas, on the other hand, reflects integrative processes, probably mediated by a central executive system. This is in accordance with the idea that slow oscillations like theta and delta are associated with integrative brain functions (Sarnthein *et al.*, 1998; von Stein & Sarnthein, 2000). The question might arise, what is the conceptual difference between these two cognitive systems reflected by local fronto-medial theta activity and interregional fronto-parietal theta coupling, respectively? Local cingulate theta activity is only obtained in tasks that require a high level of focal attention. Therefore, this kind of activation is associated with a specific attentional system that might promote the allocation of cognitive resources. In contrast to that, long-range theta phase coupling is modulated by memory load, independently of general cognitive demand. This kind of interregional theta activity reflects the central executive integrating different memory and information processing functions. As in conditions with similar memory load, these functions are similar, fronto-parietal theta phase coupling dissociated conditions of different memory load independently of task complexity. Local theta activity, on the other hand, is not mediated by memory processes per se.

Conclusion

The present study indicates that sustained attention and central executive memory processes can be dissociated by theta activity on different spatial scales. Comparing the results from local oscillatory activity to interregional connectivity in order to separate different cognitive functions is a promising approach for future cognitive neuroscientific research.

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Abbreviations

EEG, electroencephalogram; FM, fronto-mesial cortex; LORETA, low-resolution electromagnetic tomography analysis; LSM, left sensorimotor cortex; PLV, phase-locking value; ROI, region of interest; RSM, right sensorimotor cortex; TRPLV, task-related phase-locking value; TRPow, task-related power.

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