Brain Research

Research Report

The influence of mental fatigue and motivation on neural network dynamics; an EEG coherence study

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ABSTRACT

The purpose of the present study is to examine the effects of mental fatigue and motivation on neural network dynamics activated during task switching. Mental fatigue was induced by 2 h of continuous performance; after which subjects were motivated by using social comparison and monetary reward as motivating factors to perform well for an additional 20 min. EEG coherence was used as a measure of synchronization of brain activity. Electrodes of interest were identified using a data-driven pre-processing method (ten Caat, M., Lorist, M.M., Bezdan, E., Roerdink, J.B.T.M., Maurits, N.M., 2008a. High-density EEG coherence analysis using functional units applied to mental fatigue. J. Neurosci. Meth. 171, 271–278; ten Caat, M., Maurits, N.M. and Roerdink, J.B.T.M., 2008b. Data-driven visualization and group analysis of multichannel EEG coherence with functional units. IEEE T. Vis. Comp. Gr. 14, 756–771). Performance on repetition trials was faster and more accurate than on switch trials. EEG data revealed more pronounced, frequency specific fronto-parietal network activation in switch trials, while power density was higher in repetition trials. The effects of mental fatigue on power and coherence were widespread, and not limited to specific frequency bands. Moreover, these effects were independent of specific task manipulations. This increase in neuronal activity and stronger synchronization between neural networks did not result in more efficient performance; response speed decreased and the number of errors increased in fatigued subjects. A modulation of the dopamine system is proposed as a common mechanism underlying the observed the fatigue effects.

1. Introduction

Mental fatigue influences nearly all aspects of cognitive and emotional functioning in humans. It induces sub-optimal functioning, which may even lead to accidents with severe consequences. Concerning the impact of mental fatigue on daily life it is surprising that only little is known about neuro-cognitive mechanisms underlying the effects of mental fatigue.

Previous studies have indicated that higher level control functions, which orchestrate more basic cognitive functions,

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are especially sensitive to mental fatigue (Holding, 1983; Lorist et al., 2000, 2005; van der Linden et al., 2003). Lorist et al. (2000), for example, showed that control mechanisms involved in planning and preparation for future activities became less adequate and subjects made more errors with increasing mental fatigue. Moreover, fatigue was found to be associated with compromised performance monitoring, and the ability to use information from previous trials to strategically adjust behavior was severely deteriorated already after half an hour of continuous task performance (Boksem et al., 2006; Lorist et al., 2005).

These studies mainly focused on effects of mental fatigue on specific cognitive functions reflected in event-related potential (ERP) components in the EEG. However, adequate performance requires the integration of information processed in functionally specialized brain regions. Integration or binding of information processed in separate regions takes place through synchronization of brain activity in these different brain areas. Simultaneous activation in two or more functionally and anatomically distinguished brain areas is expected in case cognitive control functions are active, whereas neural synchronous oscillations occurring in more localized brain areas specialized for specific functions seem to be associated with more basic cognitive functions (Engel et al., 2001; Sauseng and Klimesch, 2008).

The purpose of the present study is to examine whether mental fatigue affects neural network dynamics as indexed by neural synchronization. To verify this we used a switch task in which cognitive control processes, involved in rapidly switching between tasks, play a crucial role, and which has shown to elicit mental fatigue (Lorist et al., 2000). Lorist et al. (2000) limited their analysis of brain activity in that study to ERP components. To investigate whether the observed effects of mental fatigue can be related to changes in network dynamics we focused on EEG coherence in the present study. The EEG signal measured at a specific electrode is supposed to reflect network activity under the electrode (in particular synchronous neural oscillations of pyramidal neurons) and EEG coherence can be regarded as a measure of interaction between two of these neuronal populations (Nunez, 2000). It is generally accepted that more synchronous activity in different brain regions will be reflected in increased coherence between EEG signals obtained from recordings directly above these areas.

Coherence in specific frequency bands has been related to different cognitive functions (Knyazev, 2007). For example, Sauseng et al. (2005) reported that global synchronization in the theta band (4–8 Hz) increases with increasing demands on cognitive control. In addition, they found that local parietal synchronization in the theta band increases with increasing task difficulty. However, the frequency specificity of these results should be interpreted carefully because Sauseng et al. limited their analysis to the alpha and theta range a priori. It is important to realize that changes in coherence values observed in a specific frequency range do not imply that a similar change in power will be observed at single electrodes involved in the interaction. An increase in EEG power indicates an increase in the number of synchronously active neurons underlying an electrode, while stronger coherence without increased power necessarily indicates increased phase locking

between neural activities recorded from two cortical areas. Kiroi and Aslanyan (2006) showed that prolonged monotonous task performance for 3–3.5 h increased power in the lower frequency bands (delta and theta) and in the beta band. Coherence levels, however, did not change with time on task, which was interpreted as a reflection of the stability of long-range neuronal relationships during continuous task performance. Similar effects of mental fatigue on EEG power were reported by Boksem et al. (2005); they found an increase in spectral power in the alpha, theta and beta band during 3 h of task performance. The increase in alpha and theta power was interpreted as a reflection of decreased arousal levels, while the increase in beta power was linked to the investment of mental effort to stay awake.

Existing evidence concerning the effects of mental fatigue on EEG synchronization is rather limited; therefore it is difficult to formulate firm hypotheses about effects of mental fatigue on brain synchronization and to identify the regions (i.e., electrodes) of interest or frequency bands of interest to be studied. Discarding a major part of information beforehand might leave brain regions or frequency bands with potentially significant contributions to the cognitive mechanism under observation undetected, which seriously limits the interpretation of research findings. Because of these disadvantages of the hypothesis-driven method under the present circumstances we applied a data-driven pre-processing method instead to identify electrodes of interest and subsequent analyses were performed over a wide range of frequency bands. The method to identify relevant electrodes of interest was developed by ten Caat et al. (2008a, 2008b), and visualizes the results of a calculation encompassing all possible coherences between electrodes. Local synchronicity is represented by functional units (FUs), representing spatially connected sets of electrode pairs of which coherence values exceed a predefined threshold level and which are presumed to represent functionally distinct brain areas. Global coherence is represented as coherence between FUs. The individual FU maps are used to calculate group mean coherence maps, visualizing dominant features from individual maps, and this information can be the basis of subsequent conventional coherence and power analysis.

The major issue in the present study is to gain more understanding of the origins and nature of changes in cognition with increasing mental fatigue. From this perspective, it is important to realize that effects of mental fatigue have been related to a lack of motivation (Boksem et al., 2006; Chaudhuri and Behan, 2000). Boksem et al. (2006) showed that after adequate motivation the adverse effects of mental fatigue could be partially reduced. They hypothesized that motivation resulted in improvements in cognitive control. As argued earlier, cognitive control processes are reflected in global synchronization between diverse cortical sites, therefore, an increase in coherence might be expected in motivated subjects compared to mentally fatigued subjects. To test this assumption, subjects were motivated in the present study after 2 h of task performance by using social comparison and monetary reward as motivating factors.

In summary, in the present study we sought to determine the effects of mental fatigue and motivation on neural network dynamics activated during task switching, using EEG coherence as a measure of synchronous activation in the

brain. Electrodes of interest were identified using a data-driven pre-processing method (ten Caat et al., 2008a, 2008b).

2. Results

2.1. Subjective measures

Subjects reported increasing levels of aversion to continue task performance with increasing time on task ($F(5,125) = 44.54$, $p < .001$); scores increased from 4.5 (SD=2.0) at the start of the experimental session to 8.8 (SD=1.7) at the end of task performance. Activation levels, as derived from the Activation–Deactivation Adjective Check List (AD–ACL; Thayer, 1989), decreased during the session (Fig. 1; $F(1,25) = 29.47$, $p < .001$ and $F(1,25) = 8.76$, $p = .007$ for general activation and high activation, respectively), while deactivation/sleep levels increased ($F(1,25) = 38.87$, $p < .001$). General deactivation levels did not change significantly ($F(1,25) = .66$, n.s.).

2.2. Behavioral data

In agreement with previous results (Lorist et al., 2000), we observed shorter reaction times (RTs) in the repetition condition (718 ms) than in the switch condition (940 ms; stimulus type: $F(1,25) = 189.49$, $p < .001$) and subjects made more incorrect responses in switch trials (9%) than in repetition trials (5%; stimulus type: $F(1,25) = 113.78$, $p < .001$; Fig. 2). In addition, they missed more trials in the switch condition (2.4%) compared to the repetition condition (1.4%; stimulus type: $F(1,25) = 13.65$, $p = .001$). RTs changed with time on task (time on task: $F(6,150) = 4.59$, $p = .003$) and this effect was dependent on stimulus type (time on task × stimulus type: $F(6,150) = 3.43$, $p = .005$). RTs in the repetition condition did not show a significant change during the first four 20-min intervals of task performance, however, in interval 5 and 6,
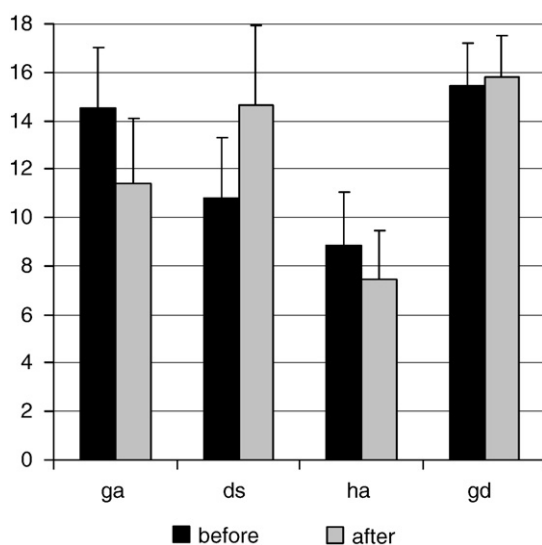

Fig. 1 – Average AD–ACL scores for the different activation states (ga=general activation, ds=deactivation/sleep, ha=high activation, gd=general deactivation). Error bars represent the standard deviation of the mean.
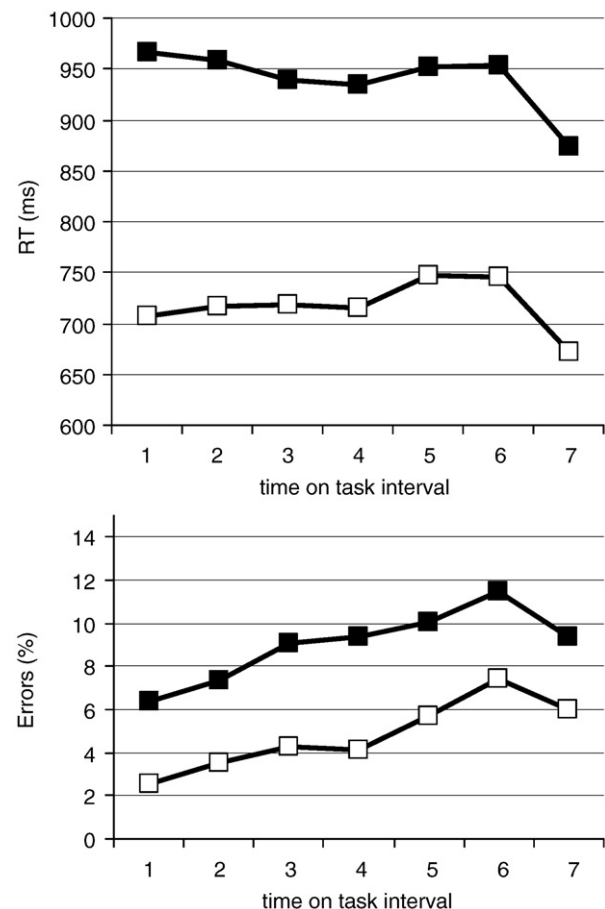

Fig. 2 – Average RTs (ms; upper panel) and percentage of errors (lower panel) for repetition (open squares) and switch trials (filled squares) in the different 20-min time on task intervals.

an increase in RT was observed (see Fig. 2). RTs in the switch condition showed a cubic relationship with time on task (time on task in switch condition: cubic trend: $F(1,25) = 12.97$, $p = .001$); subjects became faster during the first 80 min of task performance, thereafter RTs showed an increase during intervals 5 and 6. For both repetition and switch trials a significant decrease in RT was observed after the motivation manipulation, that is in interval 7 ($p = .003$ and $p = .011$, pairwise comparisons between interval 6 and interval 7 for repetition and switch trials, respectively). RTs in the switch condition became even shorter than during the first 20 min of task performance (pairwise comparisons between interval 1 and interval 7 for switch trials: $p = .016$).

The percentage of incorrect responses increased from interval 1 (0–20 min: 4.5%) to interval 6 (101–120 min: 9.5%). After the motivation instruction a non-significant improvement in performance accuracy was observed; compared to interval 6, 2% less errors were measured in interval 7 (Fig. 2; time on task: $F(6,150) = 7.47$, $p < .001$). The effects of time on task on the percentage of incorrect responses were similar for repetition and switch trials (time on task × stimulus type: $F(6,150) = .76$. n.s.). The percentage of misses did not change significantly with time on task (time on task: $F(6,150) = 2.52$, n.s.).

2.3. Coherence data

2.3.1. Group mean coherence maps

A smaller number of FUs was observed in the lower frequency bands (on average 2.8 FUs) than in the higher (alpha, beta and gamma) frequency bands (on average 6.8 FUs). Although, the number of FUs increased with increasing frequency the total number of electrodes involved in these FUs decreased, implicating the involvement of larger local networks at lower frequencies (Fig. 3). The number of significant distant connections observed in time on task interval 6 was on average larger (9.4 when averaged over the all frequency bands of interest and both conditions) than in interval 1 or 7 (7.1 and 6.2, respectively). Visual inspection of the group mean coherence maps showed that coherence between the FUs appeared most prominent between a mid-frontal FU, 2 fronto-lateral and 2 parieto-occipital FUs, situated more or less symmetrically on the left and right side of the scalp. Remarkable was the coherence between frontal and parietal sites located in contra-lateral hemispheres. Based on these findings, five electrodes of interest representing these FUs (Fz, FC5, FC6, PO7, and PO8) were selected for further conventional statistical analysis of coherence and power density. In addition to these electrodes, we used the following electrodes in the analysis: F3, F4, C3, C4, CP5, CP6, P3, P4, O1 and O2, to be able to compare our results to previous findings reported in the literature.

2.3.2. Statistical analysis of coherence[1]

In general, analysis of coherence showed that the highest coherence values were recorded in the lowest frequency bands and with increasing frequency coherences decreased significantly (1–3 Hz = .38, 4–7 Hz = .32, 8–12 Hz = .30, 13–23 Hz = .21, and 24–35 Hz = .21; main effect of frequency band: $F(4,96) = 104.21$, $p < .001$). However, post-hoc tests indicated that inter-hemispheric coherence between fronto-central and central sites (FC5–FC6, C3–C4) was higher in the gamma band (24–35 Hz) compared to the values observed in the lower frequency bands, while coherence between CP5–CP6 was relatively high in the 8–12 Hz band (Fig. 4; electrode pair: $F(14,336) = 289.10$, $p < .001$; frequency band × electrode pair: $F(56,1344) = 41.71$, $p < .001$). Follow-up analyses indicated that coherence between O1 and O2 was significantly higher in all frequency bands compared to coherence observed between all other electrode pairs. Coherences between Fz and parieto-occipital electrodes (i.e. Fz-PO7 and Fz-PO8) and the inter-hemispheric coherence values between fronto-central and parieto-occipital electrodes (i.e., FC5-PO8 and FC6-PO7) were not as high as values observed between O1–O2, however, between 1 and 23 Hz they were higher than the coherence between the other electrode pairs. Coherence between Fz-PO7

and Fz-PO8 even remained significantly higher up to 35 Hz. In addition, we observed that whereas inter-hemispheric coherence at frontal sites (F3–F4) was comparable to the fronto-parietal coherence values in the lower frequency bands (1–23 Hz), inter-hemispheric coherence at (fronto-) central sites (FC5–FC6, C3–C4) was relatively low (see also Fig. 4).

Differences in coherence between repetition and switch trials were dependent on electrode pair and frequency band (stimulus type: $F(1,24) = 5.98$, $p = .022$; electrode pair × stimulus type: $F(14,336) = 4.89$, $p < .001$; electrode pair × frequency band × stimulus type; $F(56,1344) = 1.94$, $p = .027$). Follow-up analysis indicated that coherence between frontal and parietal electrodes (Fz-PO8, FC5-PO7, FC6-PO8) and between PO7–PO8 and O1–O2 was higher in the switch condition than in the repetition condition. Moreover, the observed differences between repetition and switch trials were most pronounced in the 4–7 Hz and 13–23 Hz frequency bands The effects of stimulus type were not modulated by time on task (time on task × stimulus type: $F(6,144) = 1.08$, n.s.).

Coherence values showed an increase with time on task, and after the motivation manipulation a small, non-significant decrease was observed (Fig. 5; time on task: $F(6,144) = 3.24$, $p = .020$). The effects of time on task did not differ between frequency bands (frequency band: $F(24,576) = .93$, n.s.) or electrode pairs (electrode pair: $F(84,2016) = 1.48$, n.s.).

2.4. Power density data

We observed that overall power density decreased with increasing frequency (Fig. 6; frequency band: $F(4,960) = 266.81$, $p < .001$). Moreover, differences in power density across electrode sites were dependent on frequency (frequency band × electrode site: $F(56,1344) = 26.59$, $p < .001$). Follow-up analysis indicated that in the lower frequency bands (1–12 Hz) power density was relatively high at posterior sites (O1, O2, PO7 and PO8). In addition, power density was relatively high between 1 and 7 Hz at Fz. In the higher frequency bands (i.e., 24–35 Hz) power density was relatively high at lateral fronto-central sites (F3, F4, FC5 and FC6), while in these frequency bands power density was relatively low at P3 and P4.

In general, power density was higher in the repetition condition than in the switch condition, especially in the lower frequency bands (1–23 Hz; stimulus type: $F(1,24) = 11.68$, $p = .002$ frequency band × stimulus type: $F(4,96) = 5.46$, $p = .004$). Differences between repetition and switch trials were most pronounced at parietal and occipital electrode sites (i.e. P3, P4, PO7, PO8, O1 and O2; stimulus type × electrode site: $F(14, 336) = 6.85$, $p < .001$). Differences between repetition and switch trials did not change significantly with time on task (time on task × stimulus type: $F(6,144) = .41$, n.s.; time on task × stimulus type × electrode site: $F(84,2016) = .88$, n.s.).

With time on task a small, but significant, increase in power density was observed (Fig. 7), especially in the lower frequency bands (time on task: $F(6,144) = 11.66$, $p < .001$; time on task × frequency band: $F(24,576) = 3.01$, $p = .016$). Pairwise comparisons between time on task intervals revealed no changes in power density after the motivation manipulation. The effects of time on task were similar across electrodes (time on task × electrode site: $F(84,2016) = 1.03$, n.s.; time on task × frequency band × electrode site: $F(336,8064) = 1.14$, n.s.).

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[1] Although we use the term "coherence" hereafter, it should be noted that the statistical analysis was performed on Fisher z-transformed coherence. Coherence differs by a strictly monotonous transformation from z-transformed coherence, therefore positive and negative differences are preserved. Data of one subject contained missing data points (C3 in intervals 6 and 7) and was rejected from part of the statistical analyses.

3. Discussion

The effects of mental fatigue on neural network dynamics related to stimulus processing were examined using a switch paradigm, in which cognitive control processes play a crucial role, and which has shown to elicit mental fatigue (Lorist et al., 2000).

3.1. Stimulus type

The effects of task manipulation were similar to previous findings (e.g., Lorist et al., 2000; Rogers and Monsell, 1995); RTs were shorter and performance was more accurate on repetition trials than on switch trials. Enhanced inter-hemispheric synchronization between posterior electrode sites in the switch condition pointed to more active posterior networks in this condition than during repetition trials. Activity in parietal areas has been related to different aspects of task set reconfiguration (Sohn et al., 2000; Braver et al., 2003). Stronger coherence at parietal-occipital sites in the present study was not confounded by a parallel power increase; power density was actually higher in repetition trials, indicating that increases in coherence values in the switch condition cannot solely be explained by more activity in underlying neural networks.

In addition we found higher coherence values between several fronto-parietal electrode pairs in the switch condition compared to repetition trials. Task switching requires a continuous update of internal stimulus–response mappings represented in a task set, and adequate inhibition of inappropriate task sets. Neuro-imaging studies have shown that during these control activities a fronto-parietal network is active (Braver et al., 2003; Dove et al., 2000; Kimberg et al., 2000; Sauseng et al., 2006; Sohn et al., 2000). The coupling between fronto-parietal regions was stronger in the theta and beta band than in the alpha band. These frequency related effects of stimulus type were in agreement with findings of Sauseng et al. (2006), who assumed that theta coherence was especially related to top down control processes involved in task switching. Beta coupling has been interpreted as a reflection of enhanced processing of relevant information and, at the same time, of suppression of irrelevant information, processes crucial for adequate task set reconfiguration (Gross et al., 2003).

A remarkable finding observed in the group mean coherence maps was the strong coherence between contra-lateral frontal and parietal areas. As mentioned above, there is ample evidence that fronto-parietal networks play an important role in cognitive control (e.g., Corbetta and Shulman, 2002; Coull et al., 1996; Fassbender et al., 2006; Sauseng et al., 2005). These networks, however, are unilateral, that is, mainly confined to either the left or right hemisphere. Limited evidence for a fronto-parietal network involving contra-lateral brain areas was reported by Razoumnikova (2005); she reported that these inter-hemispheric coherences increased during problem solving in male subjects. Razoumnikova argued that inter-hemispheric connections allow the left hemisphere to exert an inhibitory influence on right-hemispheric functions thereby stimulating creative thinking. Although tentative the

stronger activation in these inter-hemispheric connections in the switch condition might be related to the inhibition of inappropriate task sets.

3.2. Time on task

Mental fatigue was induced in the present study by continuous performance for 2 h. In agreement with previous findings, this manipulation seemed successful, as reflected in increased feelings of fatigue and decreased feelings of activation with time on task. Moreover, subjects developed an aversion against prolongation of task performance, which might be regarded as a sign of mental fatigue, as well (Holding, 1983; Hockey, 1997; Lorist et al., 2000).

In general the behavioral results confirmed that mental fatigue was elicited by prolonged task performance; task performance became less efficient with time on task, response speed decreased and the number of errors increased. The observed performance deteriorations cannot be explained by a change in speed–accuracy trade-off since both speed and accuracy levels deteriorated. After the motivation information performance efficiency increased; in the switch trials subjects even reacted faster after the motivation manipulation than during the first 20 min of task performance, although the number of errors did not return to the level observed in non-fatigued subjects.

So far, subjective and behavioral results indicated that performance efficiency deteriorated with increasing mental fatigue. An important issue addressed in the present study is the effect of mental fatigue on the degree of synchronous activation in the brain. A problem was that due to the limited amount of information available on synchronization of brain activity in mentally fatigued subjects, it was difficult to formulate strong hypotheses and to identify electrodes of interest before we ran the experiment. Therefore, electrodes of interest for coherence and power analysis were identified using the data-driven visualization method introduced by ten Caat et al. (2008a, 2008b).

Concerning time on task effects, group mean coherence maps showed that the number of significant connections between brain areas increased from interval 1 to interval 6. With aging a similar phenomenon has been observed (Maurits et al., 2006). The observed more pronounced inter-hemispheric coherence in older subjects has been related to functional and adaptive compensation mechanisms used to prevent age-related performance deteriorations (Maurits et al., 2006). Although in older subjects increased neural activity was found to be related to performance improvements (Cabeza et al., 2002, 1997; Reuter-Lorenz et al., 2000; Rosen et al., 2002), we observed performance deteriorations in the present study. One can argue that due to compensation mechanisms more severe fatigue-related performance deteriorations are prevented. If this is true, it might be expected that motivation would be associated with an increase in synchronization of brain activity, since motivation is related to an increase in performance efficiency in the present study. This is contrary to what we observed; group mean coherence maps did not show an increase in significant connections from interval 6 to interval 7, that is, after the motivation manipulation. Therefore we do not have strong support for the compensation
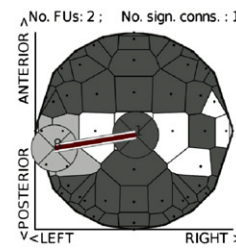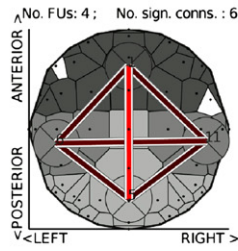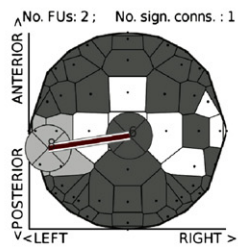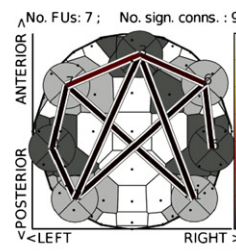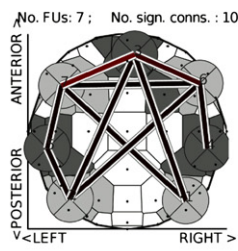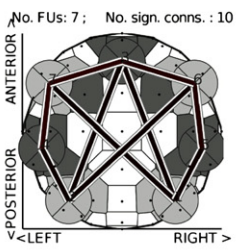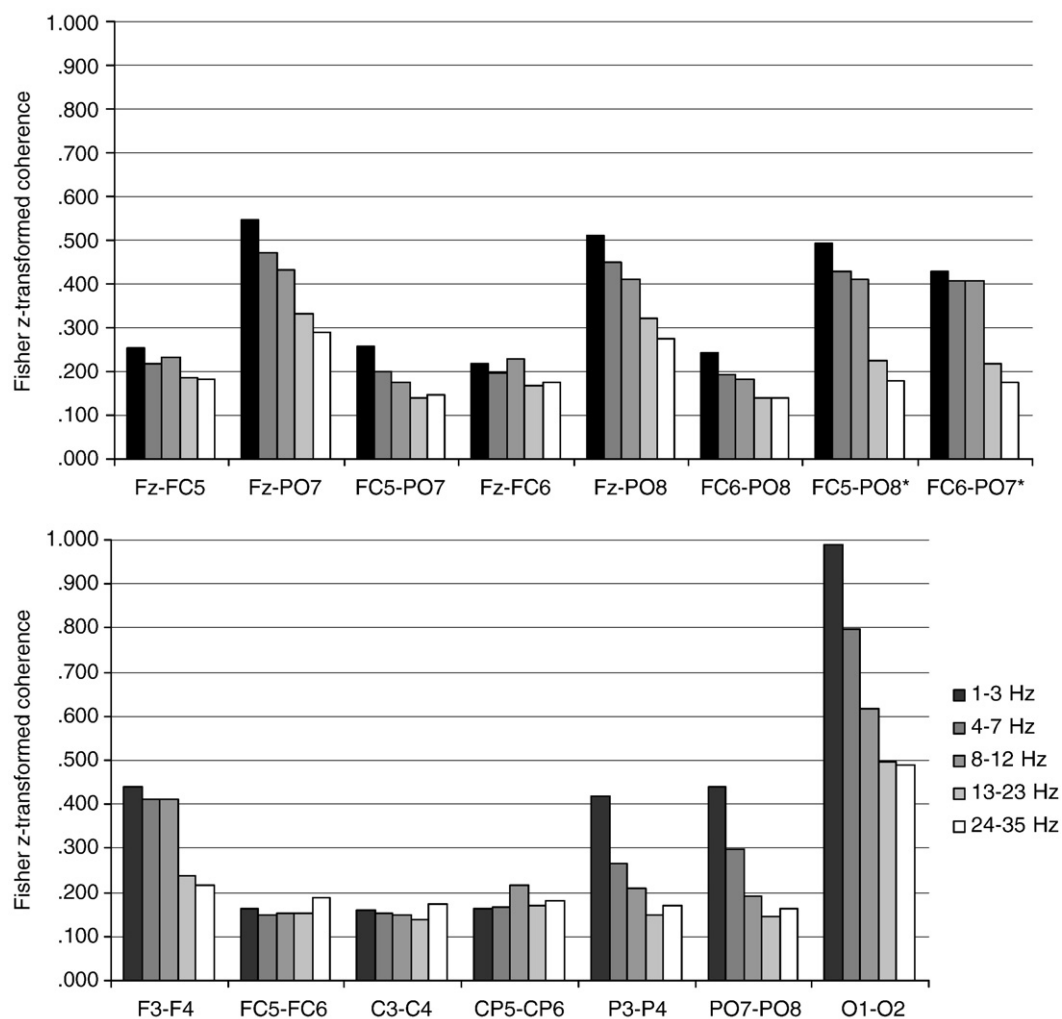
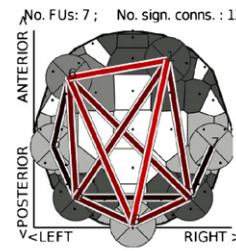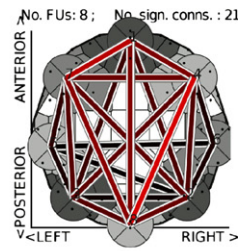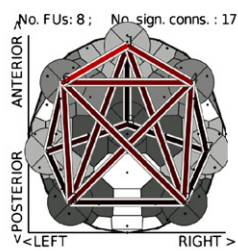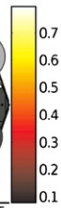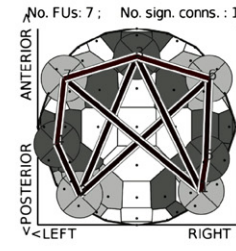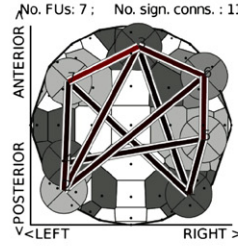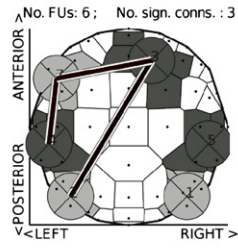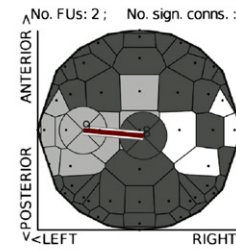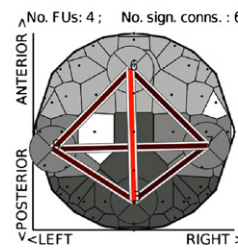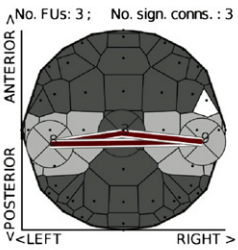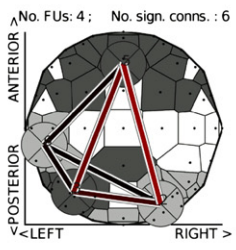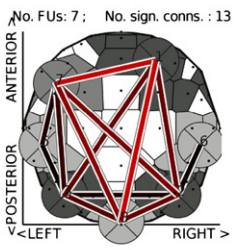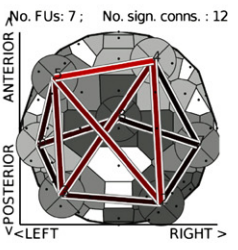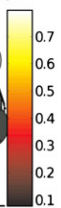Fig. 4 – Average Fisher z-transformed coherence between different electrode pairs in the different frequency bands. In the upper panel intra-hemispheric and inter-hemispheric (*) coherence is depicted. In the lower panel coherence between homologous pairs is depicted.

hypothesis to explain the increased coherence values. In line with the ageing literature, it can alternatively be argued that the increase in neural activity with increasing mental fatigue reflects non-functional changes in neural activity. These changes might be related to failures of inhibitory control, resulting in less neural specificity (Hedden and Gabrieli, 2004; Grady et al., 2006). Inhibition plays an important role in information processing, protecting the non-functional spreading of activation across neurons or neuronal networks (Nunez, 2000). Inhibition is, for example, essential for adequate task-switching performance, since task set reconfiguration not only concerns the activation of a task set required for the new task but also the inhibition of the previously activated task set (Arbuthnott and Frank, 2000). In case inappropriate

task sets remain active an increase in erroneous responses is expected, which is what we actually observed.

The conventional power and coherence analysis indicated that with time on task the amount of energy (power) in the EEG signal augmented, indicating an increase in the number of synchronously active neurons underlying an electrode with increasing mental fatigue. In addition, we observed that the synchronous activity of different neuronal populations became stronger, as reflected in higher coherence values. The effects of time on task on power and coherence in the present study were widespread, and not limited to specific brain regions or frequency bands. Moreover, the effects were independent of specific task manipulations. It is important to note that this increase in neuronal activity and the stronger

Fig. 3 – Group mean coherence maps for the switch (3 top rows) and repetition condition (3 bottom rows) for time on task intervals 1, 6 and 7 and frequency bands 1–3 Hz, 8–12 Hz and 24–35 Hz. FUs are visualized as sets of cells with identical grey values, with different grey values for adjacent FUs. White cells are part of FUs with a size smaller than 4. A line connects FUs if the inter-FU coherence exceeds the significance threshold, with its color depending on the value (see color bar, with minimum corresponding to the coherence threshold θ≈0.07; color bar is the same for all FU maps). Above each group mean coherence map the number of FUs and the number of connecting lines between FUs are displayed.
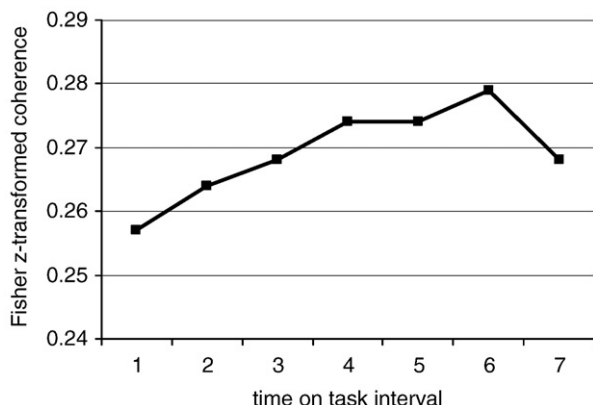
Fig. 5 – Average Fisher z-transformed coherence in the different 20-min time on task intervals superimposed for the different frequency bands and electrode pairs.

synchronization between neural networks did not result in more efficient performance; instead we observed a decline in performance efficiency with increasing mental fatigue. These results support the non-functional nature of changes in neural activity with increasing mental fatigue, supporting the "inhibition" hypothesis to explain the observed effects.

Changes in coherence might be due to stronger connections between underlying brain areas or to a common influence on both areas (Nunez, 2000). The non-specific and widespread effect on power and coherence measures of time on task favors an interpretation in terms of a common input or mechanism affecting a broad range of brain regions and cognitive functions involved in task switching. It has been argued previously that mental fatigue acts through an effect on the brain dopamine system (Boksem et al., 2006; Lorist et al., 2005; Lorist and Tops, 2003). Dopamine is known to
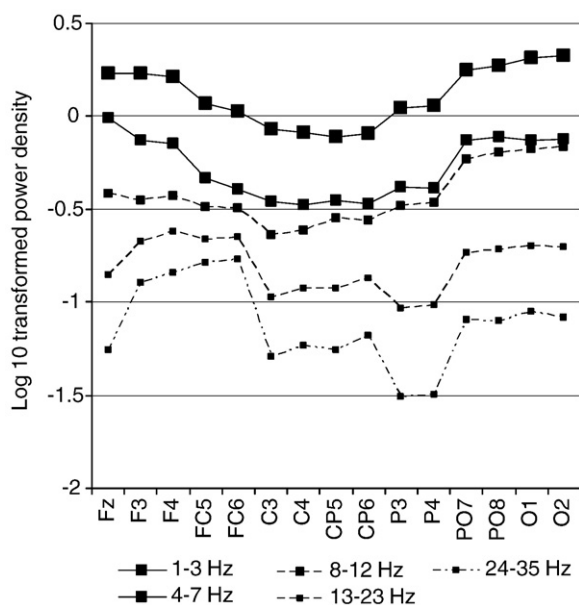

Fig. 6 – Average Log10-transformed power density for the different electrodes, superimposed for the different frequency bands and time on task intervals.
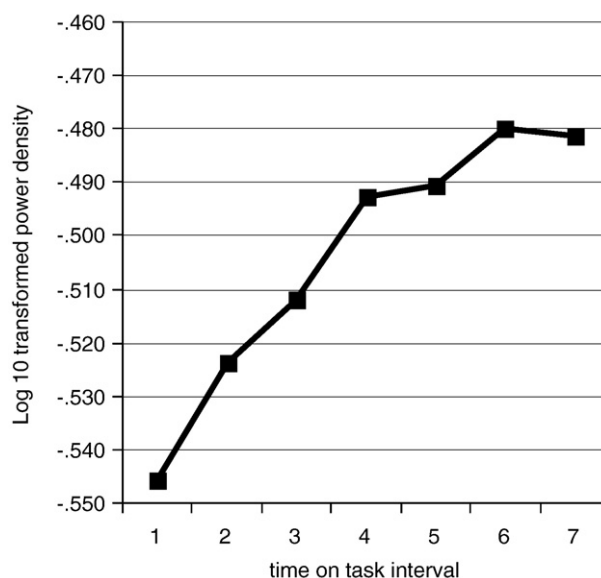

Fig. 7 – Average Log10-transformed power density for the different time on task intervals superimposed for the different frequency bands and electrodes.

operate as an important inhibitory neurotransmitter, influencing activity levels in a broad array of brain regions and cortico-cortical circuits and influencing a variety of higher order cognitive control processes (e.g., Lammel et al., 2008; Liss and Roeper, 2008; Nieoullon, 2002). In general, monoaminergic neurotransmitters suppress spontaneous neural activity, thereby improving the signal-to-noise ratio during information processing (Winterer and Weinberger, 2004). Decreased dopamine levels, as expected in mentally fatigued subjects, might result in elevated noise levels and a related increase in power, negatively affecting the quality of information processing. The increase in power due to increased noise levels might in turn be causal to the increased coherence values. The non-functional character of these changes in neural activity again favours the inhibition interpretation over a compensation interpretation of the results.

Another important characteristic of dopaminergic neurons is that they are sensitive to alterations in homeostatic balance and may inform the brain about changes in the internal environment, thereby providing the possibility for adaptive changes in behavior (Nieoullon, 2002; Schultz, 2007). Salamone et al. (1999) showed in animal studies that dopamine depletion was related to changes in processing strategies towards less demanding strategies. In case of mental fatigue changes in dopamine level might influence effort/reward evaluations, resulting in the choice of low-cost behavioral alternatives. Note that dopamine depletion does not suppress the ability to perform. However, behavior generally becomes less well adapted to environmental changes, resulting in a lack of flexibility, behavioral inhibition and shifting capacity (Tzschentke, 2001), resulting in performance difficulties as observed in fatigued subjects (e.g., Lorist, 2008; Lorist et al., 2000).

Effort/reward evaluations were manipulated in this study; subjects were motivated after 2 h of task performance by using

social comparison and monetary reward as motivating factors. This manipulation resulted in a small non-significant decrease in coherence which was accompanied by more efficient behavior. Power density did not change after the motivation manipulation. Improved performance suggests that mental fatigue can partly be undone by increasing the reward, which supports the involvement of the dopamine system in mental fatigue (Boksem et al., 2006; Lorist and Tops, 2003). However, it is important to note that although the current data fit within a dopamine framework, they are not specific enough to exclude other mechanisms contributing to the effects of mental fatigue.

In summary, the data demonstrated an effect of mental fatigue on performance and brain activity. Although the effects of task switching were dependent on electrode pair and frequency band, the changes in brain activity due to mental fatigue were broadly distributed and non-specific. A modulation of the dopamine system was proposed as a common mechanism underlying the observed the fatigue effects.

4. Experimental procedures

4.1. Subjects

Twenty-six healthy subjects (14 women) participated in this study, ranging in age from 18 to 28 years (M=21.4, SD=3.0). All subjects reported to have normal sleep patterns, not to work night shifts, and not to use prescription medication. They were right-handed and had normal or corrected to normal visual acuity. The experiment was performed in compliance with relevant laws and institutional guidelines, and was approved by the ethical committee of the University Medical Center Groningen. The subjects provided informed consent prior to the study.

4.2. Stimuli and apparatus

During task performance subjects were seated in a dimly lit, sound-attenuated room facing a color monitor at a distance of 70 cm. Stimulus presentation, as well as the registration of behavioral data, was carried out using E-prime software in conjunction with the Serial Response Box (Psychology Software Tools Inc., Pittsburgh USA).

After the presentation of the task instructions, a white square (4×4 cm), subdivided into four quadrants (2×2 cm), was displayed continuously at the center of a black screen. Stimuli were presented, one by one, in the center of one of these quadrants in a clockwise fashion, starting in the upper left square. The stimuli were randomly chosen from the characters: A, E, O, Y, U, G, K, M and R. The color of the characters was randomly chosen from the set red and blue. Stimuli were displayed in letter type Verdana in an uppercase font and were about 0.5 by 0.8 cm. Stimulus letters remained on the screen until subjects gave a response by pressing one of two response buttons, or until 2500 ms had elapsed. After a randomly chosen response–stimulus interval of 150, 600, 1500, or 2400 ms the next stimulus appeared on the screen.

The subjects were instructed to make a left- or right-hand response based on the color (red/blue) of the stimulus if the stimulus appeared in either of the two upper quadrants, and to respond based on letter identity (vowel/consonant) if the stimulus appeared in either one of the two lower quadrants. Thus, subjects were instructed to switch tasks every second trial. In the color task half of the subjects were instructed to respond to red stimuli with a left-hand button press and to blue stimuli with a right-hand response. In the identity task they were instructed to respond to a vowel with a left-hand button press and to respond to a consonant with a right-hand response. The other half of the subjects was instructed to respond vice versa on both the color task and the identity task.

4.3. Subjective measurements

The AD–ACL, consisting of 20 adjectives, was used to describe momentary activation states. Subjects indicated their activation level at that moment for each of the adjectives on a 4-point scale, ranging from 1 (definitely) to 4 (definitely not). Four clusters of adjectives stand for specific activation states: general activation, deactivation/sleep, high activation and general deactivation. Scores range between 5 and 20. In addition, subjects indicated on a simple rating scale, using verbal statements as anchors, the amount of aversion they experienced to continue task performance. Scores varied from 0 (not at all) to 10 (maximal).

4.4. EEG recording

EEG was recorded, using 59Sn electrodes attached to an electrocap (ElectroCap International), using electronically linked earlobes as reference. Electrodes were positioned according to the standard 10–10 system (American Electroencephalographic Society, 1994). The electro-oculogram (EOG) was recorded bipolarly from Sn electrodes placed at the outer canthi of both eyes and above and below the left eye. The Sn electrode for grounding the subject was placed on the sternum. Electrode impedance was kept below 5 kΩ. Signals were digitized at a rate of 500 Hz.

4.5. Procedure

Subjects were instructed to abstain from alcohol and caffeine-containing substances for at least 12 h before the experiment. It was explained to them that the study aimed at enhancing our understanding of brain mechanisms involved in task switching. They were unaware that the study also concerned effects of mental fatigue.

The experimental session started around 1.00 p.m. and lasted 3.5 to 4 h. Subjects filled out the AD–ACL and after electrode placement, they practiced the switch task for 10 min. Thereafter subjects performed the experimental task for 2 h and 20 min. They were instructed to react as fast and as accurately as possible. Every 20 min a question was asked about the level of aversion the subject felt at that moment against continuation of task performance. After 2 h of task performance an additional instruction, with a motivating content, informed subjects that the final part of the experiment followed in which they could earn a monetary reward if they reacted faster and more accurate than the other participants (social comparison). No rests were provided

during task performance. At the end of the session subjects completed the AD–ACL for the second time.

4.6. Data reduction and statistical analysis

Data was divided into seven time blocks of 20 min. We restricted our analysis to the 600 ms response–stimulus interval condition because in this interval subjects had time to prepare for the upcoming stimulus. Furthermore, task effects were found to be most clear in this RSI interval in our previous study that employed a similar switch paradigm (Lorist et al., 2000). In the 150 ms condition insufficient time to prepare adequately for task switches was available and preparation processes interfered with stimulus processing. In the 1500 ms RSI condition subjects might have difficulties maintaining the prepared state in the repetition condition, which might interfere with stimulus processing, as well.

4.6.1. Behavioral and subjective data

Trials containing premature (<150 ms) or late responses (>2200 ms) were excluded from further analysis (i.e., 1.2% of the trials). Mean reaction times (RTs) for correct trials, mean error rate (quantified as the percentage of incorrect responses within each condition), and the percentage of misses (i.e., when no response was made to a stimulus) were calculated and subjected to a GLM analysis for repeated measurements in SPSS. Within-subject factors were time on task (seven 20-min intervals) and stimulus type (switch, repetition). Analyses were performed using the $\tilde{\varepsilon}$*-adjustment procedure recommended by Quintana and Maxwell (1994). When the main analysis indicated a significant interaction between factors, additional analyses were performed, using Bonferroni adjustments. Statistical analysis of the subjective data was performed, using the same procedure, using time of measurement as within-subject variable.

4.6.2. Coherence data

In order to identify networks of synchronous brain activity and to identify electrodes of interest for coherence analysis the data-driven procedure developed by ten Caat et al. (2008a, 2008b) was used. Average referenced EEG was computed first, after which data was high-pass filtered at 0.16 Hz (48 dB/octave), notch filtered at 50 Hz (48 dB/octave) and re-sampled from 500 Hz to 512 Hz (BrainVision Analyzer 1.05, Brain Products GmbH, Munich, Germany). Subsequently, data was transferred to EEGLAB (Delorme and Makeig, 2004), running under MATLAB (The MathWorks Inc.). EEG data was segmented around stimuli that were followed by correct responses. Segments started 100 ms before stimulus onset and ended 880 ms post-stimulus. Coherence values between all pairs of electrodes were calculated, applying a procedure from Neurospec (www.neurospec.org). For each stimulus category (switch/repetition in block 1, 6 and 7) the first 40 correct trials were fed into the analysis. Coherence was determined within six frequency bands: 1–3 Hz (delta), 4–7 Hz (theta), 8–12 Hz (alpha), 13–23 Hz (beta), 24–35 Hz (gamma 1), and 36–70 Hz (gamma 2). An improved watershed based approach was used to identify functional units (FU), representing sets of neighboring electrodes, in which every two-element subset is significantly coherent. For the calculation of FUs the coherence threshold for $p < 0.05$ and $N = 40$ segments

was $\theta \approx 0.07$ (Halliday et al., 1995). Visualization of group mean coherence maps, containing the mean coherence for every electrode pair was carried out for repetition and switch trials in blocks 1, 6 and 7.

Based on visual inspection of the group mean coherence maps electrodes were selected for conventional coherence- and power analysis, using Brain Vision Analyzer (Brain Products GmbH, München, Germany). Trials with incorrect responses or trials containing movement artifacts or amplifier saturation artifacts were excluded from these analyses. First, data was low-pass filtered (45 Hz, 48 dB/octave) and re-sampled from 500 Hz to 256 Hz using spline interpolation. Thereafter one-second segments were created, starting 50 ms pre-stimulus and ending 950 ms post-stimulus. Ocular correction was performed using the Gratton and Coles method (Gratton et al., 1983). Subsequently, DC detrending was applied on individual segments using the first 100 ms as the starting point and the last 100 ms as the end point (Hennighausen et al., 1993), and segments were baseline corrected with respect to the 50 ms pre-stimulus interval.

Power density was computed using Fast Fourier Transformation (FFT), applying a 10% Hanning window. The one-second segments resulted in a frequency resolution of 1 Hz. Power density spectra were averaged over all segments for six frequency bands: 1–3 Hz (delta), 4–7 Hz (theta), 8–12 Hz (alpha), 13–23 Hz (beta), and 24–35 Hz (gamma), after normalization of power density values by a log10 transformation, using the R statistical software environment version 2.4.1 (R Development Core Team, 2006). For coherence analysis complex FFT data was used. Coherence between two EEG signals was calculated using the cross-spectrum normalized by the autospectra. Resulting coherence values were normalized using a Fisher z transformation and averaged over all segments for each frequency band mentioned above. For all coherence and power density spectra, values of zero were replaced by half the lowest level of quantification (1/2 LLOQ = 0.000025) before transformation. EEG analyses were based on an average of 60 trials per category (SD = 12).

Statistical analysis of the normalized power density- and coherence data was carried out using the GLM approach for repeated measures in SPSS. Within-subject factors were time on task (seven 20-min intervals), stimulus type (switch, repetition), frequency band (delta, theta, alpha, beta, and gamma) and electrode for power density data and electrode pair for coherence data. As for the behavior and subjective data analysis we used the $\tilde{\varepsilon}$*-adjustment procedure recommended by Quintana and Maxwell (1994). When the main analysis indicated a significant interaction ($p \leq .05$) between factors, follow-up analyses were performed, adjusting error rates according to Bonferroni. For clarity, uncorrected df values are presented.

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