NeuroImage 265 (2023) 119812

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

The neural correlates of mental fatigue and reward processing: A task-based fMRI study

Gergely Darnai[a,b,c,1], András Matuz[a,1], Husamalddin Ali Alhour[b], Gábor Perlaki[b,c,d], Gergely Orsi[c,d,e], Ákos Arató[b], Anna Szente[b], Eszter Áfra[a], Szilvia Anett Nagy[b,c,d,f], József Janszky[b,c,*], Árpád Csathó[a]

[a] Department of Behavioural Sciences, Medical School, University of Pécs, Pécs, Hungary
[b] Department of Neurology, Medical School, University of Pécs, Pécs, Hungary
[c] ELKH-PTE Clinical Neuroscience MR Research Group, Pécs, Hungary
[d] Pécs Diagnostic Centre, Pécs, Hungary
[e] Department of Neurosurgery, Medical School, University of Pécs, Pécs, Hungary
[f] Structural Neurobiology Research Group, Szentágothai Research Centre, University of Pécs, Pécs, Hungary

ARTICLE INFO

Keywords:
Psychomotor vigilance task
fMRI
Mental fatigue
Motivation
Neurocognitive framework
Insula
Middle frontal gyrus
Anterior cingulate cortex

ABSTRACT

Increasing time spent on the task (i.e., the time-on-task (ToT) effect) often results in mental fatigue. Typical effects of ToT are decreasing levels of task-related motivation and the deterioration of cognitive performance. However, a massive body of research indicates that the detrimental effects can be reversed by extrinsic motivators, for example, providing rewards to fatigued participants. Although several attempts have been made to identify brain areas involved in mental fatigue and related reward processing, the neural correlates are still less understood. In this study, we used the psychomotor vigilance task to induce mental fatigue and blood oxygen-level-dependent functional magnetic resonance imaging to investigate the neural correlates of the ToT effect and the reward effect (i.e., providing extra monetary reward after fatigue induction) in a healthy young sample. Our results were interpreted in a recently proposed neurocognitive framework. The activation of the right middle frontal gyrus, right insula and right anterior cingulate gyrus decreased as fatigue emerged and the cognitive performance dropped. However, after providing an extra reward, the cognitive performance, as well as activation of these areas, increased. Moreover, the activation levels of all of the mentioned areas were negatively associated with reaction times. Our results confirm that the middle frontal gyrus, insula and anterior cingulate cortex play crucial roles in cost-benefit evaluations, a potential background mechanism underlying fatigue, as suggested by the neurocognitive framework.

1. Introduction

Prolonged performance of cognitively demanding tasks often leads to mental fatigue (hereafter fatigue), a psychobiological state that is frequently accompanied by performance decline, increased distractibility and decreased motivation to continue the ongoing task (Csathó et al., 2012; Hopstaken et al., 2016; Pattyn et al., 2008). With increasing time spent on a demanding task, a higher level of subjective fatigue as well as a slowing in response times and an increase in the number of errors can be expected, i.e., time-on-task (ToT) effect (Boksem et al., 2005; Lorist et al., 2009; Matuz et al., 2019). The fatigue resulting from ToT has a profound negative impact on our everyday life, as it has been associated with a higher risk of traffic and occupational accidents (Nachreiner, 2001; Zeller et al., 2020). In addition, it has been shown that patients suffering from neurological conditions such as multiple sclerosis (MS; Sandry et al., 2014), stroke (Brosnan et al., 2022), as well as traumatic brain injury (Wylie and Flashman, 2017) are more sensitive to the ToT effect. This suggests, that in patients with the above-mentioned conditions, working on demanding tasks leads to a steeper performance decline and higher subjective fatigue, substantially contributing to their poor quality of life. Thus, understanding the neural underpinnings of fatigue would be beneficial for both clinical and healthy populations.

To date, only a few theoretical models have been proposed to explain the neural background of fatigue. A recently proposed neurocognitive framework posits that fatigue emerges in two distinct ways on the neu-

* Corresponding author at: Department of Neurology, Medical School, University of Pécs, Pécs, Hungary.
E-mail address: janszky.jozsef@pte.hu (J. Janszky).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.neuroimage.2022.119812.
Received 13 July 2022; Received in revised form 7 November 2022; Accepted 12 December 2022
Available online 13 December 2022.

ral level (Müller and Apps, 2019). First, as fatigue arises, a decrease in activity is observed in regions involved in task performance (*task-specific areas*). Second, the activation of *non-task-specific areas,* consisting of the insula, dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate cortex (ACC), simultaneously decreases. These regions monitor the potential task-related benefits and individuals' internal states, as well as regulating the extent of effort, taking the costs and benefits of task performance into account. Several lines of empirical evidence support the involvement of these areas in the emergence of fatigue. Lim and colleagues, for example, found decreased activity in the middle frontal gyrus (MFG, part of the DLPFC) and in the ACC after completion of a fatiguing sustained attention task (i.e. during post-task resting period) compared to the pre-task resting period (Lim et al., 2010). In addition, when investigating the ToT effect (i.e., by comparing the last quintile of the task with the first) they also found a significant activation decrease in the MFG. Similarly, Asplund and Chee (2013) found associations between ToT-induced fatigue and non-specific areas, including the MFG and anterior insula. In contrast, another study reported the opposite of the trend suggested by the framework; that is, they observed activation increases in the bilateral MFG as well as other frontal areas with increasing time spent on a fatiguing task (Gui et al., 2015). Thus, further investigations are still needed to clarify the role of non-specific areas in fatigue.

A large body of research indicated that the detrimental effects of ToT-induced fatigue can be reversed by increasing the task-related motivation levels. More specifically, providing rewards (e.g., monetary rewards) to the participants experiencing fatigue due to ToT was found to effectively improve task performance (Hopstaken et al., 2015a, 2016; Lorist et al., 2009). However, little is known about the neural effects of this motivational effect. To the best of our knowledge, only one study has been conducted that utilized fMRI to measure neural changes induced by motivational manipulation in healthy fatigued participants. In the fatigue session of the study of Gergelyfi et al. (2021), fatigue was induced by a Stroop task performed out-of-scanner and fMRI data were only recorded when the fatigued participants engaged in a working memory task under high and low monetary reward conditions. They revealed a significant reward effect in the ACC, insula, putamen, and nucleus accumbens. However, the authors did not find significant topographical overlap between reward-related brain activations and the fatigue map (i.e., the correlation map between task-induced brain activity and subjective fatigue scores), and therefore they have concluded that there is no direct link between fatigue and motivation. However, these findings are not in line with several previous studies claiming that motivation plays a crucial role in fatigue (Boksem and Tops, 2008; Dobryakova et al., 2018; Hopstaken et al., 2015b, 2015a). For example, Dobryakova et al. found that the stimulation of the fronto-striatal network through monetary reward leads to decreased fatigue in MS and healthy control. Thus, further fMRI studies are required to explore the neural background of the fatigue-motivation relationship.

In the current study, we applied the prolonged version of the psychomotor vigilance task (PVT) to induce fatigue and investigate the fatigue- and motivation-related neural mechanisms. The PVT was originally developed in 1985 as a measure of sustained attention (Dinges and Powell, 1985). Since then, it has been used for a large number of studies investigating fatigue (Angius et al., 2022; Lee et al., 2010; Smith et al., 2019). We decided to use this task for two reasons. First, the PVT is considered to be free of learning effects which may be confounding when investigating ToT-induced fatigue. Second, it has been shown to be a reliable task that is highly sensitive to fatigue-related changes (Lim et al., 2012; Sun et al., 2014). Based on the neurocognitive framework of Müller and Apps (Müller and Apps, 2019), we hypothesized decreasing activity with increasing ToT in both task-specific and non-specific areas. The second aim of the present study was to investigate the effects of reward on brain activity in fatigued participants. We manipulated the level of motivation by providing monetary rewards after inducing fatigue and expected to find activation increases in task-specific and non-specific areas.

2. Methods

2.1. Participants

Fifty-six healthy young individuals participated in this study. As depressive symptoms have been found to be associated with PVT performance (Lee et al., 2010; Plante et al., 2020), participants who reported moderate or severe depression on the Beck Depression Inventory (Beck et al., 1988) were excluded (six participants). PVT is highly sensitive to sleep propensity as well, so participants who slept for less than six hours before the day of the MRI measurements, were also excluded from analysis (five participants). To assess sleep propensity, participants were given a sleep diary that contained questions regarding the times of falling asleep and waking up for the three nights preceding the measurements. The diary was used to detect unusual sleep patterns (e.g., irregular sleep-wake rhythm) as well. Participants were also asked to abstain from alcohol-containing substances 24 h before the experiment. In addition, one participant was excluded from the study due to an excessive number (>25% of trials) of lapses (i.e. reaction times higher than 500 msec). Thus, the final sample included 44 participants (23 males). Mean age was 24.8 ± 3.1 years. A small fee (3,000 HUF) was paid to each participant as a compensation for their time and efforts. Subjects had right-hand dominance according to the Edinburgh Handedness Inventory (Oldfield, 1971). All subjects were informed about the study, and all provided written informed consent. The study was approved by the National Medical Research Council (registration number: 6843- 5/2021/EÜIG).

2.2. Stimuli

The PVT was administered in the MRI scanner. Using Presentation software (Neurobehavioral Systems, Inc., Berkeley, CA, USA), the visual stimuli were presented via MRI-compatible LCD screen with 1920 × 1200 resolution (BOLDscreen 24 LCD for fMRI, Cambridge Research Systems Ltd, Rochester, United Kingdom). Each trial started with a white fixation cross presented at the center of the screen. After an inter-stimulus-interval that varied between trials in a pseudorandom fashion and ranged between 2 and 20 s, as determined by Optseq2 (Dale, 1999), a blue circle was presented until 2 s elapsed or a response was made. Responses were collected via MRI-compatible response buttons (ResponseGrip, NordicNeuroLab AS, Bergen, Norway). Participants were instructed to press a button with the thumb of their dominant hand as soon as possible when the blue circle appeared (Fig. 1).

2.3. Experimental design and procedures

Before the task, participants were given five practice trials and reported their levels of subjective fatigue on a Visual Analogue Scale (VAS) by moving a slider from 0 to 10, with increments of 1. The extreme ends were labelled with "No fatigue at all" and "Very severe fatigue".

ToT phase (fatigue induction): the ToT phase of the experiment was intended to induce mental fatigue and consisted of three 5 min blocks of trials (15 min in total). The sequence of inter-stimulus intervals across the trials of these experimental blocks was identical within and between the participants; however, they were not informed about this invariance and none of them recognized any repeating patterns according to self-report. Prior to testing, the trial sequence was inspected by an experimental psychologist (AM) to ensure the appropriate proportion and order of trials with short and long inter-stimulus-intervals that are essential elements of the PVT. At the end of the ToT phase, subjective fatigue was registered again.

Motivational phase (motivation manipulation): after the ToT phase, participants were informed that they could get an extra fee (fix 1,000

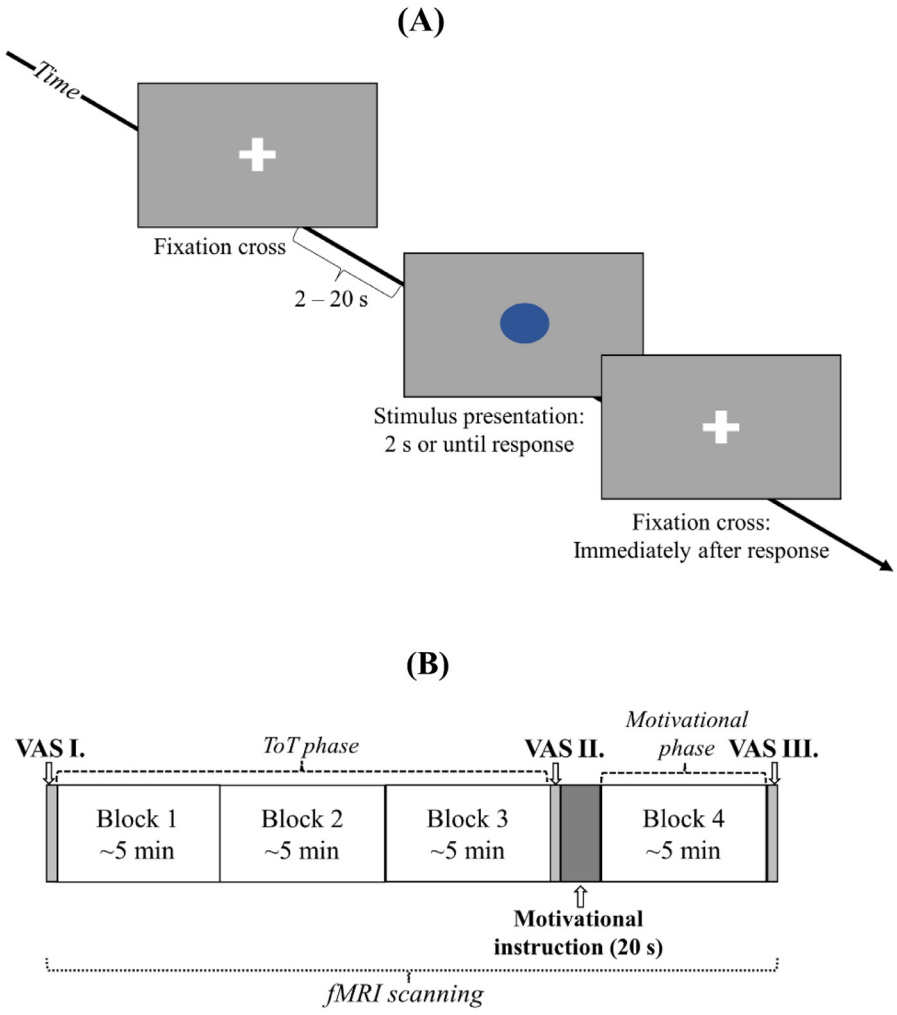

Fig. 1. Schematized sequence of a trial (A) and the schematized procedure of the experiment. VAS: visual analogue scale used to assess the level of subjective fatigue; ToT phase: Time-on-Task phase.

HUF) if they performed better in the subsequent block of trials. This fourth experimental block also lasted for 5 min and all task parameters were identical to that of the 5 min blocks in the ToT phase. After the motivational phase, participants again reported their actual level of subjective fatigue on a VAS.

2.4. MRI data acquisition

Participants were imaged using the same 3T MRI scanner (MAGNETOM Prisma^{fit}, Siemens Healthcare, Erlangen, Germany) with a 20-channel Head/Neck coil.

Functional images for the PVT task were obtained using a 2D single-shot gradient-echo echo planar imaging (EPI) sequence with the following parameters: repetition time (TR)/Echo time (TE) = 2000/30 ms; flip angle (FA) = 76°; field of view (FOV) = 210 × 210 mm^2; 70 × 70 matrix; and 36 axial slices with a thickness of 3 mm, 2040 Hz/pixel receiver bandwidth and interleaved slice order.

After the fMRI measurement, field mapping sequences (TR/TE1/TE2 = 400/4.92/7.38 ms;

FA = 60°; 36 axial slices; slice thickness = 3mm; distance factor = 25%; FOV = 210 × 210 mm^2; 70 × 70 matrix; receiver bandwidth = 290 Hz/pixel) with the same orientation and adjustment parameters as the fMRI scan were used for distortion correction.

Anatomical images were acquired using a T1-weighted 3D MPRAGE sequence (TR/TE/TI = 2530/3.41/1100 ms; FA = 7°; FOV = 256 × 256 mm^2; 256 × 256 matrix; slice thickness = 1 mm; 176 sagittal slices, 200 Hz/pixel receiver bandwidth).

2.5. Functional MRI data processing and analysis

Pre-processing and statistical analyses were performed using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library, http://www.fmrib.ox.ac.uk/fsl). Pre-processing included MCFLIRT motion correction, slice timing correction, brain extraction, spatial smoothing with 5 mm full width at half maximum, EPI distortion correction with FSL FUGUE and a high-pass temporal filter of 90 s. The single-session data sets were registered into the MNI152 standard space using a two-step process. First, the functional (EPI) image of each participant was registered to that subject's T1 structural scan using 6 degrees-of-freedom Boundary-Based Registration (BBR) which includes simultaneous distortion correction in combination with the FUGUE tool. Then, each participant's T1 image was registered to the 2 mm MNI152 standard space T1 image using a 12 degrees-of-freedom linear fit followed by nonlinear registration (FNIRT, warp resolution = 8 mm). Next, for each participant, these two registrations were combined and applied to the first-level statistical maps to take them into standard space. Whole brain general linear model (GLM) time-series statistical analyses of individual data sets were carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction.

The fMRI time series were split into four blocks (B1, B2, B3 and B4, which correspond to the 5 min experimental blocks in the ToT and motivational phases, respectively) for each individual subject, each containing 150 scans. The first-level analysis generated contrast images for task regressors for each participant. In the next step mixed-effects analyses were carried out using FLAME (FMRIB's Local Analysis of Mixed

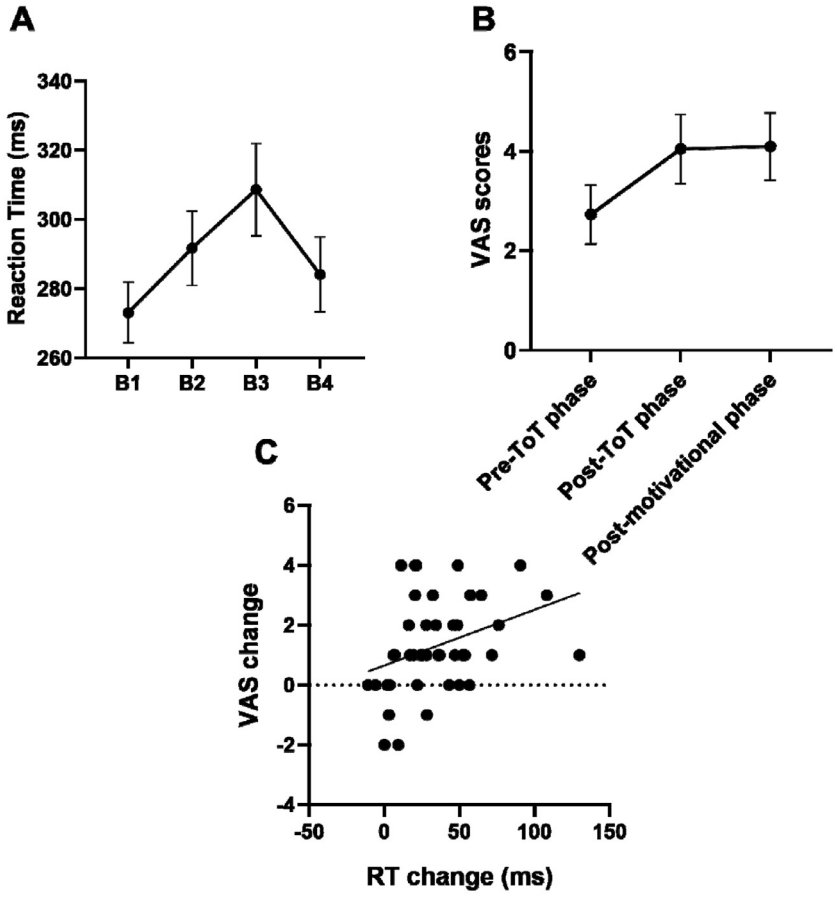

Fig. 2. (A) Mean reaction time (RT) for each experimental block. Error bars indicate ± 1 standard deviation. (B) Mean subjective fatigue scores based on the visual analogue scale (VAS) reported before and after the ToT phase and after the reward block. Error bars indicate ± 1 standard deviation. (C) Positive correlation between changes in subjective fatigue (VAS) from the pre-, to the post-ToT phase and mean RT change between the first and third blocks (Spearman's rho = 0.384, p = 0.01).

Effects, stage 1) in the following order:

1. Within-group activation differences between B1, B2, and B3 (voxel-wise F-test);
2. Within-group activation differences between B1 and B3 (B1 minus B3 and B3 minus B1);
3. Within-group activation differences between B3 and B4 (B3 minus B4 and B4 minus B3).

Since according to previous studies our primary interest is the effect of ToT (B1 minus B3) and motivation (B4 minus B3), only these contrasts will be included in the Results section (the remaining contrasts are included as supplementary materials). Statistical maps were considered to be significant at $Z > 2.3$ and a family-wise error corrected cluster significance threshold of $p = 0.05$ (Worsley et al., 2002).

Region of interest (ROI) analysis was also conducted to discover whether BOLD signal changes in the ROIs were correlated with RTs and subjective fatigue scores. Our analytical approach employs the *a priori* use of anatomically defined ROIs, including the left and right MFG, left and right insular cortex and bilateral ACC (i.e. the non-specific brain areas according to (Müller and Apps, 2019)) based on the Harvard-Oxford Structural Atlas, thresholded at 25%. For each ROI mean parameter estimates were extracted for each experimental block with FSL's Featquery tool. These values reflect the magnitude of task-evoked activity in experimental blocks (B1, B2, B3 and B4).

2.6. Statistical analysis of the behavioral data

Analysis of behavioral data was performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). To test the ToT effect, behavioral performance data were subjected to repeated measures ANOVA with Block (i.e., the three experimental blocks, B1, B2 and B3) as a within-subject factor. Subjective fatigue ratings obtained before and after the ToT period were analyzed by Wilcoxon signed rank tests. Finally, to investigate the effects of motivational instruction on the performance measures and subjective ratings, paired t-tests and Wilcoxon signed rank tests were conducted, respectively.

To examine the relationship between performance and subjective score changes, Spearman's rank correlation was performed. Performance change was defined as the mean difference in RT between B3 vs. B1, while change in the subjective scores were calculated as the difference between VAS II and VAS I (i.e. after B3 and before B1, respectively).

The associations between behavioral and subjective scores (i.e., RTs and VAS scores) with neural activation levels in the ROIs were also tested with Spearman's rank correlation for each block separately. B2-related subjective fatigue scores were not included in the statistical analysis, because the subjective measurements of fatigue were administered only before B1, after B3 and after B4. In addition, for the correlational analyses, the Benjamini-Hochberg procedure was applied to limit the Type I. error rates (Benjamini and Hochberg, 1995). The false discovery rate was set at 5%.

3. Results

3.1. Behavioral performance and subjective fatigue

Fig. 2 depicts the results of behavioral performance and subjective fatigue. The analysis of mean RT yielded a significant Block main effect ($F(2,86) = 55.433$, $p < 0.001$, $\eta_p^2 = 0.569$). Bonferroni-corrected post-hoc comparisons revealed that the mean RT was significantly lower in the first compared to the last two blocks of trials and it was significantly lower in the second than in the third block ($p < 0.001$ in all comparisons). The analysis of subjective fatigue ratings revealed that mental fatigue was significantly higher after the ToT phase than before

Table 1
Brain areas showing significantly decreased activation due to the time-on-task effect (B1 minus B3), significantly increased activation due to the reward-effect (B4 minus B3).

Cluster	Area	Voxels	Max Z-scores	MNI coordinates		
				X	Y	Z
B1 minus B3						
1	Right angular gyrus	5350	5.12	50	-38	46
	Right supramarginal gyrus					
	Right middle temporal gyrus					
	Right postcentral gyrus					
	Right cerebellum					
2	Left supramarginal gyrus	2042	4.78	-56	-22	34
	Left postcentral gyrus					
	Left angular gyrus					
3	Left lateral occipital cortex	1916	4.49	-48	-68	0
	Left middle temporal gyrus					
	Left inferior temporal gyrus					
4	Right inferior frontal gyrus	1686	4.65	32	20	-6
	Right middle frontal gyrus					
	Right frontal orbital cortex					
	Right precentral gyrus					
	Right insular cortex					
5	Left precentral gyrus	937	4.73	-58	4	30
	Left inferior frontal gyrus					
	Left insular cortex					
	Left middle frontal gyrus					
6	Right frontal pole	590	4.12	32	50	-10
7	Right paracingulate gyrus	337	4.06	8	32	34
	Cingulate gyrus, anterior division					
	Right superior frontal gyrus					
8	Left insular cortex	329	4.41	-34	20	-2
	Left frontal orbital cortex					
9	Right frontal pole	321	3.52	48	44	24
	Right middle frontal gyrus					
10	Bilateral caudate	307	3.42	10	20	-8
	Bilateral nucleus accumbens					
	Right thalamus					
B4 minus B3						
1	Right frontal pole	1731	4.02	46	42	22
	Right inferior frontal gyrus					
	Right precentral gyrus					
2	Right supramarginal gyrus	865	3.54	58	-36	36
	Right angular gyrus					
3	Left frontal pole	723	4.21	-44	36	14
	Left middle frontal gyrus					
	Left inferior frontal gyrus					
4	Right superior frontal gyrus	492	3.6	4	28	48
	Right paracingulate gyrus					
	Cingulate gyrus, anterior division					
5	Left insular cortex	342	3.51	-50	4	20
	Left middle frontal gyrus					
	Left inferior frontal gyrus					
	Left precentral gyrus					

(Z = -4.323, $p < 0.001$) (Fig. 2B). In addition, an increase in subjective fatigue (VAS change) was positively associated with elevated RT (RT change) from the first to the third block of trials (rho = 0.384, p = 0.01) (Fig. 2C). To summarize, the analysis of both the behavioral and self-reported measures indicated elevated levels of mental fatigue induced by PVT performance.

In the motivational phase (B4), we found significantly lower RTs compared to the third block (B3) of the ToT phase ($t(43) = 4.830$, $p < 0.001$) suggesting that the expectation of an extra monetary reward positively affected PVT performance. The motivational manipulation, however, had no significant effect on the subjective ratings of fatigue (Z = -0.536, p = 0.59).

3.2. Neuroimaging results

3.2.1. Changes in PVT task activation

When comparing B1 and B3 (ToT effect), significantly decreased activation was discovered in B3 bilaterally in the cerebellum, angular gyrus, supramarginal gyrus, middle temporal gyrus, postcentral gyrus, inferior frontal gyrus, MFG, frontal orbital cortex, precentral gyrus, insular cortex, caudate and nucleus accumbens, along with left lateral occipital cortex, left inferior temporal gyrus, right frontal pole, right paracingulate gyrus, right superior frontal gyrus, right thalamus and ACC (Table 1, Fig. 3A). A motivation effect (B4 vs. B3) analysis also resulted in activation differences. We found a significant activation increase in the bilateral frontal pole, inferior frontal gyrus, precentral gyrus, as well as in right supramarginal, angular, superior frontal and paracingulate gyrus, left MFG and insular cortex and ACC (Table 1, Fig. 3B). The mean activation maps in B1, B2 and B3, the results of the F test and the contrasts that were out of interest (B3 minus B1 and B3 minus B4) are presented in the Supplementary file.

3.2.2. ROI analysis

Predefined ROIs were further investigated whether subjective fatigue scores and task performance (RT) were associated with activation levels in the experimental blocks (Fig. 4). The bilateral ACC activation showed negative correlation with RTs in the B1 (rho = -0.518, $p < 0.001$), B2 (rho = -0.491, $p < 0.001$) and B3 (rho = -0.342, p = 0.023); the left

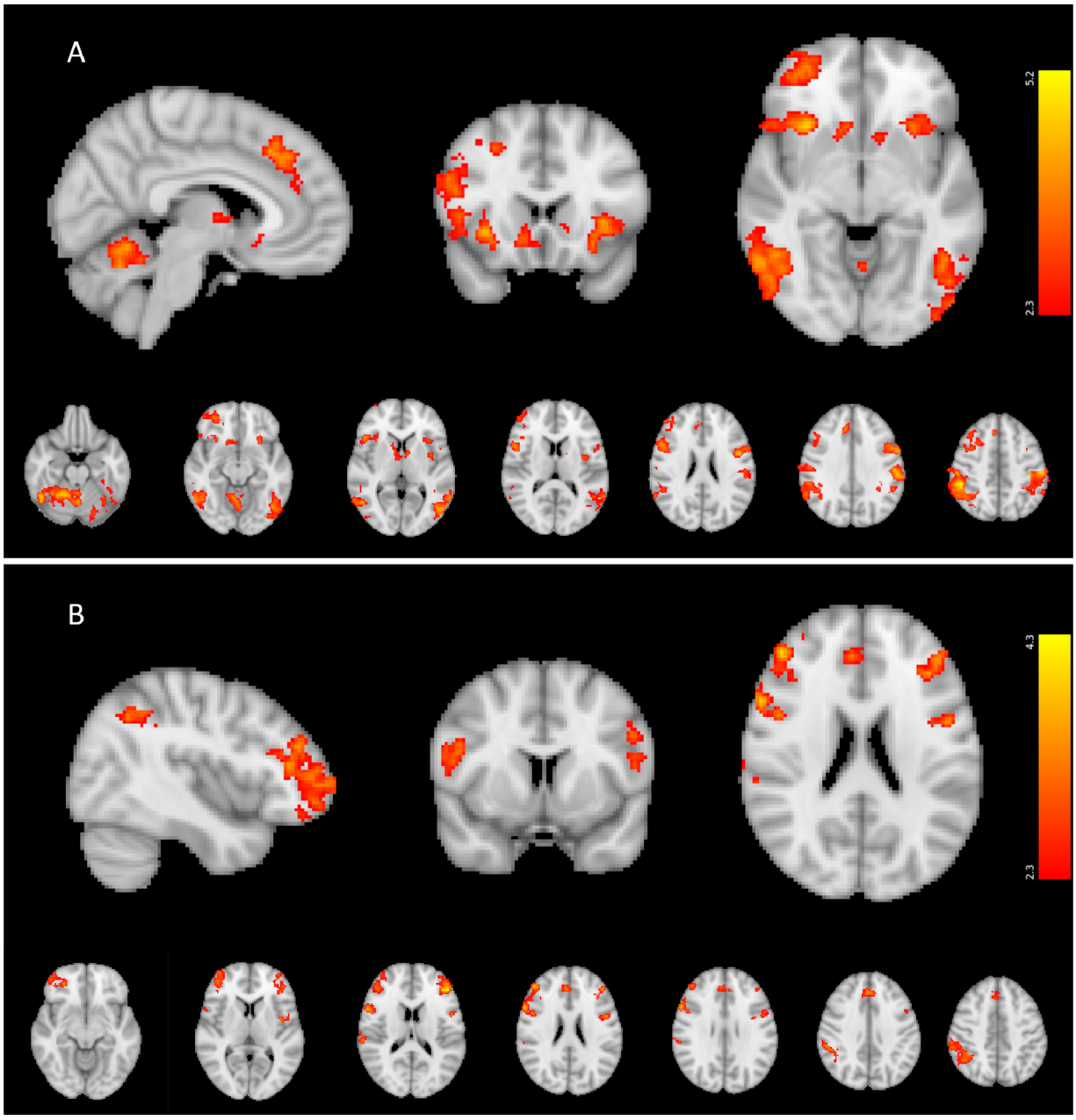

Fig. 3. (A) Group-level differences in BOLD signal changes between the first and third blocks (time-on-task effect) of the psychomotor vigilance task. (B) Group-level differences in BOLD signal changes between the fourth and third blocks (reward effect) of the psychomotor vigilance task. Images were thresholded using clusters determined by $Z > 2.3$ and a corrected cluster significance threshold of $p = 0.05$. Red-yellow color bars depict Z scores Axial slices are shown in radiological convention.

insula was also negatively correlated with RTs in the B1 (rho = -0.419, p = 0.005), B2 (rho = -0.540, p < 0.001), B3 (rho = -0.368, p = 0.014) and B4 (rho = -0.370, p = 0.013), while the left MFG activation was not related to performance or subjective feeling of fatigue.

On the right hemisphere, insular activation was negatively associated with RTs in the B1 (rho = -0.500, p < 0.001), B2 (rho = -0.475, p = 0.001), B3 (rho = -0.370, p = 0.013) and B4 (rho = -0.392, p=0.008), while the MFG showed negative correlations with RTs in the B1 (rho = -0.357, p = 0.017), B2 (rho = -0.416, p = 0.005) B3 (rho = -0.325, p = 0.031) and B4 (rho = -0.403, p = 0.007). In all cases, higher activation was associated with better performance. All of the significant correlations survived the Benjamini-Hochberg procedure. A subjective feeling of fatigue was not related to the activation levels of our ROIs.

4. Discussion

In the present study, we had two main goals. First, we used a prolonged sustained attention task (i.e., psychomotor vigilance task) to induce fatigue and investigated how neural activity changed as a function of ToT. Second, after the fatigue-induction, we provided an extra monetary reward to motivate participants for better performance and explored the reward-related changes, while participants reengaged in the task. We interpret our results in the neurocognitive framework proposed by Müller and Apps (2019).

Similarly to previous findings (Lim et al., 2012; Massar et al., 2018), fatigue was successfully induced by the PVT task as reflected in impaired task performance (i.e. slower RTs) as a function of ToT and increased levels of subjective fatigue. In line with our hypothesis, we found

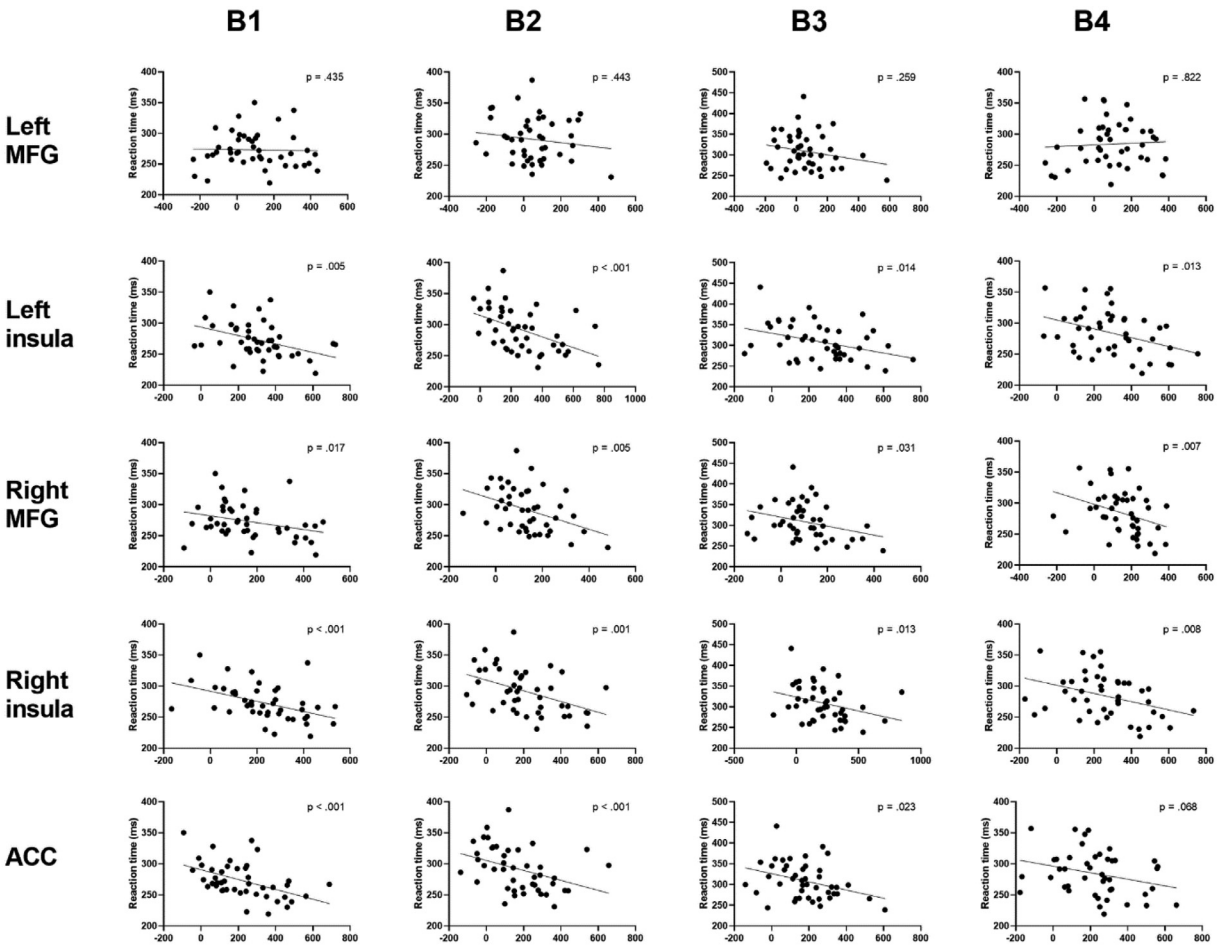

Fig. 4. Correlation analyses (Spearman) of the reaction times and activation levels of the left and right middle frontal gyrus (MFG), left and right insula and bilateral anterior cingulate cortex (ACC). B1, B2, B3, and B4 correspond to the experimental blocks of the task. Uncorrected p values are presented because all significant p values (<0.05) survived Benjamini-Hochberg correction.

that the activity of both task-specific and non-specific areas decreased as fatigue emerged. These findings are consistent with earlier works (Asplund and Chee, 2013; Breckel et al., 2011; Lim et al., 2010; but see Gui et al. 2015) and are in line with the neurocognitive framework of motivational fatigue (Müller and Apps, 2019). This model suggests that with increasing fatigue, the activity of areas linked to task-execution (i.e., task specific areas) decreases, leading to poorer performance. Accordingly, we observed decreasing activities over time in various cortical areas (including the inferior and superior frontal gyri, precentral gyrus and the occipital areas), as well as in the cerebellum, which are thought to be involved in processes required for the execution of the PVT task. More specifically, these areas are known to be involved in cognitive functions, such as sustained attention, motor control and visual processing (Cisek and Kalaska, 2010; Langner and Eickhoff, 2013). The slowing trend of reaction times could thus be explained by the reduced activation of areas related to these cognitive functions. The motivational fatigue model (Müller and Apps, 2019) claims that the processes mentioned above are associated with changes in the non-specific areas. More specifically, the model assumes that the activations of task specific regions depend on the input coming from the non-specific areas such as the MFG, ACC and insula. This input is defined as the result of certain evaluation processes controlled by these three areas. More precisely, the costs and benefits of performing the task are constantly being weighted and the final output of this evaluation process will determine whether to *exert more effort to perform well on the task*. Our results showed reduced activity in non-specific brain areas, which indicates that the costs of prolonged task performance outweighed its benefits. As a result, activity in task-specific areas also decreased, leading to deteriorated task performance. Our assumption was supported by the ROI analysis: positive associations were found between PVT performance and the activation levels of the non-specific areas suggesting their importance in the regulation of effort exertion. Our results related to the MFG is in line with the recently released neuro-metabolic model of fatigue (Blain et al., 2016; Wiehler et al., 2022). This theory claims that when performing a demanding task, cognitive control downregulation leads to lateral prefrontal cortex (lPFC) activation decrease, that results in lPFC glutamate level change. The meta-regulation adjusts this increased metabolic costs in the lPFC and the intensity of control exertion depending on task-related benefits (e.g. reward that is given when participant performs well). Increasing the impact of metabolic costs could naturally counteract the impact of expected benefits and decrease the intensity of control exertion (thus leads to decreased performance). The role of the ACC in maintaining cognitive effort is still under debate, although several frameworks have been arisen (for review see Vassena et al. 2017). For instance, the *expected value of control* framework claims that similarly to the lPFC, the ACC computes the value of exerting cognitive control but also plays crucial role in integrating different signals, including reward, costs, and choice difficulty (Shenhav et al., 2013). A more recent model specified a role for the ACC in *synchronizing brain oscillations* across various brain areas (Verguts, 2017). This framework also suggests that ACC exerts top-down control with synchronizing task-related brain areas, promoting more efficient cortical communication. This assumption is supported by the relationship between ACC activation and task performance in our study.

Although task performance as well as the activity of many brain regions decreased as fatigue emerged, we found the opposite pattern when an incentive (i.e., monetary reward) increased the perceived benefits of task performance. That is, after the motivational manipulation, the activity in the MFG, ACC, insular cortex, frontal pole as well as in right IFG, SMG and angular gyrus increased, while task performance improved, which is consistent with previous studies (Herlambang et al., 2021; Hopstaken et al., 2015b, 2015a). The effect of reward on brain activity is also in line with the work of Esterman et al. (2017). They found increased activations in the bilateral MFG, right IFG and SMG when monetary rewards were provided for the execution of a sustained attention task compared to unrewarded task blocks. In addition, we found an activation increase in the bilateral frontal pole. This area has also been suggested to play a role in the integration of costs and the risk of exerting effort, a process that is thought to determine reward-related changes in fatigued individuals (Boksem et al., 2005). These areas have been shown to be related to spatial attention (Chambers et al., 2004; Silk et al., 2010), attention control (Hampshire et al., 2010) and visuomotor processes (Bocca et al., 2015) and thus, the increased activities suggest that the improved cognitive performance in the motivation block was probably due to the better functioning of these cognitive mechanisms.

Importantly, our findings regarding the reward-related changes in neural activity can also be interpreted in the context of a motivational fatigue framework (Müller and Apps, 2019). Based on this model, the increasing activity evoked by the reward in the non-specific areas suggests that the reward affected the cost-benefit evaluation processes. More specifically, the findings imply that the perceived benefits probably outweighed the costs of task performance leading to a greater input from the MFG, insula and ACC to the task-specific areas, which is also supported by the observed activation increases in task-specific areas. On the other hand, our results are not in accordance with those of Gergelyfi et al. (2021), who found no anatomical overlap between fatigue and the reward-related changes in brain activity. This discrepancy might result from methodological differences, for example, not testing the ToT effect but comparing a fatigue session to a control session or using high and low reward conditions, while we did not manipulate the level of reward. Another crucial difference is that while Gergelyfi et al. defined the topological fatigue map as the correlation map between subjective fatigue scores and task-induced brain activity, we did not consider this kind of analytic approach because the objective and subjective markers of fatigue often show no correlation (Ackerman and Kanfer, 2009; Hockey, 2013, 1997; Matuz et al., 2019; Mehta et al., 2017). It is important to note that another discrepancy between Gergelyfi et al. and our results arises. They found motivation-related activation differences in striatum, including the putamen and nucleus accumbens. The lack of these activation changes in our results might be also the result of methodological differences between the two studies, including the different fatigue- (demanding cognitive task outside the scanner versus ToT inside the scanner) and reward-inducing (high and low reward conditions versus one-time monetary reward) strategies. These methodological differences might result in inconsistent findings regarding brain areas associated with fatigue as well. One brain area that arises again is the striatum. We found significant activation decrease in the dorsal (caudatus) and ventral striatum (nucleus accumbens). Although several other studies also showed that activation in striatum co-vary with the amount of cognitive effort required (Müller and Apps, 2019; Schmidt et al., 2012), some fMRI studies did not confirm the involvement of these subcortical structures in fatigue (Asplund and Chee, 2013; Lim et al., 2010; Paus et al., 1997). These controversial findings suggest that it is highly needed to investigate the methodology-based differences in brain activations. It might shed some light on the involvement of striatum but also on the role of other brain areas in mental fatigue. However, unfortunately our result cannot answer these questions and discrepancies.

Beside the task-specific and non-specific areas some other brain regions showed ToT-related activation decrease, including the postcentral gyrus, inferior temporal gyrus (ITG) and middle temporal gyrus (MTG). Previous studies revealed that postcentral gyrus is involved in motor control (Behroozmand et al., 2015), while ITG (Rodrigo et al., 2014) and MTG (Chehadi et al., 2018) are associated with cognitive control processes. Since it is understood that both motor and cognitive control processes are needed to perform well on the PVT (Dorrian et al., 2019), it can be assumed, that the activation decrease within these areas might also play role in the performance decline between B1 and B3. Although future studies are needed to clarify the exact role of these brain areas in fatigue: e.g. do they play more important role when higher motor (e.g., Go/No-go task) and cognitive control (e.g., Stroop task) are required.

Finally, the question arises as to how our findings reflect conditions where these neural systems are affected, including attention deficit hyperactivity disorder (ADHD). Previous studies showed increased ToT effect (Bioulac et al., 2012; George et al., 2005; Tucha et al., 2017) and altered motivation processing (Cubillo et al., 2012) in ADHD. Although previous fMRI studies revealed decreased activation in non-specific brain regions including the dlPFC (Christakou et al., 2012) and insula (Hwang et al., 2019), it is clear that the involvement of the basal ganglia structures (Plichta and Scheres, 2014), and the orbitofrontal cortex (Yang et al., 2019) are much more relevant in fatigue and motivation dysfunctions in ADHD. These results suggest that cost-benefit evaluation deficits are not the key factors, other neural features might be in charge, like the delay of brain function maturation or dysfunctions in fronto-limbic emotion-motivation circuits (Cubillo et al., 2012). Although further developmental neuroimage studies are needed to verify these speculations.

The most remarkable limitation is the correlational nature of the study. Therefore, we cannot clearly clarify the causality of the detected functional brain alterations. In addition, it would be important to validate our results on clinical cohorts. It is possible that fatigue and reward-related brain changes differ between clinical subgroups suffering from chronic mental fatigue. Thirdly, whether the brain mechanisms behind fatigue and reward are specific for PVT or generic for different types of tasks is still unknown, as similarly designed studies are sparse. Validation on other cognitive tasks (e.g. Stroop, go/no-go, n-back) are needed. Our final limitation is that, in the lack of resting-state data, we do not know whether our observations might be expanded to resting-state brain functions. Future attempts are necessary by using pre-task resting-state fMRI.

5. Conclusion

This study tested the effects of time spent on a fatiguing sustained attention task as well as increasing rewards on neural activity measured by fMRI. We found that the activation of areas linked to task performance and areas linked to motivational and evaluation processes decreased as fatigue emerged. After providing monetary rewards, however, the declining trend of task performance changed and increased back, while activation of these brain areas also increased. Our findings support the notion that beside brain areas involved in attention, motor control or visual processing, other regions such as the insula, anterior cingulate cortex and middle frontal gyrus in particular play important roles in the neural mechanisms underlying mental fatigue.

Funding

This work was supported by the Hungarian Brain Research Program [2017-1.2.1-NKP–2017-00002] government-based fund. Our research was partly financed by the Higher Education Institutional Excellence Program of the Ministry of Human Capacities in Hungary, within the framework of the 5th thematic program of the University of Pécs, Hungary [20765/3/2018/FEKUSTRAT] and by the National Research, Development and Innovation Fund of Hungary [TKP2021-EGA-16] and [TKP2021-EGA-13]. SAN was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

Data availability statement

The results of the fMRI group analyses (in NIFTI format) are available at the Open Science Framework (https://osf.io/hcx97/).

Declaration of Competing Interest

The authors declare no competing financial interests.

Credit authorship contribution statement

Gergely Darnai: Conceptualization, Formal analysis, Writing – original draft. **András Matuz:** Conceptualization, Formal analysis, Writing – original draft. **Husamalddin Ali Alhour:** Investigation, Validation. **Gábor Perlaki:** Software, Writing – review & editing. **Gergely Orsi:** Methodology, Writing – review & editing. **Ákos Arató:** Conceptualization, Data curation. **Anna Szente:** Investigation, Data curation. **Eszter Áfra:** Investigation, Data curation. **Szilvia Anett Nagy:** Writing – review & editing. **József Janszky:** Conceptualization, Supervision. **Árpád Csathó:** Writing – review & editing, Supervision.

Acknowledgement

The Authors acknowledge the contribution of the participants and the kind support of the employees of the Pécs Diagnostic Centre.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2022.119812.

References

Ackerman, P.L., Kanfer, R., 2009. Test length and cognitive fatigue: an empirical examination of effects on performance and test-taker reactions. J. Exp. Psychol. Appl. 15, 163–181. doi:10.1037/a0015719.

Angius, L., Merlini, M., Hopker, J., Bianchi, M., Fois, F., Piras, F., Cugia, P., Russell, J., Marcora, S.M., 2022. Physical and mental fatigue reduce psychomotor vigilance in professional football players. Int. J. Sports Physiol. Perform. 17, 1–8. doi:10.1123/ijspp.2021-0387.

Asplund, C.L., Chee, M.W.L., 2013. Time-on-task and sleep deprivation effects are evidenced in overlapping brain areas. Neuroimage 82, 326–335. doi:10.1016/j.neuroimage.2013.05.119.

Beck, A.T., Steer, R.A., Carbin, M.G., 1988. Psychometric properties of the beck depression inventory: twenty-five years of evaluation. Clin. Psychol. Rev. 8, 77–100. doi:10.1016/0272-7358(88)90050-5.

Behroozmand, R., Shebek, R., Hansen, D.R., Oya, H., Robin, D.A., Howard, M.A., Greenlee, J.D.W., 2015. Sensory-motor networks involved in speech production and motor control: an fMRI study. Neuroimage 109, 418–428. doi:10.1016/j.neuroimage.2015.01.040.

Benjamini, Y., Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J. R. Stat. Soc. Ser. C 57, 289–300. doi:10.2307/2346101.

Bioulac, S., Lallemand, S., Rizzo, A., Philip, P., Fabrigoule, C., Bouvard, M.P., 2012. Impact of time on task on ADHD patient's performances in a virtual classroom. Eur. J. Paediatr. Neurol. 16, 514–521. doi:10.1016/J.EJPN.2012.01.006.

Blain, B., Hollard, G., Pessiglione, M., 2016. Neural mechanisms underlying the impact of daylong cognitive work on economic decisions. Proc. Natl. Acad. Sci. USA 113, 6967–6972. doi:10.1073/pnas.1520527113.

Bocca, F., Töllner, T., Müller, H.J., Taylor, P.C., 2015. The right angular gyrus combines perceptual and response-related expectancies in visual search: TMS-EEG evidence. Brain Stimul. 8, 816–822. doi:10.1016/j.brs.2015.02.001.

Boksem, M.A.S., Meijman, T.F., Lorist, M.M., 2005. Effects of mental fatigue on attention: an ERP study. Brain Res. Cogn. Brain Res. 25, 107–116. doi:10.1016/j.cogbrainres.2005.04.011.

Boksem, M.A.S., Tops, M., 2008. Mental fatigue: costs and benefits. Brain Res. Rev. 59, 125–139. doi:10.1016/j.brainresrev.2008.07.001.

Breckel, T.P.K., Giessing, C., Thiel, C.M., 2011. Impact of brain networks involved in vigilance on processing irrelevant visual motion. Neuroimage 55, 1754–1762. doi:10.1016/j.neuroimage.2011.01.025.

Brosnan, M.B., Dockree, P.M., Harty, S., Pearce, D.J., Levenstein, J.M., Gillebert, C.R., Bellgrove, M.A., O'Connell, R.G., Robertson, I.H., Demeyere, N., 2022. Lost in time: temporal monitoring elicits clinical decrements in sustained attention post-stroke. J. Int. Neuropsychol. Soc. 28, 249–257. doi:10.1017/S1355617721000242.

Chambers, C.D., Payne, J.M., Stokes, M.G., Mattingley, J.B., 2004. Fast and slow parietal pathways mediate spatial attention. Nat. Neurosci. 7, 217–218. doi:10.1038/nn1203.

Chehadi, O., Rusu, A.C., Konietzny, K., Schulz, E., Köster, O., Schmidt-Wilcke, T., Hasenbring, M.I., 2018. Brain structural alterations associated with dysfunctional cognitive control of pain in patients with low back pain. Eur. J. Pain 22, 745–755. doi:10.1002/EJP.1159.

Christakou, A., Murphy, C.M., Chantiluke, K., Cubillo, A.I., Smith, A.B., Giampietro, V., Daly, E., Ecker, C., Robertson, D., Murphy, D.G., Rubia, K., 2012. Disorder-specific functional abnormalities during sustained attention in youth with Attention Deficit Hyperactivity Disorder (ADHD) and with Autism. Mol. Psychiatry 18 (2), 236–244. doi:10.1038/mp.2011.185, 201318.

Cisek, P., Kalaska, J.F., 2010. Neural mechanisms for interacting with a world full of action choices. Annu. Rev. Neurosci. 33, 269–298. doi:10.1146/annurev.neuro.051508.135409.

Csathó, Á., Van Der Linden, D., Hernádi, I., Buzás, P., Kalmár, G., 2012. Effects of mental fatigue on the capacity limits of visual attention. J. Cogn. Psychol. 24, 511–524. doi:10.1080/20445911.2012.658039.

Cubillo, A., Halari, R., Smith, A., Taylor, E., Rubia, K., 2012. A review of fronto-striatal and fronto-cortical brain abnormalities in children and adults with Attention Deficit Hyperactivity Disorder (ADHD) and new evidence for dysfunction in adults with ADHD during motivation and attention. Cortex 48, 194–215. doi:10.1016/J.CORTEX.2011.04.007.

Dale, A.M., 1999. Optimal experimental design for event-related fMRI, in: Hum. Brain Mapp.. pp. 109-114. doi:10.1002/(SICI)1097-0193(1999)8:2/3<109::AID-HBM7>3.0.CO;2-W.

Dinges, D.F., Powell, J.W., 1985. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. Behav. Res. Methods Instrum. Comput. 17, 652–655. doi:10.3758/BF03200977.

Dobryakova, E., Hulst, H.E., Spirou, A., Chiaravalloti, N.D., Genova, H.M., Wylie, G.R., DeLuca, J., 2018. Fronto-striatal network activation leads to less fatigue in multiple sclerosis. Mult. Scler. 24, 1174–1182. doi:10.1177/1352458517717087.

Dorrian, J., Rogers, N.L., Dinges, D.F., 2019. Psychomotor vigilance performance: neurocognitive assay sensitive to sleep loss. In: Sleep Deprivation. CRC Press, pp. 39–70. doi:10.3109/9780203998007-4.

Esterman, M., Poole, V., Liu, G., DeGutis, J., 2017. Modulating reward induces differential neurocognitive approaches to sustained attention. Cereb. Cortex 27, 4022–4032. doi:10.1093/cercor/bhw214.

George, M., Dobler, V., Nicholls, E., Manly, T., 2005. Spatial awareness, alertness, and ADHD: The re-emergence of unilateral neglect with time-on-task. Brain Cogn. 57, 264–275. doi:10.1016/J.BANDC.2004.09.003.

Gergelyfi, M., Sanz-Arigita, E.J., Solopchuk, O., Dricot, L., Jacob, B., Zénon, A., 2021. Mental fatigue correlates with depression of task-related network and augmented DMN activity but spares the reward circuit. Neuroimage 243, 118532. doi:10.1016/j.neuroimage.2021.118532.

Gui, D., Xu, S., Zhu, S., Fang, Z., Spaeth, A.M., Xin, Y., Feng, T., Rao, H., 2015. Resting spontaneous activity in the default mode network predicts performance decline during prolonged attention workload. Neuroimage 120, 323–330. doi:10.1016/j.neuroimage.2015.07.030.

Hampshire, A., Chamberlain, S.R., Monti, M.M., Duncan, J., Owen, A.M., 2010. The role of the right inferior frontal gyrus: inhibition and attentional control. Neuroimage 50, 1313–1319. doi:10.1016/j.neuroimage.2009.12.109.

Herlambang, M.B., Taatgen, N.A., Cnossen, F., 2021. Modeling motivation using goal competition in mental fatigue studies. J. Math. Psychol. 102, 102540. doi:10.1016/j.jmp.2021.102540.

Hockey, G.R.J., 2013. The psychology of fatigue: work, effort and control, The Psychology of Fatigue: Work, Effort and Control. doi:10.1017/CBO9781139015394.

Hockey, G.R.J., 1997. Compensatory control in the regulation of human performance under stress and high workload: a cognitive-energetical framework. Biol. Psychol. 73–93. doi:10.1016/S0301-0511(96)05223-4.

Hopstaken, J.F., van der Linden, D., Bakker, A.B., Kompier, M.A.J., 2015a. A multifaceted investigation of the link between mental fatigue and task disengagement. Psychophysiology 52, 305–315. doi:10.1111/psyp.12339.

Hopstaken, J.F., van der Linden, D., Bakker, A.B., Kompier, M.A.J., 2015b. The window of my eyes: task disengagement and mental fatigue covary with pupil dynamics. Biol. Psychol. 110, 100–106. doi:10.1016/j.biopsycho.2015.06.013.

Hopstaken, J.F., van der Linden, D., Bakker, A.B., Kompier, M.A.J., Leung, Y.K., 2016. Shifts in attention during mental fatigue: evidence from subjective, behavioral, physiological, and eye-tracking data. J. Exp. Psychol. Hum. Percept. Perform. 42, 878–889. doi:10.1037/xhp0000189.

Hwang, S., Meffert, H., Parsley, I., Tyler, P.M., Erway, A.K., Botkin, M.L., Pope, K., Blair, R.J.R., 2019. Segregating sustained attention from response inhibition in ADHD: an fMRI study. Neuroimage Clin. 21, 101677. doi:10.1016/j.nicl.2019.101677.

Langner, R., Eickhoff, S.B., 2013. Sustaining attention to simple tasks: a meta-analytic review of the neural mechanisms of vigilant attention. Psychol. Bull. 139, 870–900. doi:10.1037/a0030694.

Lee, I.S., Bardwell, W.A., Ancoli-Israel, S., Dimsdale, J.E., 2010. Number of lapses during the psychomotor vigilance task as an objective measure of fatigue. J. Clin. Sleep Med. 6, 163–168. doi:10.5664/jcsm.27766.

Lim, J., Ebstein, R., Tse, C.Y., Monakhov, M., Lai, P.S., Dinges, D.F., Kwok, K., 2012. Dopaminergic polymorphisms associated with time-on-task declines and fatigue in the psychomotor vigilance test. PLoS One 7. doi:10.1371/journal.pone.0033767.

Lim, J., Wu, W.Chau, Wang, J., Detre, J.A., Dinges, D.F., Rao, H., 2010. Imaging brain fatigue from sustained mental workload: an ASL perfusion study of the time-on-task effect. Neuroimage 49, 3426–3435. doi:10.1016/j.neuroimage.2009.11.020.

Lorist, M.M., Bezdan, E., ten Caat, M., Span, M.M., Roerdink, J.B.T.M., Maurits, N.M., 2009. The influence of mental fatigue and motivation on neural network dynamics; an EEG coherence study. Brain Res. 1270, 95–106. doi:10.1016/j.brainres.2009.03.015.

Massar, S.A.A., Sasmita, K., Lim, J., Chee, M.W.L., 2018. Motivation alters implicit temporal attention through sustained and transient mechanisms: a behavioral and pupillometric study. Psychophysiology 55. doi:10.1111/psyp.13275.

Matuz, A., Van der Linden, D., Topa, K., Csathó, Á., 2019. Cross-modal conflict increases with time-on-task in a temporal discrimination task. Front. Psychol. 10, 2429. doi:10.3389/fpsyg.2019.02429.

Mehta, R.K., Peres, S.C., Kannan, P., Rhee, J., Shortz, A.E., Sam Mannan, M., 2017. Comparison of objective and subjective operator fatigue assessment methods in offshore shiftwork. J. Loss Prev. Process Ind. 48, 376–381. doi:10.1016/j.jlp.2017.02.009.

Müller, T., Apps, M.A.J., 2019. Motivational fatigue: A neurocognitive framework for the impact of effortful exertion on subsequent motivation. Neuropsychologia 123, 141–151. doi:10.1016/j.neuropsychologia.2018.04.030.

Nachreiner, F., 2001. Time on task effects on safety. J. Hum. Ergol. (Tokyo) 30, 97–102. doi:10.1016/j.aap.2009.11.011.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113. doi:10.1016/0028-3932(71)90067-4.

Pattyn, N., Neyt, X., Henderickx, D., Soetens, E., 2008. Psychophysiological investigation of vigilance decrement: boredom or cognitive fatigue? Physiol. Behav. 93, 369–378. doi:10.1016/j.physbeh.2007.09.016.

Paus, T., Zatorre, R.J., Hofle, N., Caramanos, Z., Gotman, J., Petrides, M., Evans, A.C., 1997. Time-related changes in neural systems underlying attention and arousal during the performance of an auditory vigilance task. J. Cogn. Neurosci. 9, 392–408. doi:10.1162/jocn.1997.9.3.392.

Plante, D.T., Hagen, E.W., Ravelo, L.A., Peppard, P.E., 2020. Impaired neurobehavioral alertness quantified by the psychomotor vigilance task is associated with depression in the Wisconsin Sleep Cohort study. Sleep Med. 67, 66–70. doi:10.1016/J.SLEEP.2019.11.1248.

Plichta, M.M., Scheres, A., 2014. Ventral-striatal responsiveness during reward anticipation in ADHD and its relation to trait impulsivity in the healthy population: A meta-analytic review of the fMRI literature. Neurosci. Biobehav. Rev. 38, 125–134. doi:10.1016/j.neubiorev.2013.07.012.

Rodrigo, M.J., Padrón, I., de Vega, M., Ferstl, E.C., 2014. Adolescents' risky decision-making activates neural networks related to social cognition and cognitive control processes. Front. Hum. Neurosci. 8, 60. doi:10.3389/FNHUM.2014.00060/BIBTEX.

Sandry, J., Genova, H.M., Dobryakova, E., DeLuca, J., Wylie, G., 2014. Subjective cognitive fatigue in multiple sclerosis depends on task length. Front. Neurol. 5, 214. doi:10.3389/fneur.2014.00214.

Schmidt, L., Lebreton, M., Cléry-Melin, M.L., Daunizeau, J., Pessiglione, M., 2012. Neural mechanisms underlying motivation of mental versus physical effort. PLoS Biol. 10, e1001266. doi:10.1371/JOURNAL.PBIO.1001266.

Shenhav, A., Botvinick, M.M., Cohen, J.D., 2013. The expected value of control: an integrative theory of anterior cingulate cortex function. Neuron 79, 217–240. doi:10.1016/j.neuron.2013.07.007.

Silk, T.J., Bellgrove, M.A., Wrafter, P., Mattingley, J.B., Cunnington, R., 2010. Spatial working memory and spatial attention rely on common neural processes in the intraparietal sulcus. Neuroimage 53, 718–724. doi:10.1016/j.neuroimage.2010.06.068.

Smith, M.R., Chai, R., Nguyen, H.T., Marcora, S.M., Coutts, A.J., 2019. Comparing the effects of three cognitive tasks on indicators of mental fatigue. J. Psychol. 153, 759–783. doi:10.1080/00223980.2019.1611530.

Sun, Y., Lim, J., Kwok, K., Bezerianos, A., 2014. Functional cortical connectivity analysis of mental fatigue unmasks hemispheric asymmetry and changes in small-world networks. Brain Cogn. 85, 220–230. doi:10.1016/j.bandc.2013.12.011.

Tucha, L., Fuermaier, A.B.M., Koerts, J., Buggenthin, R., Aschenbrenner, S., Weisbrod, M., Thome, J., Lange, K.W., Tucha, O., 2017. Sustained attention in adult ADHD: time-on-task effects of various measures of attention. J. Neural Transm. 124, 39–53. doi:10.1007/s00702-015-1426-0.

Vassena, E., Holroyd, C.B., Alexander, W.H., 2017. Computational models of anterior cingulate cortex: at the crossroads between prediction and effort. Front. Neurosci. 11, 316. doi:10.3389/fnins.2017.00316.

Verguts, T., 2017. Binding by random bursts: a computational model of cognitive control. J. Cogn. Neurosci. 29, 1103–1118. doi:10.1162/jocn_a_01117.

Wiehler, A., Branzoli, F., Adanyeguh, I., Mochel, F., Pessiglione, M., 2022. A neuro-metabolic account of why daylong cognitive work alters the control of economic decisions. Curr. Biol. 32, 3564–3575. doi:10.1016/j.cub.2022.07.010, e5.

Worsley, K.J., Liao, C.H., Aston, J., Petre, V., Duncan, G.H., Morales, F., Evans, A.C., 2002. A general statistical analysis for fMRI data. Neuroimage 15, 1–15. doi:10.1006/nimg.2001.0933.

Wylie, G.R., Flashman, L.A., 2017. Understanding the interplay between mild traumatic brain injury and cognitive fatigue: models and treatments. Concussion 2, CNC50. doi:10.2217/cnc-2017-0003.

Yang, D.Y., Chi, M.H., Chu, C.L., Lin, C.Y., Hsu, S.E., Chen, K.C., Lee, I.H., Chen, P.S., Yang, Y.K., 2019. Orbitofrontal dysfunction during the reward process in adults with ADHD: an fMRI study. Clin. Neurophysiol. 130, 627–633. doi:10.1016/j.clinph.2019.01.022.

Zeller, R., Williamson, A., Friswell, R., 2020. The effect of sleep-need and time-on-task on driver fatigue. Transp. Res. Part F Traffic Psychol. Behav. 74, 15–29. doi:10.1016/j.trf.2020.08.001.