The Cocktail Party Effect in Post-Stroke Fatigue: an EEG study

Running head: Sensory filtering in post-stroke fatigue

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Abstract

Objective: An inability to selectively attend away from task irrelevant stimuli is thought to drive post-stroke fatigue. In this study we investigated if neural processing of task relevant stimuli, in the presence of noise (task-irrelevant stimuli), is compromised in post-stroke fatigue.

Methods: An auditory oddball task consisting of target, standard and novel tones was carried out with and without background noise while recording neural responses using electroencephalography. Participants responded to target tones with a button press. After each block, participants rated how effortful the block felt. Fatigue was measured using the fatigue severity scale. The effect of fatigue and noise on behaviour (response time, accuracy, and effort rating) and neural responses (amplitude and latency) was examined using mixed model ANOVAS.

Results: Those with fatigue had slower responses both in 'noise' and 'no noise' conditions. The response amplitude to the novel tones in the 'noise' condition was smaller, than 'no noise' condition, which was modulated by fatigue. The latency of response was longer, in the 'noise' when compared to 'no noise' condition which was not modulated by fatigue. likewise, perceived effort was also greater in the 'noise' condition, but not modulated by fatigue.

Interpretation: Processing of novel stimuli in the presence of background noise is significantly altered in post-stroke fatigue, indicating a problem with attentional switching processes, one that selectively contributes to the feeling of fatigue without affecting performance.

Introduction

Post-stroke fatigue (PSF), a feeling of extreme exhaustion, is a commonly reported symptom with a major impact on quality of life and mortality[1–4]. Despite the high prevalence of fatigue, an understanding of the mechanisms that underlie this complex symptom is currently lacking.

The ability to focus one's attention on task relevant stimulus while suppressing task-irrelevant stimuli, termed as the cocktail party effect, is a near impossible task for stroke survivors reporting high levels of fatigue. In other words, although stroke survivors with high levels of fatigue can hold a conversation, doing so in a crowded environment, triggers fatigue. Such reports of inability to modulate attention away from distractor stimuli and focus on target stimuli, are consistent with a recently proposed mechanism of PSF, where an inability to modulate attention away from predictable sensory information is the basis of high effort that underpins fatigue[5,6]. Perceptual processing capacity is a finite resource, and under the perceptual load theory, all stimuli (both relevant and irrelevant to a task) are processed within perceptual capacity limits[7,8]. The attention allocated to task-irrelevant stimuli is determined by the perceptual load of the target task, in that targets with high perceptual load take up more attentional capacity and less is left for processing of stimuli unrelated to the task[9]. In other words, perceptual load is a major factor in determining selective attention[7].

A reliable method to study selective attention is using event-related potentials (ERPs) recorded using electroencephalography (EEG) during an auditory oddball paradigm. A novel or unpredictable tone is presented among a stream of familiar events, which involuntarily captures attention and evokes an orienting response termed the P300. The early component of the P300, termed P300a, reflects an automatic shift of attentional processes related to unpredictable and rare stimuli (bottom-up processing), while the later component, P300b, reflects top-down attentional processes associated with the detection of anticipated targets[10–12]. Another component of the ERP (the N100), evoked by all tones within such a paradigm, reflects perceptual information processing and is increased when an attended stimulus can be more easily distinguished from other stimuli[13]. Performing an auditory oddball task in the presence of background sounds compared to a silent environment, affects the amplitude of the various components of the ERP, in line with the perceptual load theory[14].

The aim of this study was to study selective attention in the presence and absence of distractors in chronic stroke survivors with varying severity of fatigue using a three-tone auditory oddball task. If PSF is driven by an inability to shift attention away from predictable sensory information, we would expect the amplitude of evoked responses in those with PSF to be smaller in the presence of distractors when compared to those without fatigue. Such a paradigm, will also allow us to identify whether such changes are primarily driven by top-down or bottom-up processing (or both), that may give further insight into the mechanisms of PSF.

Material and Methods

Participants

This was a cross-sectional observational study approved by the London Bromley Research Ethics Committee (REC reference number: 16/LO/0714). Stroke survivors were recruited via the Clinical Research Network from the University College NHS Trust Hospital (UCLH), a departmental Stroke Database and from the community. All stroke survivors were screened prior to the study based on the following criteria: first-time ischaemic or haemorrhagic stroke; stroke occurred at least 3 months prior to the study; no clinical diagnosis of any other neurological disorder; physically well recovered following their stroke defined as grip strength and manual dexterity of the affected hand being at least 60% of the unaffected hand assessed using a hand-held dynamometer and the nine-hole peg test (NHPT) respectively; not taking anti-depressants or any other medication that has a direct effect on the central nervous system; not clinically depressed with depression scores ≤ 11 assessed using the Hospital Anxiety and Depression Scale (HADS). [15]. Following written informed consent in accordance with the Declaration of Helsinki, twenty-nine stroke survivors participated in the study (Table 1).

Fatigue

Two measures of fatigue were captured at the start of the study, trait and state fatigue. Trait fatigue represents the experience and impact of fatigue on day to day living for a pre-determined time leading up to the day of testing, whereas state fatigue characterizes fatigue at a given moment in time. Trait fatigue was quantified using the FSS-7, a seven-item questionnaire that rates fatigue over a 1 week period preceding the date of testing[16]. State fatigue was quantified using a visual analogue scale (VAS) ranging from zero to ten in steps of 1 (Not at all tired to extremely tired).

Stimuli and Procedure

Participants were seated 70 centimeters from the monitor (Dell U240 24-inch monitor, at a screen resolution of 1280x768) and made their responses using a standard USB keyboard. The experiment was controlled using the Psychophysics Toolbox for Matlab[17,18], running on a Windows computer. A three-stimulus auditory oddball paradigm was used to elicit N100, P300a and P300b event-related potentials (ERPs) both in the presence and absence of noise (Figure 1). Stimuli consisted of 1,200 binaural, 80 dB tones of 150 ms duration presented to the participants through headphones (Sennheiser, HD 569), divided into twelve blocks (100 stimuli per block) lasting approximately four minutes each. In 50% of the blocks (6 of 12), participants performed the oddball task with no noise, while in the remaining 50% of the blocks, participants performed the oddball task in the presence of noise. The 'noise' was an ecologically valid recording of chatter in the café (babble) played at 65 dB. The order of block presentation was counterbalanced across participants. Twelve percent of the stimuli (144 in total, 12 per block) were target tones (1.5 kHz tone), 12% of the stimuli (144 in total, 12 per block) were "novel" sounds (a cricket sound, a sneeze etc), and 76% were standard tones (1 kHz tone), with an inter-stimulus interval varying between 1.8 and 2.2 seconds. Participants were instructed to press a button on the keyboard with the index finger of their right hand in response to target tones only, while keeping their eyes on a fixation cross. This allowed us to have a measure of response time (time from auditory stimulus onset to button press) and accuracy (% correct of button press) for each participant. Participants were also asked to rate the effort required to complete a block of the task, on a VAS ranging from zero (very easy) to ten (very hard). Before the start of the experiment participants completed

practice trials (15 correct trials), both in the presence and absence of background noise, to ensure they familiarized themselves with the task demands.

EEG Acquisition

Whole-scalp electroencephalography (EEG) data was recorded using a 64-channel cap array (ActiCap, Herrsching, Germany) and a BrainAmp EEG amplifier system (BrainProducts, Gilching, Germany). The 64 electrodes were positioned on the cap in accordance with the 10-20 international EEG electrode array. During online recordings, channels FCz and AFz were used as the reference and ground respectively. Impedances were kept below 10 kΩ throughout the recording. The EEG signal was sampled at 1 kHz and visualized online using the BrainVision Recorder Software (BrainVision Recorder, Version 1.21.0102 Brain Products GmbH, Gilching, Germany). Event markers were sent from the stimulus presentation PC to the BrainAmp amplifier via the TriggerBox which allows one to send accurate triggers via a USB port with millisecond precision.

EEG Analysis

EEG data were pre-processed and analysed offline using EEGLAB[19], ERPLAB[20] and customized MATLAB scripts (Mathworks, Inc., MA, USA). EEG data was down-sampled to 250 Hz and subsequently band-pass filtered between 0.5 and 30 Hz with a zero phase-shift IIR Butterworth filter (24 dB/Oct). Noisy channels were identified and removed using automated procedures. To identify and remove ocular movements and blink artefacts from the EEG data, an independent component analysis (ICA) implemented within EEGLAB was used. The components were visually inspected and those containing ocular movements or blink artifacts were removed. The previously removed channels were then interpolated back into the dataset and finally, the EEG data was re-referenced against the grand average of all scalp electrodes.

ERP

The pre-processed EEG data was segmented into epochs of -200 ms to 800 ms time locked to the auditory stimulus onset and baseline corrected using the 200 ms pre-stimulus period. Individual epochs were inspected using a 200 ms sliding time window in steps of 100 ms across the entire length of the epoch for voltages exceeding ± 100 μV. These trials were subsequently excluded from the analysis (2.5 % ± 3.4) of trials. All artefact-free epochs were then averaged for each of the three conditions (Standard, Target, Novel) and filtered using a low-pass IIR Butterworth filter of 12 Hz. The mean number of trials remaining was comparable between groups for each condition (Table 2).

The mismatch negativity (MMN) wave was estimated by subtracting the grand average of the standard tones from the grand average of the novel tones (MMNa) and from the grand average of the target tones (MMNb) in each participant. The N100 amplitude was defined as the instantaneous peak negative amplitude between 50 and 200 ms from the auditory stimulus onset at electrode Cz across the three conditions; the P300a amplitude was defined as the instantaneous peak positive amplitude between 250 and 450 ms from the auditory stimulus onset at electrode CPz in MMNa wave; the P300b amplitude was defined as the instantaneous peak positive amplitude between 280 and 650 ms from the auditory stimulus onset at electrode Pz in the MMNb

wave. The latency of each peak across the three ERPs was also recorded for statistical analysis. These three midline locations were chosen as ERP responses were largest at these electrode sites.

Statistical Analysis

All statistical analyses were performed using R (RStudio Version 1.2.5033). Spearman rank correlations were used to identify the association between trait fatigue (FSS-7) and all continuous demographic measures (age, grip strength, NHPT, HADS-Depression, HADS-Anxiety and Time Post-Stroke), while Wilcoxon rank sum tests were used to identify the association between trait fatigue and all categorical demographic measures (sex, hemisphere affected, type of stroke and vascular territory affected).

The distribution of the dependent variable was assessed using the Shapiro-Wilk's test of normality, while homogeneity of variances was assessed using the Levene's test. As all data was normally distributed, group differences in the behavioural (response time, accuracy, and effort) and ERP data (amplitude and latency) were examined using a mixed analysis of variance with group (Low Fatigue and High Fatigue) as the between subject factor and noise (Off/On) as the within subject factor. Differences were considered statistically significant at the level of $p < 0.05$. Generalised eta squared (η^2) was reported for the group effect sizes. Bonferroni corrected pairwise t-tests were used to assess simple main effects in the post-hoc analysis.

Results

Participant Demographics

Twenty-nine stroke survivors completed the study (11 females and 18 males). The median FSS-7 score was 5.29 (IQR = 2.57) in females and 2.50 (IQR = 2.46) in males. The Wilcoxon test showed that the difference in FSS-7 score was marginally non-significant ($p = 0.05$, effect size = 0.37). Spearman rank correlations between trait fatigue (FSS-7) and all continuous demographic measures revealed a significant positive association between trait fatigue and HADS-Depression (Spearman $\rho = 0.41$, $p = 0.03$), while no other variable correlated with trait fatigue. The median FSS-7 score in those with right and left hemisphere strokes was 4.43 (IQR = 3.00) and 2.71 (IQR = 3.75) respectively (Wilcoxon test: $p = 0.50$, effect size = 0.13). The median FSS-7 score in ischemic strokes was 2.93 (IQR = 3.46) and 3.86 (IQR = 2.29) in hemorrhagic strokes (Wilcoxon test: $p = 0.51$, effect size $r = 0.13$). The median FSS-7 score in ACA strokes was 6.85, in MCA strokes was 3.36 (IQR = 3.25), in PCA strokes was 3.07 (IQR = 2.07), and 4.21 (IQR = 2.68) in Brainstem/Cerebellum strokes (Kruskal-Wallis test: $p = 0.57$, $\eta^2 = -0.04$). A spearman rank correlation between FSS-7 and the Time Post-Stroke showed no significant association (Spearman $\rho = 0.08$, $p = 0.67$). Any meaningful interpretation of the effect of the type of stroke and vascular territory affected on FSS-7 in the current cohort of stroke survivors is difficult given the skewed numbers.

Behaviour

The response time (RT) results are shown in Figure 2A. As the RT data was not normally distributed, the data were log transformed and entered into a mixed ANOVA with noise (Off/On) as the within-subject factor and fatigue (Low Fatigue/High Fatigue) as the between subject factor. There was a main effect of noise ($F_{(1,27)} = 8.12$, $p = 0.01$, $\eta^2 = 0.01$) and a main effect of fatigue

($F_{(1,27)} = 5.40$, $p = 0.03$, $\eta^2 = 0.16$) but no interaction between noise and fatigue ($F_{(1,27)} = 0.17$, $p = 0.69$, $\eta^2 < 0.01$). Pairwise t-tests showed a significant difference in RT between the two fatigue groups in the noise off ($p = 0.025$) and the noise on ($p = 0.036$) conditions.

The accuracy results are shown in Figure 2B. The mixed ANOVA revealed no effect of noise ($F_{(1,27)} = 1.21$, $p = 0.28$, $\eta^2 = 0.01$), no effect of fatigue ($F_{(1,27)} = 3.36$, $p = 0.08$, $\eta^2 = 0.10$) and no interaction between noise and fatigue ($F_{(1,27)} = 0.45$, $p = 0.51$, $\eta^2 < 0.01$).

The effort rating results are shown in Figure 2C. The mixed ANOVA revealed a main effect of noise ($F_{(1,27)} = 10.50$, $p < 0.01$, $\eta^2 = 0.05$), no effect of fatigue ($F_{(1,27)} = 2.80$, $p = 0.11$, $\eta^2 = 0.08$) and no interaction between noise and fatigue ($F_{(1,27)} = 0.37$, $p = 0.55$, $\eta^2 < 0.01$).

P300a amplitude and latency

Grand average waveforms and topographic maps for P300a are shown in Figure 3. The mixed ANOVA with the amplitude of the P300a as the dependent variable revealed a main effect of noise ($F_{(1,27)} = 37.18$, $p < 0.01$, $\eta^2 = 0.12$), no effect of fatigue ($F_{(1,27)} = 3.36$, $p = 0.08$, $\eta^2 = 0.10$) and a significant interaction between noise and fatigue ($F_{(1,27)} = 8.50$, $p < 0.01$, $\eta^2 = 0.03$). Pairwise t-test showed that there was a significant difference in the amplitude of the P300a between the two fatigue groups in the noise on ($p = 0.02$) but not in the noise off ($p = 0.45$) conditions (Figure 4A). To further examine how the presence of noise differentially modulates the amplitude of the P300a across the two fatigue groups, the change in amplitude between the noise off and on conditions was calculated and compared between the two fatigue groups using a t-test (t-statistic = -2.75, df = 17.8, $p = 0.01$; Figure 4B).

The mixed ANOVA with the latency of P300a as the dependent variable (Figure 4C) revealed a main effect of noise ($F_{(1,27)} = 13.80$, $p < 0.01$, $\eta^2 = 0.09$), no effect of fatigue ($F_{(1,27)} = 0.12$, $p = 0.74$, $\eta^2 < 0.01$) and a significant interaction between noise and fatigue ($F_{(1,27)} = 4.59$, $p = 0.04$, $\eta^2 = 0.03$). Pairwise t-tests showed a significant difference in the latency of the P300a between the two noise conditions in the low fatigue group (t-statistic = -4.87, df = 15, $p < 0.01$) but not in the high fatigue group (t-statistic = -0.95, df = 12, $p = 0.36$).

P300b amplitude and latency

The mixed ANOVA with the amplitude of P300b as the dependent variable (Figure 5A) revealed no effect of noise ($F_{(1,27)} = 0.03$, $p = 0.85$, $\eta^2 < 0.01$), no effect of fatigue ($F_{(1,27)} = 0.002$, $p = 0.97$, $\eta^2 < 0.01$) and no significant interaction between noise and fatigue ($F_{(1,27)} = 0.00006$, $p = 0.99$, $\eta^2 < 0.01$). The mixed ANOVA with the latency of the P300b as the dependent variable (Figure 5B) revealed no effect of noise ($F_{(1,27)} = 0.03$, $p = 0.88$, $\eta^2 < 0.01$), no effect of fatigue ($F_{(1,27)} = 0.53$, $p = 0.47$, $\eta^2 = 0.012$) and no significant interaction between noise and fatigue ($F_{(1,27)} = 0.04$, $p = 0.84$, $\eta^2 < 0.01$).

N100 amplitude and latency

The mixed ANOVA with the amplitude of the N100 as the dependent variable (Figure 5C) had an additional within-subject factor of Condition (Standard, Target, Novel) to examine whether the

amplitude of the N100 was differentially modulated across the different conditions. The mixed ANOVA revealed no effect of condition ($F_{(2,54)} = 0.69$, $p = 0.44$, $\eta^2 = 0.01$). The amplitude of the N100 was therefore averaged across the three conditions, and a mixed ANOVA was re-computed with noise as the only within-subject factor. The mixed ANOVA revealed a main effect of noise ($F_{(1,27)} = 42.06$, $p < 0.01$, $\eta^2 = 0.12$), no effect of fatigue ($F_{(1,27)} = 0.14$, $p = 0.71$, $\eta^2 < 0.01$) and no significant interaction between noise and fatigue ($F_{(1,27)} =1.17$, $p = 0.21$, $\eta^2 < 0.01$). The mixed ANOVA with the latency of the N100 as the dependent variable (Figure 5D) revealed an effect of noise ($F_{(1,27)} = 5.28$, $p = 0.03$, $\eta^2 = 0.06$), no effect of fatigue ($F_{(1,27)} = 0.06$, $p = 0.81$, $\eta^2 < 0.01$) and no significant interaction between noise and fatigue ($F_{(1,27)} = 0.83$, $p = 0.37$, $\eta^2 = 0.01$).

Discussion

In twenty-nine minimally impaired, non-depressed, chronic stroke survivors, we show that trait fatigue is predictive of slower responses to target stimuli in an auditory oddball paradigm. Response times were significantly slower in the presence of background noise (distractors) too, however there was no interaction between trait fatigue and the effect of background noise on response times. Accuracy of responses was affected neither by noise nor fatigue, however the amount of effort required to perform the task, as indicated by self-report, was higher in the presence of background noise and not affected by fatigue. Analysis of the electrophysiological responses showed that the P300a had a lower amplitude in the presence of background noise that was more evident in those with high levels fatigue, while the latency of the response was prolonged in the presence of background noise and more so in those with low levels of fatigue. The P300b on the other hand, was affected neither by noise nor fatigue, while the amplitude of the N100 was smaller in the presence of background noise and not affected by fatigue.

Post-stroke fatigue has been associated with deficits in various cognitive domains, including attention[21,22]. Attention forms an integral aspect of perception and by modulating attention to or away from various internal and external stimuli, one can modulate perception. A recent account of PSF proposes that altered perception can explain both the motor and cognitive deficits seen in PSF[5,6]. Sensory information arising from the external or internal environment, in the form of auditory/visual or proprioceptive information respectively, when self-generated or anticipated, is attenuated, and hence not perceive it. When taking the example of a muscle contraction to perform a simple movement, the sensory information arising from the peripheral musculature is predictable and therefore attenuated, resulting in the subsequent movement being perceived as effortless. The perception of effort associated with voluntary muscle contractions is higher in those with PSF, which is in line with patient report of simple day-to-day tasks requiring a lot more effort when compared to before the stroke, despite no physical impairment[23]. This phenomenon is not specific to muscle contractions, and those with high levels of fatigue report high effort related to processing exteroceptive information. In our study, we show using an oddball paradigm, the inability to attenuate processing of task-irrelevant auditory stimuli can make performing a simple auditory task, feel more effortful.

Response times were slower in the presence of background noise, and even slower in those with high levels of fatigue, with no interaction between fatigue and noise. Previous studies show that while PSF patients exhibit slower movement speeds, response times are not compramised[24]. It is possible that the button press which registered the response in this instance, is a combination of both reaction time and movement speed, therefore, is a reflection of slower movement speeds and not altered reaction times. The lack of interaction between fatigue and noise on response times, is

in support of such an explanation, as the extent of perceptual processing increases as the task demands increase and should thus have resulted in a greater effect of fatigue on perceptual processing. However, in the absence of such an effect, we can conclude that slower response times is indicative of slower movement times and not reaction times.

A novelty-oddball paradigm, consisting of both target and novel stimuli, areas activates both the dorsal and ventral attentional streams, with the dorsal stream active during top-down selective attention, and ventral during bottom-up control of attention. Optimal control of attention is dependent on the effective interaction of these two networks[25]. The current study suggests that those with high levels of fatigue exhibit deficits in the bottom-up control of attention, indicated by a greater change in the amplitude of the P300a component in the presence of noise compared to the silent condition. The P300a component, a centrally distributed positive deflection, represents the process of an involuntary switch in attention captured by an unexpected event beyond the immediate perceptual field, representing a bottom-up mechanism of redirecting attentional resources[26]. When the task requires more attention, as is the case in the presence of background noise, less attentional resources are invested in processing task irrelevant stimuli[14]. However, if one is unable to shift attention from task-irrelevant stimuli, as proposed in PSF, less attentional resources are available to invest in the task, indicated by a smaller amplitude of the P300a and a larger difference in the amplitude of the P300a across the noise conditions. Similar findings of reduced amplitude of the P300a component have been shown in Parkinson's disease patients suffering from chronic pathological fatigue, pointing towards common underlying mechanisms across different neurological conditions[11]. The P300b component on the other hand, has a more posterior distribution with a longer latency than the P300a component and reflects brain activity related to attention and working memory that is engaged in the selection of task-relevant stimuli and responses[12,27]. The lack of effect of both noise and fatigue on the amplitude of the P300b component suggests that top-down modulation of attention is not affected by fatigue and is similar to previous findings in healthy controls and PD patients[11,14].

The lack of modulation of the N100 component by fatigue is another interesting finding in this study. The auditory N100 component is a negative deflection with a central distribution that appears to be sensitive to auditory stimulus properties and is increased when an attended stimulus can be more easily distinguished from other stimuli[28]. Given that the amplitude of the N100 component was lower and the latency was longer in the presence of background noise compared to the silent condition confirms the abovementioned statement and is in line with previous reports[13,14]. The amplitude of the N100 was not modulated by fatigue or noise condition, suggesting that those with high levels of fatigue were still able to distinguish the auditory properties of the different stimuli and were able to distinguish the various tones from the background noise just as well as those with low levels of fatigue. The electrophysiological findings, when taken together with the behavioural measure of accuracy, suggest that PSF patients do not show any difference in performance metrics and are still able to achieve the same levels of performance as those with low levels of fatigue. This is in line with previous findings showing that reaction times and the completion of motor tasks are not affected by fatigue[23,29].

In summary, we show that processing of novel stimuli in the presence of background noise is significantly altered in PSF, indicating a problem with attentional switching processes, one that selectively contributes to the feeling of fatigue without affecting performance. This evidence provides a physiological basis for self-reported fatigue-related difficulties of processing several streams of sensory information. Therefore, by providing experimental evidence for a theoretically informed explanation of poor sensory processing in high fatigue, this study lays the foundation for an attentional mechanism of fatigue that may be common to chronic fatigue across disease conditions.

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Author Contributions
Conception and design (AK, WDD); acquisition and analysis of data (WDD); drafting a significant portion of the manuscript or figures (WDD).

Conflicts of Interest
The authors report no competing interests.

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Figure Legends

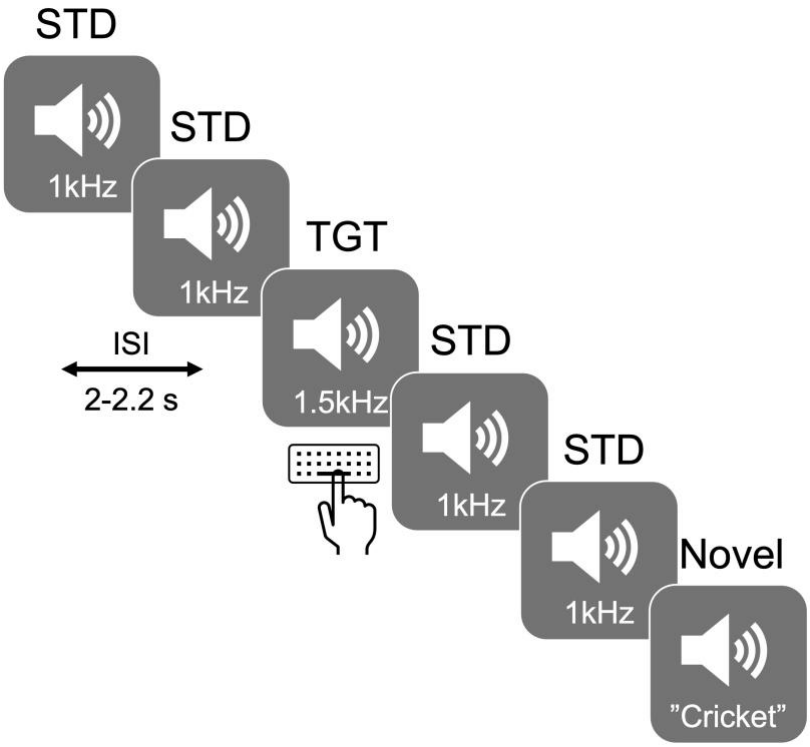

Figure 1. Illustration of the task design. Target (TGT) tones at 1.5 kHz requiring a requiring a response via a keyboard and Novel tones were presented amongst a sequence of standard (STD) tones at 1 kHz.

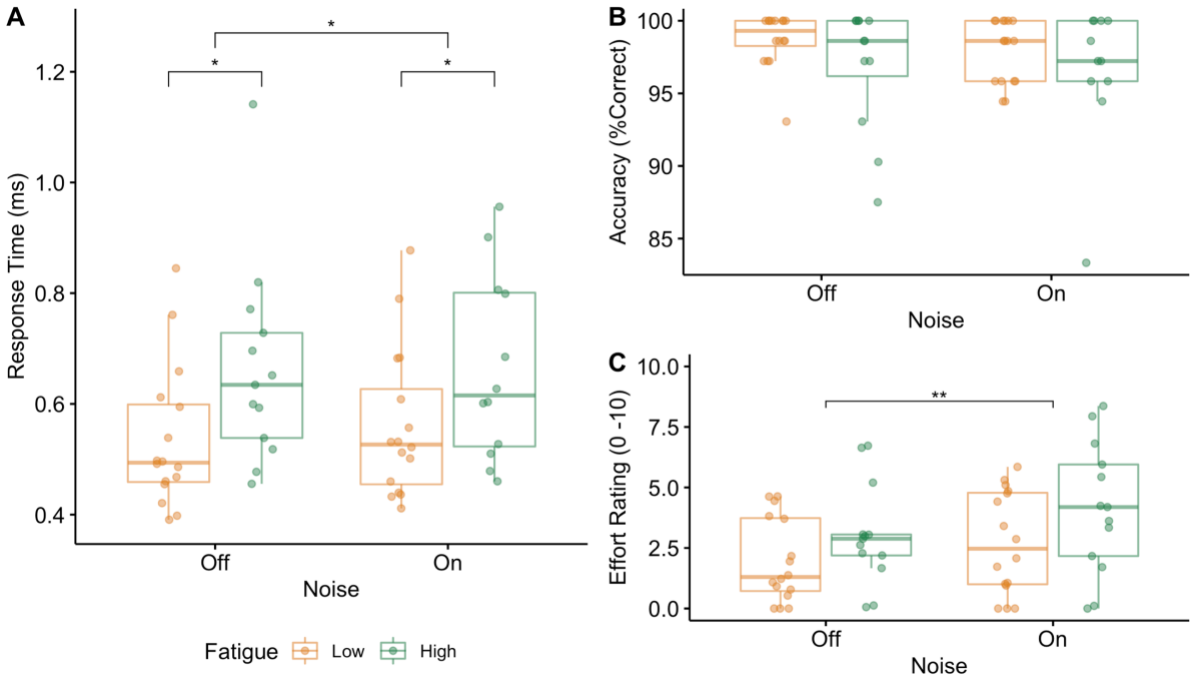

Figure 2. Behavioural results. Box plots with individual data points for the low fatigue group in yellow and the high fatigue group in green for response time (A), accuracy (B) and effort rating (C) across the two background noise conditions (Off and On). Significant differences between the groups are indicated with asterisks (*$p < 0.05$).

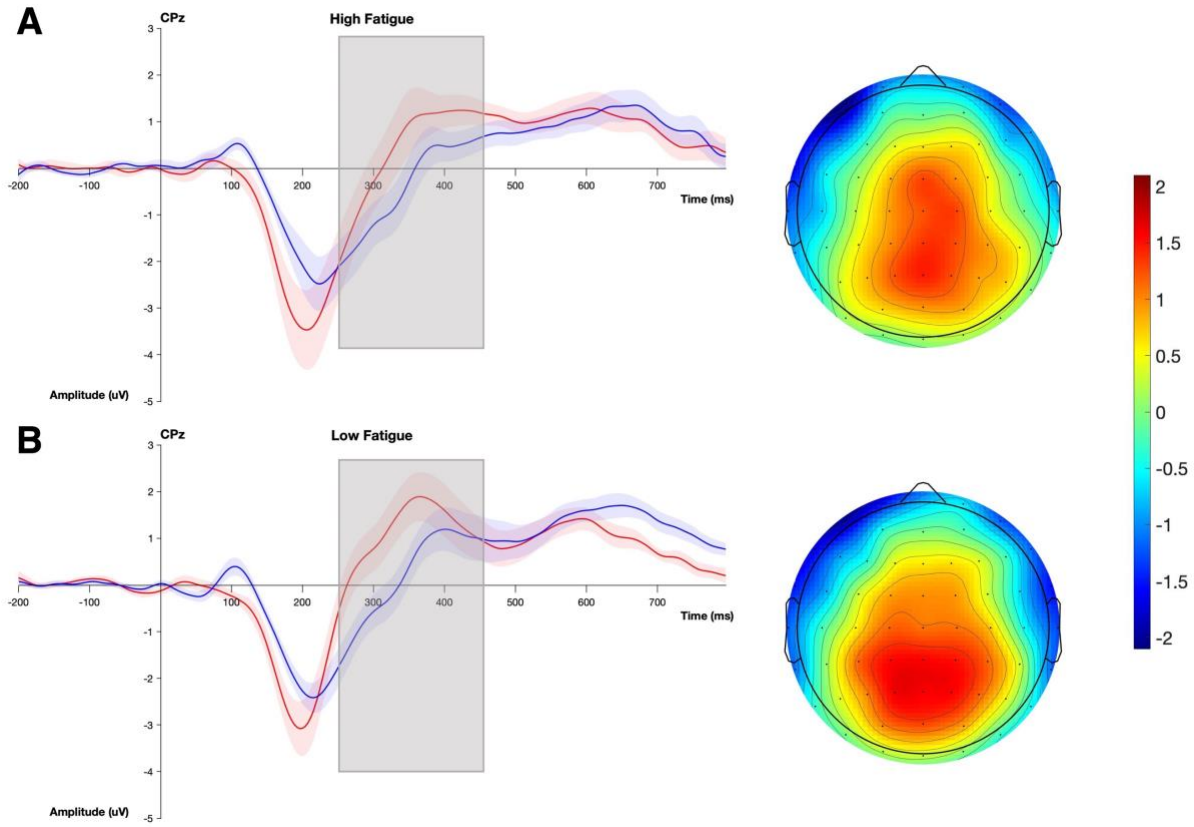

Figure 3. Grand average ERP of the P300a at electrode CPz and topographical plot for the high (A) and low (B) fatigue groups. The noise off condition is in red and the noise on condition is in blue. The topographical plots illustrate the difference between the two noise conditions. The grey box indicates the time window within which the P300a was measured

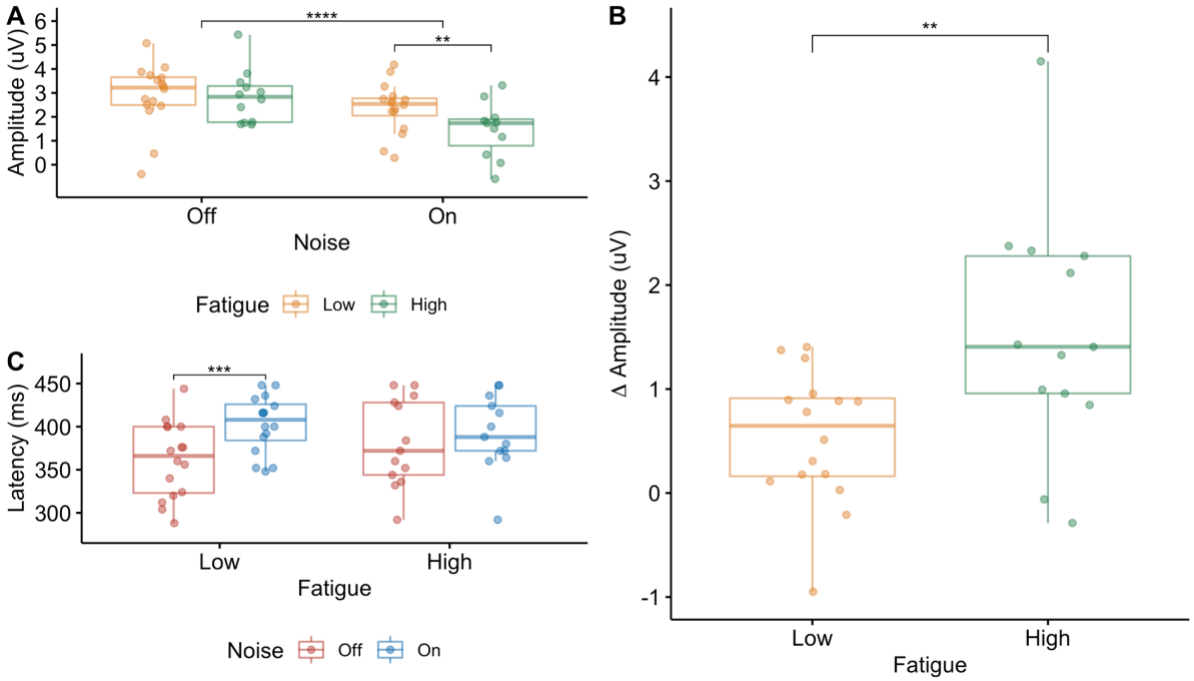

Figure 4. P300a results. Box plots with individual data points for the low fatigue group in yellow and the high fatigue group in green for the amplitude (A) and the difference in amplitude across the two noise conditions (B) for each fatigue group of the P300a. Box plots with individual data points for the latency of

the P300a across the different noise conditions, with noise off in red and noise on in blue, is shown in panel C. Significant differences between the groups are indicated with asterisks (*p < 0.05).

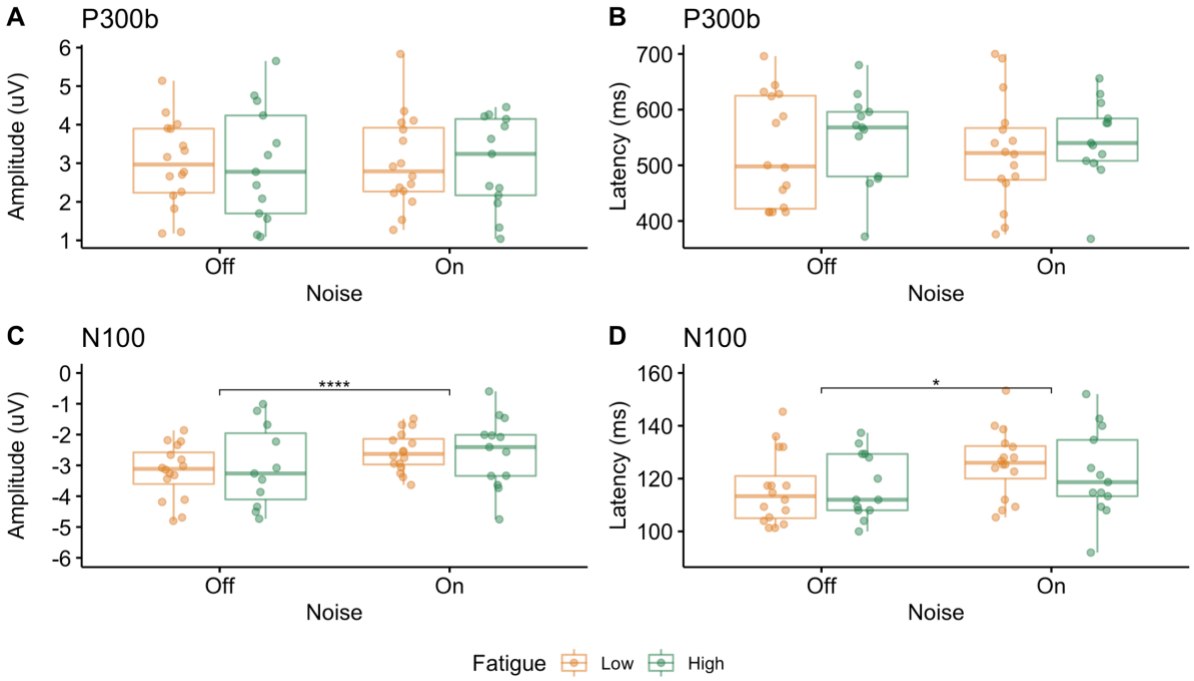

Figure 5. P300b and N100. Box plots with individual data points for the low fatigue group in yellow and the high fatigue group in green for the amplitude (A) and latency (B) of the P300b, as well as the amplitude (C) and latency (D) of the N100. Significant differences between the groups are indicated with asterisks (*p < 0.05).

Tables

	Fatigue Group	
Variable	Low Fatigue, N = 16[1]	High Fatigue, N = 13[1]
FSS-7	2.1 (1.4,2.4)	5.6 (5.3,6.00)
Age (years)	61.7 (55.6,64.8)	62.9 (56.1,68.1)
Sex		
Male | Female	13 | 3	5 | 8
Grip Strength (% unaffected hand)	98.4 (89.9,107.3)	92.3 (79.7,103.3)
NHPT (% unaffected hand)	94.3 (86.0,105.3)	87.7 (69.4,94.8)
SDMT	1.0 (0.8,1.2)	0.8 (0.5,1.0)
HADS - Anxiety	4.0 (2.8,7.6)	9.0 (3.0,10.0)
HADS - Depression	4.0 (3.0,5.0)	7.0 (3.0,9.0)
Hemisphere Affected		
Left | Right	10 | 6	6 | 7
Type of Stroke		
Ischaemic | Hemorrhagic	14 | 2	12 | 1
Vascular Territory Affected		
ACA | MCA | PCA | Brainstem/Cerebellum	0 | 8 | 1 | 3	1 | 8 | 1 | 3
Time Post-Stroke (years)	5.3 (4.2,6.8)	7.4 (5.4,11.1)

[1]Median (25%,75%); n

Table 1. Demographics of the high and low fatigue groups that took part in the study. The median and interquartile range is shown for continuous variables, while the count is shown for categorical variables. NHPT = Nine Hole Peg Test, SDMT = Symbol Digit Modalities Test, HADS = Hospital Anxiety and Depression Scale, ACA = Anterior Cerebral Artery, MCA = Middle Cerebral Artery, PCA = Posterior Cerebral Artery.

	Fatigue Group		
Tone Type	Low, N = 16[1]	High, N = 13[1]	p-value[2]
Standard	445.94 (14.06)	443.62 (15.76)	0.6
Standard with Noise	439.75 (25.40)	444.92 (23.62)	0.9
Target	70.44 (1.90)	70.23 (3.03)	0.8
Target with Noise	67.69 (6.39)	70.92 (2.10)	0.093
Novel	71.06 (1.34)	70.15 (2.85)	0.7
Novel with Noise	69.56 (4.35)	70.69 (2.69)	0.9

[1]Mean (SD)

[2]Wilcoxon rank sum test

Table 2. Number of trials for each condition across the two fatigue groups. The mean number of trials and the standard deviation across each condition, as well as the p-value for the difference between the two groups is shown.