Steady-state visual evoked potentials are unchanged following physical and cognitive exertion paradigms

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Abstract

**Background:** There is a need for objective biomarkers of sports-related concussion that are unaffected by physical and cognitive exertion. Electroencephalography-based biomarkers such as steady-state visually evoked potentials (SSVEPs) have been proposed as one such biomarker. The aim of this study was to investigate the effects of cognitive and physical exertion on SSVEP signal-to-noise ratio (SNR).

**Methods:** This study involved two experiments. The first experiment was performed in a controlled laboratory environment and involved a treadmill run designed to induce physical fatigue and a Stroop task designed to induce mental fatigue, completed in a randomized order on two separate visits. SSVEPs were evoked using a 15-Hz strobe using a Nurochek headset before and after each task. Changes in the 15-Hz SSVEP SNR and self-reported fatigue (visual analog scales) were assessed. In the second experiment, SSVEP SNR was measured before and after real-world boxing matches. Paired t-tests compared pre- and post-task SSVEP SNR and fatigue scores.

**Results:** Eighteen participants were recruited for experiment 1. Following the treadmill run, participants reported higher physical fatigue, mental fatigue, and overall fatigue ($p \leq 0.005; d \geq 0.90$). Following the Stroop task, participants reported higher mental fatigue and overall fatigue ($p < 0.001; d \geq 1.16$), but not physical fatigue. SSVEP SNR scores were unchanged following either the Stroop task ($p = 0.059$) or the treadmill task ($p = 0.590$). Seven participants were recruited for experiment 2. SSVEP SNR scores were unchanged following the boxing matches ($p = 0.967$).

**Conclusions:** The results of both experiments demonstrate that SSVEP SNR scores were not different following the treadmill run, Stroop task or amateur boxing match. These findings provide preliminary evidence that SSVEP fidelity may not be significantly affected by physical and cognitive exertion paradigms.

**Keywords**
Biomarker, EEG, electroencephalography, fatigue, sports-related concussion, SSVEP

Introduction

Mild traumatic brain injury, also known as concussion, is a common injury among adult and youth athletes. In the United States alone, there are an estimated 1.6 to 3.8 million sports-related concussions each year.1 Moreover, as many as 50% of sports-related concussions may go unreported.2 While the etiology of concussion is widely agreed upon, no single objective measure or combination of measures exist to diagnose concussion.2

In the acute evaluation of suspected sports-related concussions, healthcare providers have relied upon the Sport Concussion Assessment Tool (SCAT), King-Devick (KD) test, and the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) tool.3–5 These sideline assessment tools use some combination of neuropsychological testing to assess injured athletes for concussion and to monitor...
Though they provide rapid results, they are all fallible in some regard. Previous research shows that the results of both the SCAT and KD test may be confounded by physical or mental fatigue in the context of sports-related activities,\textsuperscript{4,6,7} while the ImPACT’s requirement for a baseline limits its implementation among athletes without previously established standards.\textsuperscript{8,9} These tests appraise neuropsychological function to assist healthcare providers in making a clinical assessment, but ultimately these methods of evaluation are subject to either player test performance or clinician interpretation. As such, there is a need to identify objective measures that are robust to the effects of fatigue and other confounders.

To remedy this, the use of blood- or neuroimaging-based biomarkers as objective assessment tools has been proposed as potential future biomarkers of concussion.\textsuperscript{10} Blood biomarkers might be used to detect both acute axonal injury and astroglial injury, notable sequelae of some sports-related injuries. For example, T-tau protein levels were found to increase following a sports-related concussion, in one study.\textsuperscript{11} Another example is the Banyan Brain Trauma Indicator, a blood test kit used to detect levels of UCH-L1 and GFAP, biomarkers associated with acute intracranial lesions observed on CT scans.\textsuperscript{12} However, although blood biomarkers show promise as objective assessment tools that may be useful in clinical decision making, current blood biomarkers do not provide real-time decision-making capability, which might be required for use in sports.

Electroencephalography (EEG) is one of several neuroimaging methods that have been used to measure the state of the brain in response to concussion. Previous studies have indicated a variety of quantitative EEG metrics may be sensitive to neurophysiological changes after concussion.\textsuperscript{13} More recently, steady-state visual evoked potentials (SSVEPs) have been identified as one potential EEG biomarker with a lower signal-to-noise ratio (SNR) observed in concussed rugby union players compared to baseline and following recovery.\textsuperscript{14} If the SSVEP is to be adopted as a biomarker of sports-related concussion, it is important to understand how various external factors may influence this measure. Previous studies have identified changes in SSVEPs during the performance of exercise.\textsuperscript{15,16} However, EEG-based biomarkers of concussion in real-world sporting contexts, such as sideline concussion assessment, would be recorded at rest following sports participation. Despite this, to the authors’ knowledge, there is no research regarding the effects of prior cognitive and physical exertion on resting-state SSVEPs.

The aim of this study was to evaluate the fidelity of resting-state SSVEPs following physically or cognitively demanding tasks. This involved two experiments. The first experiment measured SSVEPs before and after physically and cognitively fatiguing paradigms applied in a controlled laboratory environment. The second experiment measured SSVEPs before and after participation in a boxing match (i.e. real-world environment).

## Methods

### Experiment 1: Laboratory-based tasks

#### Experiment 1 - Participants. Eighteen healthy participants were recruited for experiment 1 (12 males and 6 females; 26 ± 5 years of age). One male participant completed the Stroop task but withdrew from the study for personal reasons prior to completing the treadmill running task (see below). Experiment 1 was conducted at the Department of Rehabilitation and Human Performance at Mount Sinai Hospital, New York. Exclusion criteria were known history of epilepsy or a seizure disorder, legal blindness in one or both eyes, or concussion or other head injury within the previous year. The Physical Activity Readiness Questionnaire was used to screen for adverse indications for exercise participation. Each participant provided written informed consent prior to this study, which was approved by the Icahn School of Medicine Institutional Review Board (#19-02167).

#### Experiment 1 - Protocol. Experiment 1 consisted of two visits approximately one week apart. In one visit, participants completed a treadmill run designed to be physically fatiguing. In the other visit, participants completed a computerized Stroop task designed to be cognitively fatiguing. The order of the two visits was randomly assigned for each participant using simple randomization.

For both visits, a baseline SSVEP measurement was recorded prior to completing the treadmill/Stroop task (see: SSVEP Protocol). Participants then self-reported their baseline physical fatigue, mental fatigue, and overall fatigue level on three separate visual analog scales (VAS), which required participants to mark a 100-mm line where 0 indicated “not at all fatigued” and 100 indicated “extremely fatigued.” Immediately following the treadmill/Stroop task, self-reported fatigue was reassessed using the VAS scales, and post-task SSVEPs were then recorded approximately 3 min after task completion.

#### Treadmill task. Participants completed a treadmill run during which they were asked to cover the greatest possible distance in 20 min. Participants completed a 10-min warm up of their preference immediately prior to the run. Participants self-selected the starting treadmill belt speed and were permitted to adjust the speed of the treadmill belt throughout the 20 min. Verbal and motivational feedback was provided when 5 min remained in the trial and water was available ad libitum. Heart rate was recorded during the final 30 s of the run.

#### SSVEP Protocol

- **Experiment 1 – Laboratory-based tasks**
  - Participants self-selected the starting treadmill belt speed and were permitted to adjust the speed of the treadmill belt throughout the 20 min. The Physical Activity Readiness Questionnaire was used to screen for adverse indications for exercise participation. Each participant provided written informed consent prior to this study, which was approved by the Icahn School of Medicine Institutional Review Board (#19-02167).
  - For both visits, a baseline SSVEP measurement was recorded prior to completing the treadmill/Stroop task (see: SSVEP Protocol). Participants then self-reported their baseline physical fatigue, mental fatigue, and overall fatigue level on three separate visual analog scales (VAS), which required participants to mark a 100-mm line where 0 indicated “not at all fatigued” and 100 indicated “extremely fatigued.” Immediately following the treadmill/Stroop task, self-reported fatigue was reassessed using the VAS scales, and post-task SSVEPs were then recorded approximately 3 min after task completion.

- **Treadmill task.** Participants completed a treadmill run during which they were asked to cover the greatest possible distance in 20 min. Participants completed a 10-min warm up of their preference immediately prior to the run. Participants self-selected the starting treadmill belt speed and were permitted to adjust the speed of the treadmill belt throughout the 20 min. Verbal and motivational feedback was provided when 5 min remained in the trial and water was available ad libitum. Heart rate was recorded during the final 30 s of the run.
Stroop task. Participants performed a computerized Stroop Task (Stroop, 1935) for 15 min. In this task, a series of color words (“red”, “blue”, or “green”) appeared on the screen in a randomly assigned font color (red, blue, or green). Participants were asked to press a response key corresponding to the font color of each word as quickly as possible. The task included both congruent and incongruent trials. Subsequent trials appeared immediately following each response key press.

Experiment 2: Real-world amateur boxing match

Experiment 2: Participants. Seven amateur boxers from a novice boxing program in Sydney, Australia, were recruited to participate in experiment 2 (7 males; 30 ± 9 years of age). Exclusion criteria were known history of epilepsy or a seizure disorder, legal blindness in one or both eyes, or concussion or other head injury within the previous year. Each participant provided written informed consent prior to this study, which was approved by the Bellberry Human Research Ethics Committee (#2018-10-891).

Experiment 2: Protocol. Each participant underwent an individual boxing match consisting of three two-minute rounds. The match was a scheduled exhibition at the end of a 12-week intensive program for novice boxers and was run in accordance with NSWABL (New South Wales Australian Boxing League) rules and regulations, with participants wearing headgear and 16 oz gloves for protection. A baseline SSVEP measurement was obtained for each participant within 2 h prior to the start of their boxing match. A post-match SSVEP measurement was obtained within 15 min following their match. All participants were medically cleared before and after their match by a licensed physician on the day of the match.

SSVEP protocol

All participants in both experiments underwent a standardized approach to SSVEP measurement. SSVEPs were recorded using Nurochek (Headsafe, Sydney, Australia), which is a hybrid EEG and visual stimulation device that measures the EEG signal from three electrodes over the occipital region of the brain (O1, O2 and Oz) in response to a 15 Hz stimulus displayed on a visor positioned over the eyes. Two parietal electrodes (P1 and P2) serve as the reference and ground respectively, with the system displaying impedance values in real time via a mobile application. Impedances of <15 kΩ were required at two of the three recording electrodes prior to initiating the stimulus. The visual stimulus is provided by 5 white LEDs arranged in a cross shape in front of each eye (10 LEDs total). The LEDs are simultaneously alternated between an on/off power state at 15 Hz, creating a flickering stimulus with a duty cycle of 50%. The construction of the visor ensures the LEDs are at a fixed distance to the eyes on each test.

The SSVEP stimulus was 30 s in duration and performed twice with an approximately 30 s rest between. EEG during the second 30 s series was recorded at a sampling frequency of 250 Hz. These recordings were filtered using a 5–35 Hz third-order Butterworth bandpass filter before being normalized by dividing each channel’s amplitude by its mean amplitude and multiplying by the mean amplitude of all three recording channels. The signals were then transformed into the frequency domain for analysis using a fast Fourier transform (2ⁿ+2 padding). The spectral resolution of the transformed signal was 0.01 Hz. The spectra of the three recording channels were then summed and SSVEP results were reported as the SNR, where the signal is amplitude at 15 Hz and the noise is mean amplitude across the 5–35 Hz window (Figure 1). All processing was performed automatically by the Nurochek.

Statistical analyses

Visualization of the data indicated a positive skew in both SSVEP SNR and VAS scores, which Shapiro-Wilk tests confirmed to be non-normally distributed. Subsequently, all SNR and VAS data were transformed using the square root function. Paired t-tests were then used to test for differences between pre- and post-task Nurochek and VAS values. To account for the multiple comparisons made using the three VAS scales (overall-, physical-, and mental-fatigue), these p-values were subjected to Bonferroni adjustments. Confidence intervals (95% CI) and effect sizes (Cohen’s d) were calculated alongside the t-tests. Pearson’s correlation coefficients (r) were also calculated between pre- and post-task measurements to gauge the reliability of the SSVEP SNR following the interventions of experiments 1 and 2. Absolute percentage change in SSVEP SNR was calculated for each participant using the untransformed data. Data are presented as mean ± standard deviation unless otherwise stated.

Results

Experiment 1: Laboratory-based tasks

Participants covered 3.6 ± 0.5 km during the 20-min treadmill run. Heart rate in the last 30 s of the run was 185 ± 12 beats per minute. In the Stroop task, mean reaction time was 828 ± 173 ms, with an accuracy of 96.0 ± 3.0%.

Both the treadmill running and Stroop tasks induced self-reported fatigue as measured by the VAS scales (Figure 2). Specifically, following the treadmill running task, participants reported higher VAS scores for overall fatigue ($t_{(16)} = 8.67$, 95% CI: 4.04–6.66; $p < 0.001$; $d = 2.10$), physical fatigue ($t_{(16)} = 10.8$, 95% CI: 4.56–6.78; $p < 0.001$; $d = 2.63$), and mental fatigue ($t_{(16)} = 3.77$, 95% CI: 1.95–3.30; $p < 0.001$; $d = 0.83$).
CI: 0.91–3.24; p = 0.005; d = 0.90). Following the Stroop task, participants reported higher overall fatigue (t(17) = 4.91, 95% confidence interval [CI]: 1.31–3.30; p < 0.001; Cohen’s d = 1.16) and mental fatigue (t(17) = 5.30, 95% CI: 1.76–4.10; p < 0.001; d = 1.25), but VAS scores for physical fatigue were unchanged (t(17) = 1.35; 95% CI: −0.22–0.99; p = 0.588; d = 0.32).

The SSVEP SNRs were not significantly different after either the treadmill running tasks (t(16) = 0.55; 95% CI: −0.29–0.49; p = 0.590; d = 0.13) or Stroop (t(17) = 2.02; 95% CI: −0.01–0.68; p = 0.059; d = 0.48) (Figure 3).

**Figure 1.** A processed EEG response. The combined response is the sum of the spectra from the three recording electrodes. SNR is calculated as the amplitude at 15 Hz divided by the mean amplitude between 5-35 Hz (dashed line). Presented results are from a representative EEG response (median SNR from all recordings across experiments 1 and 2).

**Figure 2.** Self-reported state of fatigue before and after the treadmill task (A) and Stroop task (B). Data are mean ± standard error.

**Figure 3.** SSVEP SNR before and after the treadmill task and Stroop task. Data are mean ± standard error.
Post-task SSVEP SNR values were moderately correlated with pre-task values following the treadmill run ($r = 0.61$) and Stroop task ($r = 0.33$). Absolute percentage change in SSVEP SNR was $53.0 \pm 40.2\%$ following the treadmill run and $62.5 \pm 46.0\%$ following the Stroop task.

**Experiment 2: Real-world amateur boxing match**

SSVEP SNR scores were not significantly different following the boxing matches ($t_{60} = -0.04$, 95% CI: $-0.99$–$0.96$; $p = 0.967$; $d = 0.02$; Figure 4). Post-match SSVEP SNR values were weakly correlated with pre-match values ($r = 0.26$). Absolute percentage change in SSVEP SNR was $49.7 \pm 31.4\%$ following the boxing match. No indication of concussion was present during the medical assessments of the attending physician.

**Discussion**

This study involved two experiments that evaluated the fidelity of SSVEPs following physically or cognitively demanding tasks. In experiment 1, we found that SSVEP SNR scores did not differ significantly following a maximal treadmill run or Stroop task in a controlled laboratory environment. In experiment 2, we found that SSVEP SNR scores were unchanged following an amateur boxing match. These results indicate that SSVEP SNR, which may be decreased in concussion, is robust to both physical and cognitive exertion, a necessary requirement for SSVEPs to serve as a biomarker of sports-related concussion.

The results from experiment 1 found no difference in SSVEP SNR following the maximal treadmill task. This is seemingly in contrast to previous studies that found increased SSVEP amplitude during physical activity compared to baseline measurements. Hocking found an increased amplitude and decreased latency of SSVEPs during a physically demanding treadmill task in a thermally strenuous environment. Similarly, Bullock and colleagues reported greater SSVEP amplitude in response to the presentation of an orientation discrimination task during both low- and high-intensity cycling exercise compared to rest. In contrast to these studies, our study compared SSVEP SNR at baseline to recordings taken minutes after the treadmill run to determine the fidelity of resting-state SSVEPs in response to the residual effects of physical activity. Collectively, these findings suggest that SSVEP responses may be more pronounced during physical activity than at rest, even when resting-state measurements are recorded shortly after vigorous physical activity.

Experiment 1 also found no significant difference in SSVEP SNR following the Stroop task. This is in contrast to two previous studies that found SSVEP SNR significantly decreased with accumulated fatigue during prolonged, continuous use of an SSVEP-based brain computer interface. Moreover, Peng and colleagues reported a significant correlation between participants’ subjective fatigue scores and changes in SSVEP SNR. However, in both of these studies, participants were exposed to prolonged periods of photic stimuli to control the brain computer interface. It is therefore unclear whether the duration of photic stimulation, duration of task, timing of SSVEP assessment (during brain computer interface control task compared to following the Stroop task), or a combination of these variables may have contributed to the difference in results versus experiment 1.

Experiment 2 found no changes in SSVEP SNR following the amateur boxing matches, despite the participants receiving impacts to the head. These results build upon one previous study that found no change in SSVEP SNR between baseline and retest scores recorded across the course of a rugby season (at an average of 32 days apart) for players that did not suffer a concussion between measurements. None of the participants in the real-world boxing experiment exhibited any clinical indication of concussion in the opinion of the attending sports physician.

Collectively, the results of experiments 1 and 2 indicate SSVEP SNR measurements may be unchanged following physical and cognitive exertion in both controlled and real-world environments. This is a crucial characteristic of any potential sports-related concussion biomarker that has been suggested to confound existing sideline assessments for concussion. For example, Lee and colleagues found that professional athletes reported more symptoms, committed more errors on the modified balance error scoring system, and required more time to complete the tandem gait test on the SCAT3 when examined following exercise. Fox et al. also found impaired performance on the balance error scoring system following both aerobic and anaerobic exercise. Conversely, Devilbiss and colleagues reported improved performance on both the standardized assessment of concussion component of the SCAT and the King-Devick test following a 1-mile run. Factors such as testing environment, testing instructions, sleep, and fatigue...
have also been shown to affect the validity of the ImPACT tool, another concussion assessment instrument. Moreover, clinicians have noted the phenomenon of “sandbagging” among athletes, characterized as providing suboptimal effort in order to return to their baseline cognitive scores and return to play more quickly, which might further decrease the validity of neurocognitive assessment batteries, and highlights the need for objective physiological biomarkers.

This study has some limitations that require consideration. The small sample size in experiment 2 was limited by the number of individuals participating in the boxing exhibition. The statistical power to detect difference between the repeated measures of SSVEP SNR would therefore have been limited for this experiment. We include these results here in combination with the results of experiment 1 and advise a cautious interpretation of the results of experiment 2 in isolation.

Although the results from experiment 1 found no significant difference between SSVEP SNR before and after the Stroop task, increases in SSVEP SNR were approaching significance for this paradigm. It is therefore conceivable that a greater cognitive exertion may have led to differences in the measured SSVEP SNR. In experiment 1, the Stroop task was performed for 15 min. While this duration of Stroop task participation may be sufficient to produce significant deficits in cognition, longer durations of Stroop task performance could have produced a more pronounced effect on SSVEP SNR. Further investigation involving longer durations of ecologically valid cognitively demanding tasks may therefore be required to determine their effects on SSVEP recordings.

Finally, although the results of this study may not be generalizable to all sporting contexts, the combination of the two experiments demonstrates that the results from the highly controlled laboratory exercises were replicated in the small number of participants in the real-world boxing match paradigm. These results showed that no systematic changes in SSVEP SNR were observed in either experiment, however, the results of both experiments also found absolute percentage changes in SSVEP SNR of approximately 50% and the correlation coefficients indicated poor reliability of repeat measurements following the interventions. Further research is necessary to determine the test-retest reliability of SSVEP signals (without intervention) before the reliability of SSVEP SNR following the interventions of experiments 1 and 2 can be fully interpreted. This might also be necessary before SSVEP-based biomarkers are included within sports-related concussion batteries.

In conclusion, this study found that the SSVEP SNR was not different following either physically or cognitively demanding laboratory tasks or following an amateur boxing match. While the utility of SSVEP-based biomarkers in sports-related concussion remains under investigation, it is necessary to understand how various factors including physical and cognitive exertion may influence this measure prior to adoption within sports-related concussion batteries.

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**Conflicts of interest**

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