EEG correlates of fatigue during administration of a neuropsychological test battery

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HIGHLIGHTS

- Prolonged administration of neuropsychological testing induces increased self-reported and performance-related fatigue.
- Modulation of EEG activity during neuropsychological testing is an index of fatigue rather than a training effect.
- Fatigue effect should be taken into consideration during administration of a neuropsychological test battery in clinical populations.

ABSTRACT

Objective: Mental fatigue, a poorly understood symptom of sports-related concussion, ideally requires assessment across multiple modalities. Our study aimed to examine mental fatigue effects among 10 neurologically normal, athletically active students undergoing typical concussion testing. It is our intention to ultimately address the question whether fatigue effects due to mild traumatic brain injury (mTBI) may become confounded with fatigue effects due to testing effort.
Methods: Fourteen athletically active and neurologically normal volunteers were initially recruited from Penn State University. Self-reported fatigue, neuropsychological performance, and electroencephalographic (EEG) activity were measured throughout the whole testing duration. EEG measures in frequency domain (e.g., relative power of theta, alpha, and beta bands) were examined over the course of neuropsychological (NP) test administration.
Results: Predicted fatigue effects over the course of testing included: (a) increased self-reported fatigue; (b) increased errors on the Stroop Interference Test; (c) significantly increased relative power of theta activity during the Stroop Interference Test in frontal–central and parietal regions; and (d) migration of alpha activation from the occipital to anterior (left parietal and pre-central) regions during the Stroop Interference task administered at the beginning compared with the end of testing.
Conclusions: Results supported predictions related to subjective fatigue and cognitive performance and offered partial support for predictions related to EEG activation patterns over the course of administering the NP testing.
Significance: Neurologically intact and athletically active college students demonstrate effects related to fatigue after undergoing a typical sports concussion assessment battery, including an increase in subjectively experienced fatigue, a decrease in cognitive task performance accuracy and associated modulations in EEG activity. This finding should be considered by clinical practitioners while evaluating the symptoms of concussion and making a decision regarding the return-to-sport participation.

1. Introduction

Fatigue is believed to be a gradual and cumulative process associated with a disinclination for effort, reduced efficiency and alertness, and impaired mental performance (Grandjean, 1970; cf: Lal and Craig, 2001). Mental fatigue is defined as a state of reduced mental alertness that impairs performance. Recently, several studies reported on the feasibility of measuring mental fatigue via participants' performance, based on EEG data in sustained attention experiments (Makeig and Jung, 1995; Makeig and Inlow, 1993; Lal and Craig, 2002; Jones and Harrison, 2001). More recently, advanced use of EEG to measure mental fatigue using multi-class

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support vector machines (SVM) with confidence estimates has been proposed (Shen et al., 2008). Although numerous physiological indicators are available to measure level of alertness, the EEG signal may be one of the most predictive and reliable.

A recent conference on sports concussion in Zurich (2008) emphasized the need to develop a better understanding of fatigue, a common symptom after sports concussion (McCrory et al., 2005; Moser et al., 2007). Guidelines for managing post-concussion fatigue increasingly have highlighted the need for refraining from both physical and mental exertion after concussion to prevent a return of symptoms and to allow brain functioning to recover (Gioia, 2008). Despite its frequency and importance as a symptom of brain injury, no comprehensive study of fatigue relevant to sports concussion has been conducted to date.

Fatigue may result from sleep deprivation, physical exhaustion, or boredom, among other factors. All of these processes share the feature of reduced activation or arousal in the central nervous system, which leads to decreased alertness and increased drowsiness (Lal and Craig, 2001). Fatigue can be characterized by a sensation of weariness, reduction in motivation, attenuation in efficiency, or impairments in vigilance and task performance (Grandjean, 1970; Mosso, 1904); it is a multidimensional construct with subjective, behavioral, and physiological components (Chaudhuri and Behan, 2004; DeLuca, 2007; Grandjean, 1970; Mosso, 1904). A comprehensive characterization of fatigue thus requires the assessment of all three domains.

In the assessment of different functional domains after sports concussion, self-reports are used to characterize the subjective experience of symptoms (Hutchison et al., 2009; McCrea et al., 2003), neuropsychological tests are used to measure cognitive functioning (Bellanger and Vanderploeg, 2005), and electroencephalographic activity (EEG) or cerebral blood flow (CBF) are used to characterize changes in neurophysiology (Chen et al., 2004; Dupuis et al., 2000; Nuwer et al., 2005). In sports concussion investigations, as well as other studies of mild traumatic brain injury caused by other factors, fatigue is typically evaluated in only one domain or, less commonly, in two domains simultaneously (Broglio and Puetz, 2008; Stulemeijer et al., 2006).

The only study to date that has evaluated post-concussion symptoms, including fatigue, across multiple modalities did not include a control group of non-injured, neurologically normal individuals (Thompson, 2007). This consideration becomes particularly important given that the neuropsychological test batteries used to identify post-concussion symptoms often require considerable cognitive effort, which can itself be fatiguing. Thus, fatigue effects due to brain injury may become confounded with fatigue effects due to testing effort. Evaluating a non-injured sample to establish a baseline for typical fatigue effects would represent an important first step in developing a better understanding of fatigue as a symptom among concussed athletes.

Characterizing possible fatigue effects that might arise during a neuropsychological concussion assessment battery requires not only the measurement of fatigue across multiple domains but the measurement, within each domain, of aspects relevant to such effects. In the domain of subjectively experienced fatigue, for example, widely used self-report measures for assessing fatigue exist (e.g., Fisk et al., 1994; Krupp et al., 1989; Stein et al., 2001; Whitehead, 2009). However, all of these measures elicit information about the experience of fatigue during daily activities. A better alternative for the assessment of more immediate effects of fatigue on neuropsychological test performance would involve assessing fatigue during the testing session.

Prior research on cognitive functioning has shown that fatigue disrupts lower-level cognitive processes such as alertness as well as higher-level cognitive processes involving executive functioning (Beebe et al., 2003; Durmer and Dinges, 2005). On neuropsycholog-

ical tests, increasing fatigue is associated with decrements in task performance, including increased error rate and decreased efficiency (Grandjean, 1970; Lal and Craig, 2001). Studies investigating fatigue have used tests requiring sustained attention, such as psychomotor vigilance tasks, as well as tests assessing executive function, like the Stroop test (Jones and Harrison, 2001; Lim and Dinges, 2008).

The Stroop test is especially relevant to investigating fatigue in sports concussion. First, it is widely used in concussion assessment batteries, where has been shown to be sensitive to concussion effects (Rosenbaum et al., 2006). Second, it calls upon both lower- and higher-level cognitive abilities, with the more automatic Word condition requiring the former, and the more effortful Interference condition requiring the latter.

In the physiological domain, changes in brain electrical activity or metabolic rate are often used to monitor fatigue. Although previous research has used a variety of physiological parameters to assess levels of alertness or fatigue, EEG continues to be among the most promising and reliable (Lal and Craig, 2001; Papadelis et al., 2007). The EEG signal represents postsynaptic cortical neuronal potentials, which summate in the cortex and are captured as they propagate through the scalp. This electrical activity in the brain is defined in terms of frequency bands, including delta (0–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–20 Hz). Different aspects of a specific frequency band can be measured, such as amplitude (power) and frequency (cycles per second) within the bandwidth (Stern et al., 2000).

Changes in EEG spectral activity during drowsiness, as well as in response to fluctuations in vigilance, have been long observed (De Gennaro et al., 2007; Loomis et al., 1937; Santamaria and Chiappa, 1987). In studies that have examined EEG patterns, the most consistent findings have been increases in delta and theta rhythms as drowsiness and fatigue build up, especially in frontal and central areas, and decreases in beta rhythms as alertness declines, especially in posterior regions (De Gennaro et al., 2007; Makeig and Jung, 1995; Matousek and Petersen, 1983; Lal and Craig, 2002; Santamaria and Chiappa, 1987; Tinguely et al., 2006). Increased theta activity, in particular, has been correlated with decrements in cognitive task performance (Corsi-Cabrera et al., 2003; Horváth et al., 1976; Makeig and Jung, 1995).

Findings related to alpha rhythms are less consistent. Investigators have found both decreases and increases in alpha activity with the onset of drowsiness and attenuation of alertness (Cajochen et al., 1995; Makeig and Jung, 1995; Torsvall and Akerstedt, 1987). The direction of change appears to depend upon various factors, including scalp recording site and time of measurement. One pattern commonly seen with drowsiness onset is the attenuation or disappearance of alpha activity in occipital areas accompanied or followed by the enhancement of alpha activity in central and frontal areas (Lal and Craig, 2001; Santamaria and Chiappa, 1987).

Incorporating the above considerations, we designed a study examining subjective, cognitive, and physiological indicators of fatigue in a nonconcussed, neurologically normal, and athletically active group of participants undergoing a typical neuropsychological concussion test battery. Our goal was to create a template for studying multimodal fatigue effects in the context of such an assessment that could then be applied to clinical populations, e.g., concussed individuals. We reasoned that, if multimodal fatigue effects were evident in this normal population, further study would be warranted in concussed athletes, given that such effects might be expected to be even more pronounced in these individuals who are known to be especially susceptible to fatigue.

Our study focused on fatigue as the main outcome variable across three domains. To capture the subjective experience of fatigue, we used a self-report measure that asks about fatigue experienced in relation to neuropsychological testing. To assess cognitive

or mental fatigue, we used the Stroop test, a neuropsychological task shown to be sensitive to concussion (Rosenbaum et al., 2006). To examine physiological changes related to fatigue, we administered the concussion assessment battery while recording EEG activity simultaneously, including theta, alpha, and beta bandwidths across four regions (frontal, central, parietal, and occipital) in both brain hemispheres.

After undergoing a typical 90-min assessment battery, we hypothesized that participants would show an increase in subjectively experienced fatigue from pretest to posttest on the self-report measure. On the neuropsychological measure, which was administered at three time points, we hypothesized that participants would show improved or maintained speed on both Stroop conditions due to practice effects, but that they would exhibit decreased accuracy due to fatigue only on the more effortful Interference condition. We further anticipated that participants would show changes in EEG power density or peak frequency from pretest to posttest contingent upon neuropsychological task, bandwidth, and brain region.

First, we expected participants to display increases in theta power in frontal and central regions from pretest to posttest under both Stroop conditions due to the effects of increasing fatigue, but we hypothesized that these effects would be more pronounced for the cognitively demanding Interference condition. Second, we expected participants to display decreases in beta peak frequency in posterior regions due to decreasing vigilance from pretest to posttest under both Stroop conditions, but again we hypothesized that these effects would be more pronounced for the Interference condition. Finally, we expected participants to show a pretest to posttest attenuation of occipital alpha power accompanied by a concomitant enhancement of alpha power in central and frontal areas under both Stroop conditions.

2. Method

2.1. Subjects

Data were collected from 14 athletically active and neurologically normal undergraduate students recruited from the Pennsylvania State University. Average age was 21.4 years ($SD = 1.3$) and average estimated IQ, based upon Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001) test scores, was 108.9 ($SD = 6.4$). The sample was 70% male and 30% female. The reported racial/ethnic composition was 70% Caucasian American, 10% African American, 10% Asian American, and 10% mixed. Overall, subject percentages can be presented as 10% multiples, given the usable sample consisted of 10 subjects. All participants had become involved in sports between ages 4 and 8 years old and had maintained their involvement, at either the recreational or collegiate level, as students at the university.

All participants were right-handed (Chapman and Chapman, 1987), and none were taking medications known to affect EEG measurement. We ensured that participants were neurologically normal through a telephone screening questionnaire. Participants were excluded if they reported a prior history of (a) traumatic brain injury, (b) learning disability or attention deficit hyperactivity disorder, (c) alcohol or drug abuse or dependence, (d) a neurological condition, or (e) a psychiatric disorder. Participants were also excluded if English was not their first language. All participants reported that they had slept 7–8 h the night before testing. Half of the subjects were tested between 10:00am and noon, and the other half were tested between noon and 2:00 pm. Subjects were requested to avoid taking any beverages containing caffeine at least 3 h prior to testing.

2.2. Measures and apparatus

2.2.1. Beatty Pretest and Posttest Fatigue Rating

The Beatty is a 16-item measure of cognitive fatigue (7 items), physical fatigue (8 items), and overall fatigue (1 item) which is administered before and after a neuropsychological test battery in order to determine how much change has occurred in these domains over the course of testing. For the pretest fatigue measure, items related to cognitive fatigue and physical fatigue are rated on a five-point Likert scale ranging from 1 (*not at all*) to 5 (*a great deal*). For the posttest fatigue measure, respondents rate how much difficulty they are having on these same items after testing has finished as compared to before testing started, using a five-point Likert scale ranging from 1 (*much less*) to 3 (*the same*) to 5 (*much more*). Dependent variables were cognitive, physical, and total fatigue raw scores at pretest and posttest.

2.2.2. The Stroop Neuropsychological Screening Test (Stroop; Trenerry et al., 1989)

The Stroop test is a measure of processing speed, attention, and cognitive control which assesses lower-level cognitive abilities, such as sustaining attention, as well as higher-level cognitive abilities, such as initiating or inhibiting responses, shifting between response modes, and monitoring cognitive performance. In the Word condition, participants are asked to read aloud 112 color words that are printed in colored ink. In the Interference condition, they are asked to state aloud the ink color in which the 112 color words are printed. Dependent variables were total time and total errors for the Word and Interference conditions.

2.3. EEG recording

EEG data were acquired using Ag/AgCl electrodes mounted in a 64 channels electrode helmet. This *Quik-Cap* elastic nylon cap holds 64 Ag–AgCL electrodes from Neuromedical Supplies, Sterling, VA. According to company reference/specs, the configuration of the electrode arrangement in the cap is based on the 10% system. Recording diameter is 6 mm and cavity depth is 5 mm for each electrode. Conducting gel (Electro-gel™, Electro-Cap International Inc., Eaton, OH) was injected into each electrode to connect the recording surface of the electrode with the scalp. The ground electrode was located 10% anterior to FZ, with linked earlobes serving as references, and impedances were kept below 5 kΩ. It should be noted that there is no 'gold standard' for reference electrode/sites in EEG studies. It is possible that the type of referencing (i.e., common reference, linked ears, linked mastoid, forehead, virtual reference free montage, etc. commonly reported in EEG literature) may influence topographical distribution of EEG signal. The EEG signals were amplified using a programmable DC coupled broadband SynAmps amplifier (NeuroScan, Inc., El Paso, TX). The EEG data were sampled at 250 Hz and then segmented in 500-ms epochs. Data were digitized and stored offline.

2.4. Procedures

Participants were recruited and screened by phone and informed that they would be reimbursed for their participation ($10/hour). If participants met inclusionary criteria and agreed to participate in the study, a testing appointment was scheduled. Neuropsychological testing and EEG recording were conducted by Ph.D.'s level graduate students.

Testing and recording took place in an electrically shielded experimental room. On the day of testing, the assessor reviewed study protocols with participants and obtained informed consent in accordance with Institutional Review Board guidelines. Participants were then asked to fill out questionnaires while they were

connected to the EEG monitor, which took approximately 30 min. They were instructed to limit eye, facial, and limb movements during testing and recording sessions. Neuropsychological testing commenced, with EEG activity recorded simultaneously and continuously throughout each test.

The neuropsychological test battery took approximately 90 min to complete. Participants were administered a measure of cognitive performance (Stroop) at the beginning, middle, and end of the battery, and a measure of subjective fatigue (Beatty) at the beginning and end of the battery. In addition to these measures, the battery included computerized tests and pencil-and-paper measures typically used in sports concussion: ImPACT, Hopkins Verbal Learning Test-Revised, Brief Visuospatial Memory Test-Revised, Trail Making Tests A & B, and the Computerized Assessment of Response Bias (CARB).

2.5. EEG data processing and analysis

To reduce the number of independent variables (Oken and Chiappa, 1986), we collapsed 62 EEG channels into four topographical regions of interest (frontal, central, parietal, and occipital) in each hemisphere: (a) frontal right (FP2, AF4, F6, F4, F2) and left (FP1, AF3, F5, F3, F1); (b) central right (FC6, FC4, FC2, C6, C4, C2, CP6, CP4, CP2) and left (FC5, FC3, FC1, C5, C3, C1, CP5, CP3, CP1); (c) parietal right (P6, P4, P2, PO6, PO4) and left (P5, P3, P1, PO5, PO3); and (d) occipital right (CB2, O2) and left (CB1, O1). We combined data for left and right hemispheres in each region as we were not predicting differential hemispheric activation. We excluded the temporal area and the delta bandwidth to reduce the chance of including muscle artifacts.

Data were processed offline with EEGLAB 5.03 software (Delorme and Makeig, 2004) using Matlab open source toolbox (Mathworks, Natick, USA). Epochs were baseline normalized and then visually screened for unique, nonstereotypic artifacts such as eye blinks, eye movements, heartbeats, and muscle activity, which were eliminated. To compute power spectra during cognitive testing, Fast Fourier Transform power calculations were performed within each epoch and then averaged across them for each frequency band (theta, alpha, and beta). To ensure homogeneous data processing, relative power for each frequency band was used instead of absolute power.

3. Results

Results from the fatigue rating scales and neuropsychological measures are shown in Table 1 and Fig. 1. A standard statistical t-test including degrees of freedom ($n = 9$ in parentheses) values
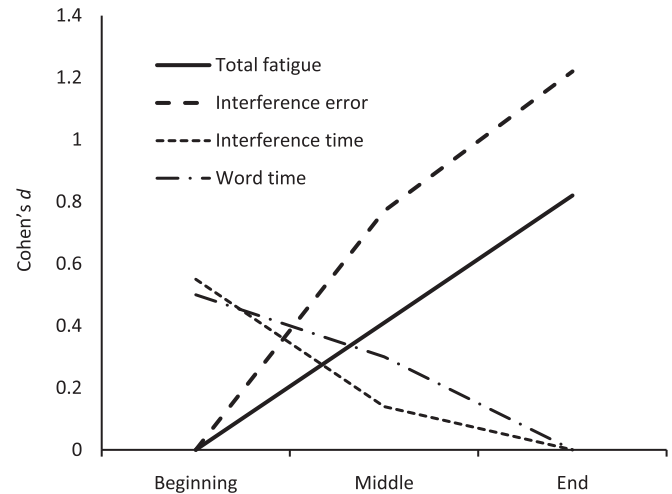
Fig. 1. Cohen's standardized differences (Cohen's d) at beginning, middle, and end of test battery for fatigue and neuropsychological performance variables. To show increasing or decreasing trends, Cohen's d was calculated for Beatty total fatigue (Total fatigue), Stroop Color-Word Interference total errors (Interference error), and total completion time for both Stroop Color-Word (Word time) and Color-Word Interference (Interference time) conditions. Note: To show the increasing trend in total fatigue and in total errors, Cohen's d was calculated using the formula (mean at other times – mean at beginning)/pooled standard deviation. To show the decreasing trend on total completion times, Cohen's d was calculated using the formula (mean at other times – mean at end)/pooled standard deviation.

was used to examine the differences in NP data as testing was progressed from pretest to post-test. Consistent with hypotheses, participants reported a significant increase in overall fatigue from pretest to posttest, $t(9) = 2.90$, $p < .05$. For the subscales, reported increases in physical fatigue were significant, $t(9) = 2.32$, $p < .05$, whereas reported increases in cognitive fatigue approached significance, $t(9) = 2.03$, $p = .07$. Also consistent with predictions, participants showed a significant decrease in time required to complete the task administered at the beginning compared with the end of the test battery on both the Stroop Word task, $t(9) = 3.15$, $p < .05$, and the Interference task, $t(9) = 3.36$, $p < .01$. Furthermore as expected, a significant increase occurred from the administration at the beginning compared with the end in total errors on the Interference task, $t(9) = 2.49$, $p < .05$, but not on the Word task, $t(9) = 1.40$, $p > .10$.

The results from EEG analyses are shown in Fig. 2. Consistent with predictions, there were significant changes in theta power activation during the Stroop Interference condition administered at the beginning compared with the end of the testing session in frontal, $F(2, 18) = 13.78$, $p < .01$, central, $F(2, 18) = 7.30$, $p < .01$, and parietal,

Table 1
Reported fatigue and neuropsychological test scores at pretest and posttest.

| Measure administered	Pretest	Posttest	Test statistic	
	M (SD)	M (SD)	t-test	p-value
Self-reported fatigue:				
Beatty Pretest and Posttest Fatigue Rating				
Cognitive fatigue	9.5 (2.8)	11.4 (4.7)	2.03	.073
Physical fatigue	10.9 (3.3)	13.7 (4.8)	2.32	**.046**[*]
Total fatigue	22.6 (6.1)	29.3 (10.3)	2.90	**.018**[*]
Neuropsychological test performance:				
Stroop Color-Word (Word) and Color-Word Interference (Interference)				
Word total time	50.9 (7.9)	47.3 (6.4)	3.15	.012[*]
Interference total time	101.4 (25.5)	88.4 (21.6)	3.36	**.008**[**]
Word total errors	0.0 (0.0)	0.3 (0.7)	1.40	>.10
Interference total errors	0.5 (0.7)	1.9 (1.6)	2.49	**.034**[*]

P values in Bold identified as significant.
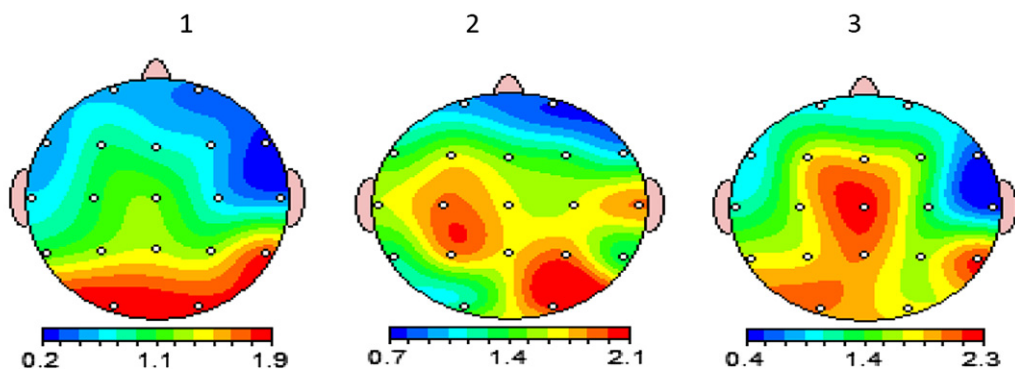[*] $p < .05$.
[**] $p < .01$..

(A) Theta Power (4- 7 Hz) Evolution from pre-test to post-test on Stroop Interference Condition
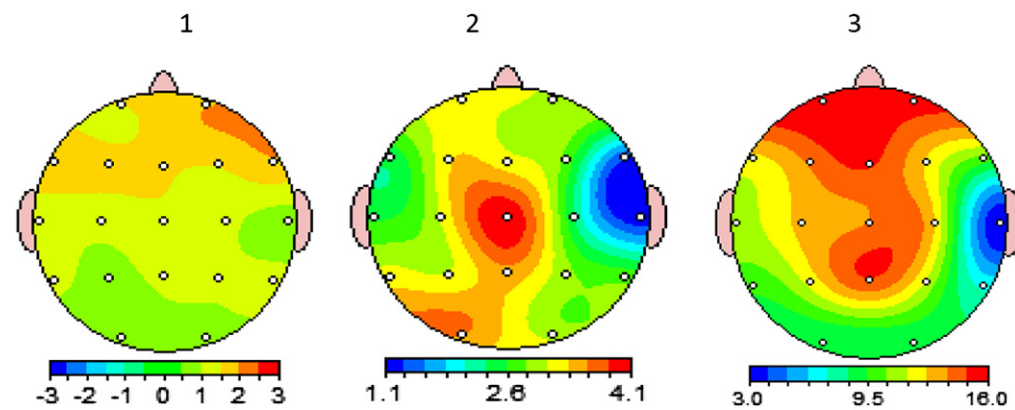
(B) Alpha Power (8-12 HZ) Evolution from pre-test to post-test on Stroop Interference Condition

Fig. 2. Topographical distribution of the Grand Averaged Evolution of theta (4–7 Hz) and alpha (8–12 Hz) EEG power during the Stroop Interference task administered at the beginning (1), middle (2), and at the end (3) of the testing battery. Note a progressive enhancement of theta power at frontal–central and parietal areas (A). Also notice a migration of alpha power from predominantly occipital areas during the Stroop test administered at the beginning of the battery, to anterior (left parietal and pre-central) regions when the Stroop was administered at the end of the battery (B). The maps were calculated using EEGLab adjusted for 19 footage sites on the scalp according 10% system.

$F(1.4, 12.5) = 5.16$, $p < .05$ areas. Effect sizes were greatest in frontal areas ($\eta^2 = .61$) and declined across central ($\eta^2 = .45$) and parietal ($\eta^2 = .36$) areas. As shown in Fig. 2, there was a significant increase of *theta* power during the Stroop Interference condition as the testing progressed. Specifically, this *theta* increment was obvious initially at central areas with further diffusion to frontal electrode sites. This finding is consistent with previous reports suggesting increase of *theta* power as a function of progressive mental fatigue (Makeig and Inlow, 1993). The effect across time for *theta* power was not significant during the Stroop Word condition.

For *beta* peak frequency, significant linear trends ($p < .05$) emerged in central and parietal regions for the Stroop Interference condition associated small effect sizes ($\eta^2 = .41$ and .32, respectively). Follow-up *t* tests showed significant decreases in *beta* peak frequency in both parietal, $t(9) = 2.42$, $p < .05$, and central, $t(9) = 2.69$, $p < .05$, areas from pretest to posttest. No significant changes in *beta* power occurred over time during the Stroop Word condition.

Alpha power showed a significant change in central, $F(1.3, 11.4) = 8.97$, $p < .01$, and parietal, $F(1.3, 11.4) = 22.91$, $p < .01$, regions during the Stroop Interference condition administered at the three time points, with a correspondingly large effect size in the parietal area, $\eta^2 = .70$, and a moderate effect size in the central area, $\eta^2 = .50$. Significant linear trends ($p < .05$) also appeared in frontal and occipital areas on this same task, but with somewhat smaller effect sizes ($\eta^2 = .34$ and .30 respectively). Follow-up *t* tests showed increases in *alpha* power in frontal, $t(9) = 2.46$, $p < .05$, and occipital, $t(9) = 2.58$, $p < .05$, regions during the Stroop Interference condition administered at the beginning compared with the end of the test battery. As displayed in Fig. 2, there was a shift of topographical distribution of alpha power from predominantly occipital areas to parietal and then to central areas with localized focus at the Cz electrode site. A similar pattern of *alpha* shift from posterior to anterior regions was previously suggested as an index of mental fatigue (Trejo et al., 1995). No significant increases in *alpha* power occurred for any regions on the Stroop Word condition.

4. Discussion

In this study, we examined subjective, cognitive, and physiological indicators of fatigue in a nonconcussed, neurologically normal sample of athletically active students undergoing a typical neuropsychological concussion assessment battery in conjunction with EEG recording. In support of the first hypothesis, participants reported a significant increase in subjectively experienced fatigue from pretest to posttest. In support of the second hypothesis, participants demonstrated significantly faster performance under both conditions of the Stroop task from pretest to posttest, but they exhibited significantly decreased accuracy on the more effortful Interference condition.

Predictions regarding EEG activity were partially supported. As predicted in the first hypothesis, participants showed significant increases in *theta* power in frontal and central regions from pretest to posttest under the more effortful Stroop Interference condition, with effect sizes increasing linearly from posterior to anterior regions. For the less effortful Word condition, *theta* power also increased significantly from pretest to posttest but only in frontal regions, and the effect size was less marked than for the Interference condition. As predicted in the second hypothesis, participants displayed significant decreases in *beta* peak frequency in posterior (parietal) regions from pretest to posttest. However, these changes were apparent only upon examining linear trends and follow-up tests, and they occurred only under the more effortful Interference condition and not under the less effortful Word condition.

Finally, as predicted in the third hypothesis, participants showed significant increases in *alpha* power in central areas but only under the Stroop Interference condition. Although they also displayed increases in frontal areas, these changes emerged only upon examining linear trends and follow-up tests. Furthermore, contrary to prediction, the greatest increases in *alpha* power appeared in parietal areas. Also contrary to prediction, participants actually showed a significant, albeit slight, increase in *alpha* power in occipital areas rather than the predicted pretest to posttest attenuation.

In this study we were concerned with decrement in cognitive functions arising from sustained mental work in a controlled laboratory experiment. We refer to these decrements as cognitive fatigue to distinguish them from effects of sleepiness, motivation, or practice effects (learning). We accept the definition of cognitive fatigue as the unwillingness of alert, motivated participants to continue performance of mental work (Trejo et al., 1995).

It may be argued that 90 min of neurocognitive assessment may not be sufficient to induce mental fatigue. However, it should be noted that in another EEG study, evidence of fatigue from sustained mental effort (sustained information processing for a 70-min intelligence test) induced EEG changes consistent with mental fatigue (Smith et al., 1999). Specifically, *theta* power increased most robustly at Fz electrode site. No changes were observed in *beta* power band. However, Kiroy et al. (1996) found an increase in both *theta* and *beta* power in participants who performed mental tasks, something that may reflect compensatory mechanisms for their low vigilance level.

A number of EEG studies have demonstrated increased *theta* power after mental effort, something that may reflect alteration of vigilance. However, basing such an interpretation on one EEG variable is unlikely to be as reliable as detecting simultaneous changes that occur at other frequency bands, as in our study. We added location of alteration concomitant with cognitive performance measures (Lal and Craig, 2002). Therefore, we analyzed EEG at various frequency bands, spatial locations, and also included behavioral data and subjective reports.

Alteration of *theta* should also be considered as a function of task difficulty. For example, increased frontal *theta* has been observed under conditions requiring more focused attention (Gevins et al., 1997) or time pressure (Slobounov et al., 2000). The Fm *theta* increases as a function of task difficulty and practice (Gevins et al., 1997). In essence, an Fm-theta peak of 6.5 Hz is the equivalent of the power of frontal , which was observed in a number of previous midline (Fz, Cz) thetaEEG studies. Specifically, an increase in visuomotor task complexity systematically induced the increase of Fm-theta power (Slobounov et al., 2000), similar to other cognitive (Smith et al., 1999) and visuomotor (Karni et al., 1998) tasks. Overall, it was suggested that midline Fm-theta might be a good index of task complexity, which is related with changes in focused attention during task performance. It should be noted, however, that practice should induce performance enhancement, unlike what oc-curred with our results, so changes in EEG were more likely to reflect fatigue, not practice effects.

An inverse relationship between *alpha* and task difficulty has been reported, and interpreted as *alpha* sensitivity to task difficulty, cortical idling or disengagement (Buzsaki, 2006). The subjective reports of increased fatigue available in our study, along with increased errors on the Stroop Interference task over time allow for greater clarity in interpretation. Given these concomitant reports it seems most likely that the increased *alpha* in anterior regions that occurred on the Stroop from the beginning to the end of the battery would seem to be most likely due to increased fatigue.

The degree of convergence between initial hypotheses and experimental results supports several conclusions. First, neurologically intact and athletically active college students demonstrate effects related to fatigue after undergoing a typical sports concussion assessment battery, including an increase in subjectively experienced fatigue and a decrease in cognitive task performance accuracy, as has been found in other studies (Beebe et al., 2003; Grandjean, 1970; Lim and Dinges, 2008). Also as shown in prior work, changes in EEG activity associated with increasing fatigue and decreasing alertness appear after undergoing such a battery, including an increase in frontal *theta* power and a concomitant decrease in posterior *beta* peak frequency (Corsi-Cabrera et al., 2003; Horváth et al., 1976; Lal and Craig, 2002; Makeig and Jung, 1995). Although participants reported a slightly greater increase in physical than cognitive fatigue from pretest to posttest, this difference was extremely small and not likely to be meaningful.

A second conclusion from our work is that the Stroop Interference condition, like other executive functioning tasks, appears to be differentially sensitive to fatigue effects (Beebe et al., 2003; Jones and Harrison, 2001). Performance accuracy declined significantly from pretest to posttest only under the more effortful Stroop Interference condition but not under the less effortful Word condition. The differential effects of fatigue on these two tasks were further borne out by different EEG activation patterns during them. Under the Interference condition, *theta* power, which is associated with fatigue, increased to a significantly greater degree in frontal, central, and even parietal regions. On the Word condition, however, it increased only in frontal areas and to a much lesser degree.

A third inference from our study relates to the decrease in *beta* peak frequency in parietal regions that emerged on the Interference task but not on the Word task. Although contrary to our prediction, this finding is consistent with the idea that the Interference task is more sensitive to effects associated with decreasing alertness. Whereas the Word task is overlearned and largely automatic, and thus may be less susceptible to declines in vigilance, the Interference task is both novel and cognitively demanding, and thus may be more susceptible to decreasing alertness. These findings may have particular relevance when attempting to use neuropsychological tasks along with EEG recording to better characterize fatigue as a symptom in sports concussion.

Differences in task-related demands might also explain the Stroop-related activation patterns for *alpha* power, which were the least supported of our hypotheses. Rather than decreasing in occipital areas while simultaneously or subsequently increasing in frontal and central areas, as we predicted for our participants and as commonly occurs with the onset of fatigue (Lal and Craig, 2001; Santamaria and Chiappa, 1987), *alpha* power increased across all four topographical regions, with the greatest increases in parietal followed by central areas. However, these increases occurred only under the Stroop Interference condition.

In conclusion, the results of our study offer evidence that non-concussed and athletically active students experience the effects of increased fatigue in multiple modalities, including subjective, cognitive, and physiological domains, over the course of a sports concussion assessment battery. Fatigue effects should thus be

taken into account – either controlled for or further explored – when administering similar test batteries to concussed athletes. With this examination, we hope to provide an initial reference point for interpreting fatigue effects in future multimodal studies examining this symptom in concussed college athletes.

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