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Research Report

Effect of cognitive load on eye-target synchronization during smooth pursuit eye movement

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ABSTRACT

In mild traumatic brain injury (mTBI), the fiber tracts that connect the frontal cortex with the cerebellum may suffer shear damage, leading to attention deficits and performance variability. This damage also disrupts the enhancement of eye-target synchronization that can be affected by cognitive load when subjects are tested using a concurrent eye-tracking test and word-recall test. We investigated the effect of cognitive load on eye-target synchronization in normal and mTBI patients using the nonlinear dynamical technique of stochastic phase synchronization. Results demonstrate that eye-target synchronization was negatively affected by cognitive load in mTBI subjects. In contrast, eye-target synchronization improved under intermediate cognitive load in young (≤40 years old) normal subjects.

1. Introduction

Although mild traumatic brain injury (mTBI) affects millions of people, most methods used for its diagnosis are relatively unreliable. This poses a serious clinical problem, since early pathological identification of mTBI is critical for appropriate treatment of the patient. Variability in how normal and mTBI subjects can track a moving target, and how this tracking is affected by engaging the subject's attention, may provide crucial clues to the differences in brain function between injured and non-injured populations. Recent results (Contreras et al., 2008) suggest that the nonlinear-dynamics-based technique of stochastic phase synchronization, applied to human visual pursuit of a moving target, may provide a powerful aid in this investigation.

Smooth pursuit eye movement (SPEM) is a voluntary behavior that becomes active when a moving target appears in the visual field. Abundant previous research in this area supports the fact that SPEM and attentional processes have a shared neural substrate (Chen et al., 2002; Hultsch and MacDonald. 2004; Hutton and Tegally, 2005; Kowler, 1989; Van Donkelaar and Drew, 2002). The frontal areas of the brain, such as frontal eye fields, supplementary eye fields, prefrontal cortex, and parietal cortex, which are actively implicated in attention, are also directly connected to the cerebellum, one of the brain regions that directly control SPEM. These cortico-

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cerebellar connections are not only the longest white matter tracts of the brain but are also believed to be among the most vulnerable tracts to mTBI. Studies have shown that mild traumatic brain injury correlates with attentional deficits, as well as higher variability in the performance of SPEM (Dockree et al., 2006; Robertson et al., 1997; Suh et al., 2006a, 2006b; Maruta et al., 2010; Vanderploeg et al., 2005; Van Donkelaar and Drew, 2002).

The effect of working recall memory load, which requires time-to-time attention, on eye tracking (Suh et al., 2008) as well as on other behavioral performance (Hetherington et al., 1996; Hultsch and MacDonald, 2004; Stuss et al., 1994) has recently been investigated, using a technique based on performance variability. The results support the hypothesis that SPEM and cognitive performance have an interdependent relationship. However, this method might leave unattended useful information about the dynamics of eye-target synchronization.

Any two systems in nature that oscillate, and are coupled to each other, are capable of becoming entrained, or synchronized. This phenomenon was studied as early as the seventeenth century by Christian Huygens, who noticed the synchronization of two pendulum clocks hung from the same beam in a room. More recently, a host of oscillating, coupled systems have been studied in biology, ranging from the firing of neurons or cardiac myocytes to periodic gene expression and circadian rhythms. As awareness of synchronization in biological oscillators — and of its role in both normal and pathological processes — has grown, the nonlinear dynamics community has developed tools for quantifying synchronization (Pikovsky et al., 2001), and these tools have been increasingly applied by the biological community. A particularly powerful approach has been to study the *stochastic phase synchronization* between two oscillators. This approach considers the phase difference between two oscillators, and extends the idea of synchrony to include oscillators which are not in phase, but maintain a relatively fixed phase difference. This phase difference will fluctuate in any real system, particularly a biological one (hence "stochastic"). As discussed in more detail below, this synchrony can be quantified by a measure called the synchronization index, which describes how constant the phase difference remains during some time interval: in essence, providing the dispersion of phase values between the oscillators. A narrow distribution of phase differences corresponds to well-synchronized oscillators, whereas a broad distribution indicates relatively poor synchronization.

In the present paper, stochastic phase synchronization is applied to the concurrent eye tracking and word-recall test in order to obtain further insight into the dynamics of attention. This approach has been applied to study other neurological pathologies, such as Parkinson's disease (Gross et al., 2000; Pikovsky et al. 2001; Tass et al., 1998, 2003) and epilepsy (Bahar, 2004; Takeshita et al., 2007).

Stochastic phase synchronization is particularly powerful for highlighting rapid changes in synchronization, such as those induced by fatigue in mTBI patients during SPEM (Contreras et al., 2008). In addition, the technique can reveal

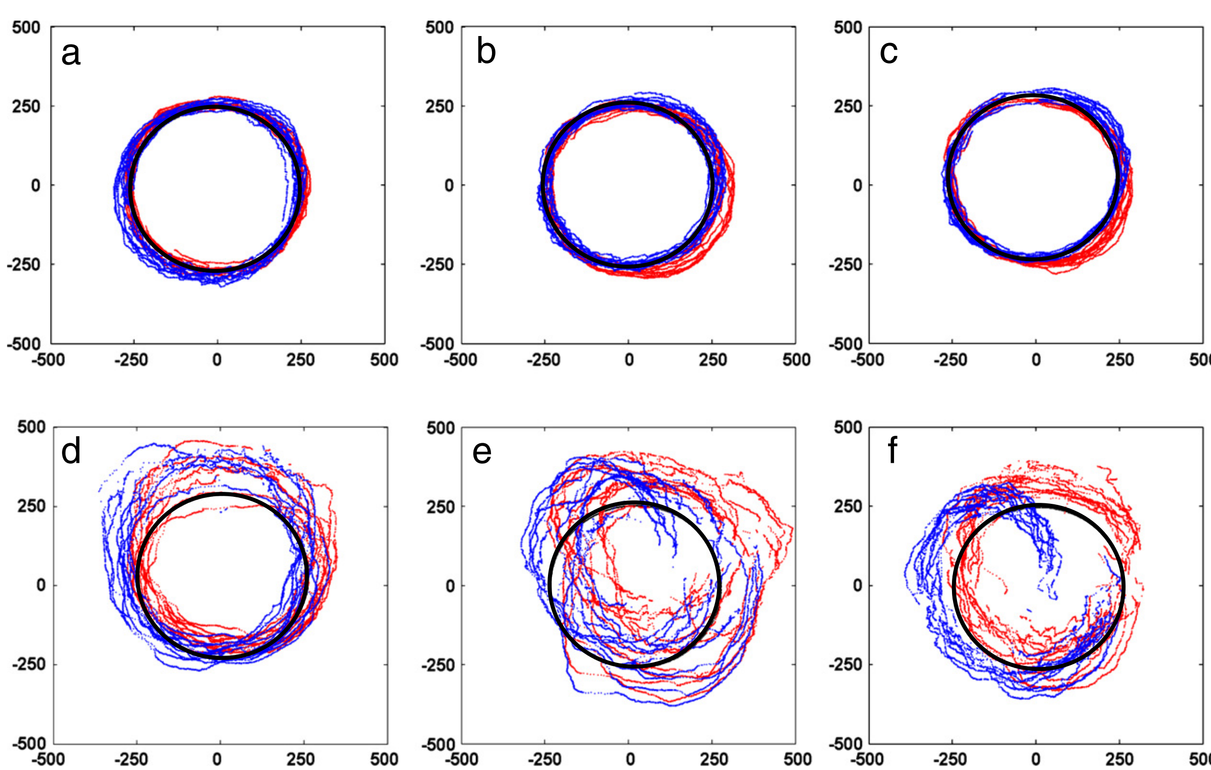

Fig. 1 – Eye trajectories for various cognitive loads for a normal subject (a–c) and an mTBI patient (d–f). (a,d) No cognitive load; (b,e) 1 word; (c,f) 5 words. Black circles represent the target trajectory. Red trajectories correspond to right eye movement and blue to left eye.

subtle differences in attentional response that other techniques might be unable to capture. For example, while a study based on velocity error (VE) (Suh et al., 2008) found no correlation between age and variability in VE, a synchronization-based study (Contreras et al., 2008) showed significant differences in behavior between younger and older subgroups of control subjects, suggesting an effect of age on SPEM performance. In the present paper, we use this technique to investigate the effects of cognitive load on SPEM in normal and mTBI subjects. Due to the age effects just mentioned, we restrict the present study to subjects aged 40 years and younger, for both control subjects and mTBI patient groups.

2. Results

2.1. *Effects of cognitive load on eye-target synchrony in normal subjects and mTBI patients*

Typical eye movement paths followed by a control subject and an mTBI patient are shown in Fig. 1, in order to illustrate the range of behaviors under various cognitive loads. The mTBI group recalled 0.9 ± 0.3 words for the 1-word recall condition, and 3.9 ± 1.2 words for the 5-word recall condition. The normal group recalled 1 ± 0 word for 1-word recall condition, and 4.4 ± 0.7 words for the 5-word recall condition. Statistical comparison cannot be made for the 1-word condition, since the standard deviation for the normal group's performance is zero; however, performance appears to be well matched between groups, with all but one of the mTBI patients recalling 1/1 words. For the 5-word condition, there was no statistically significant difference in performance between the groups ($p = 0.3673$, Mann–Whitney). Note that word-recall data was available only for 10 of the 12 normal subjects, and thus, for this comparison, $N = 12$ for the mTBI group and $N = 10$ for the normal group.

Synchronization indices between eye position and target position were determined for all subjects. As shown in Table 1, and discussed further below, the synchronization of each eye's horizontal coordinate and the horizontal coordinate of the target was calculated; likewise, we calculated the synchronization index between the vertical coordinates of the eye and the target. Moreover, due to the fatigue effects observed by Contreras et al. (2008), synchronization indices were calculated separately for the first and second halves of each trial. Thus "X1" represents the synchronization between the horizontal eye and target positions during the first half of a trial, and "X2" represents the second half of the trial. For each group, 12 subjects were studied; data from each eye was recorded, and thus $N = 24$ for each group. Unless explicitly stated, all analyses discussed below concern the first half of each trial in order to avoid fatigue effects during the test (see Section 2.3).

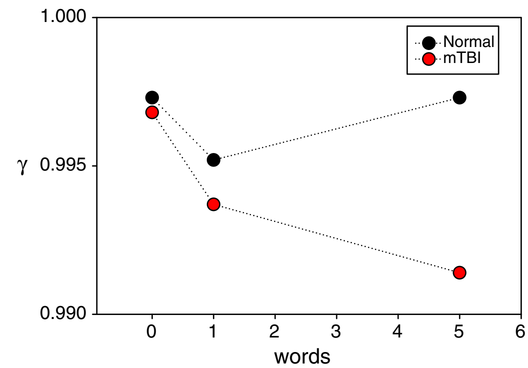

Fig. 2 – Median synchronization index γ as a function of cognitive load for normal subjects and mTBI patients. Error bars show standard deviation.

For each condition in the horizontal component, both the mean and median values of the synchronization index for the horizontal direction were larger for the normal subjects than were the corresponding values for mTBI patients. The median values of synchronization indices for the horizontal components are shown in Fig. 2. A Mann–Whitney test comparing the synchronization indices between the two groups showed a statistically significant difference for the horizontal coordinate at 5 words ($p = 0.0005$, U-statistic 119.0), as well as for the vertical component at 1 word ($p = 0.0490$, U-statistic 192.0) and at 5 words ($p = 0.0006$, U-statistic 122.00). For the vertical component at 1 word, however, the mTBI subjects outperformed the normal subjects, as measured by the mean synchronization index (normal, 0.9412 vs. mTBI, 0.9459), though the median index was greater for the normal subjects

Table 1 – Synchronization indices for normal subjects and mTBI patients. N = 12 for each subject group.

	Mean 0 w	Median 0 w	Std 0 w	Mean 1 w	Median 1 w	Std 1 w	Mean 5 w	Median 5 w	Std 5 w
Normal subjects									
X1	0.9872	0.9973	0.03528	0.9933	0.9952	0.006957	0.9965	0.9973	0.003236
X2	0.9843	0.9956	0.03532	0.9924	0.9961	0.007934	0.9949	0.9955	0.005288
Y1	0.9469	0.9884	0.08448	0.9412	0.9877	0.1545	0.9622	0.9906	0.09022
Y2	0.9429	0.9850	0.1302	0.9125	0.9888	0.2254	0.9497	0.9853	0.1295
TBI patients									
X1	0.9809	0.9968	0.06717	0.9807	0.9937	0.04798	0.9849	0.9914	0.02257
X2	0.9495	0.9959	0.1902	0.9784	0.9936	0.04241	0.9818	0.9921	0.02368
Y1	0.9734	0.9820	0.02717	0.9459	0.9811	0.09044	0.9387	0.9622	0.06637
Y2	0.9485	0.9771	0.09038	0.9452	0.9797	0.08738	0.9578	0.9725	0.03744

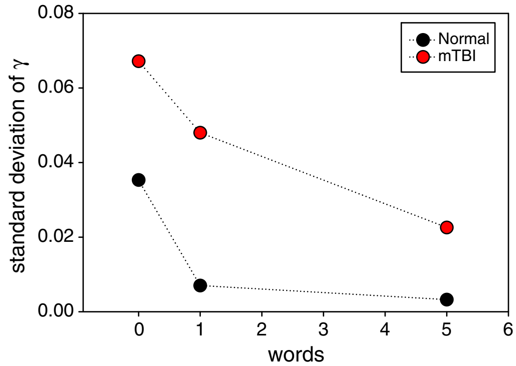

Fig. 3 – Standard deviation of synchronization index γ for normal subjects and mTBI patients.

(normal, 0.9877 vs. mTBI, 0.9811). For the 5-word condition, the normal subjects strongly outperformed the mTBI patients, in both horizontal and vertical directions, and as measured by both mean and median values.

As shown in Fig. 3, the standard deviation within groups diminishes as a function of cognitive load. The normal subjects achieve consistently lower values in all cases, although the trend is the same in both groups. This result suggests that *higher cognitive load provides a consistently more reliable measure of synchronization*.

What of the effect of cognitive load itself, within each group? A Friedman test (nonparametric repeated measures ANOVA) performed on mTBI patients to compare their performance at different cognitive loads of both components reveals that memory tasks have a detrimental impact on their performance in both the horizontal ($p=0.0007$) and vertical ($p=0.0015$) directions. Note that, as with the results discussed in Figs. 2 and 3, this analysis was performed on data from the first half of each trial, in order to disallow possible fatigue effects.

For normal subjects, while inspection of the trend in Fig. 2 suggests that cognitive load might increase the subjects' performance, a Friedman test shows no significant results, giving $p=0.1353$, (Friedman statistic 4.00) for the horizontal direction (data shown in Fig. 2) and $p=0.8825$ (Friedman statistic 0.25) for the vertical direction. A different approach, however, does reveal a cognitive load effect in normal subjects. A Wilcoxon matched-pairs test, applied to the *improvement* in synchronization, $(\gamma_i-\gamma_0)/\gamma_0$, with i the number of words and γ_0 the synchronization index under zero cognitive load, shows that the improvement in performance at $i=5$ is significantly greater than the improvement when $i=1$ ($p=0.0072$). For the vertical component, the difference between these performance changes is insignificant (Wilcoxon matched-pairs, $p=0.3478$).

2.2. *Horizontal vs. vertical component*

The results discussed above suggest a difference between the horizontal and vertical components of SPEM. This is borne out by a direct comparison of synchronization in the two directions within subject groups (in contrast to the between-group comparisons discussed in Section 2.1 above). Figs. 4 and 5 show representative examples of phase difference histograms for the horizontal and vertical components, respectively. As discussed in Section 4.2 below, the sharpness of the peak

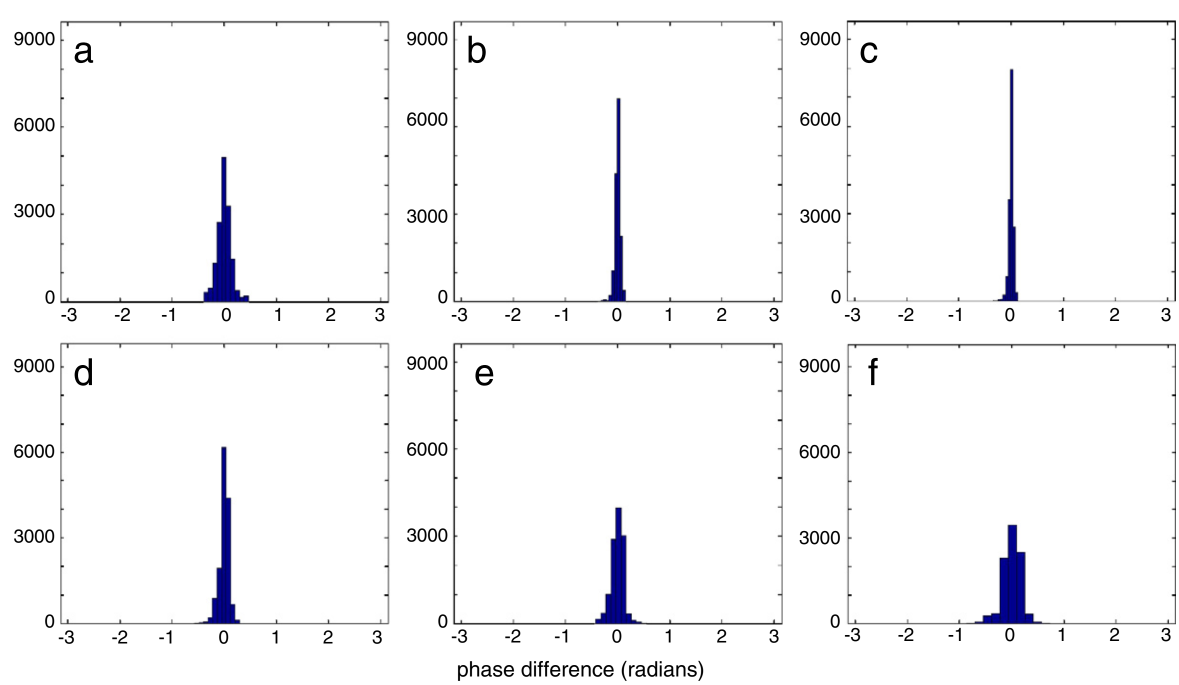

Fig. 4 – Phase difference histograms showing the phase differences between the horizontal component of eye movement and the horizontal component of target movement for a normal subject (a–c) and an mTBI patient (d–f). Histograms are shown for zero cognitive load (a,d), 1 word (b,e) and 5 words (c,f). Horizontal axes show phase differences from –π to π, and vertical axes show number of time points with a given phase difference.

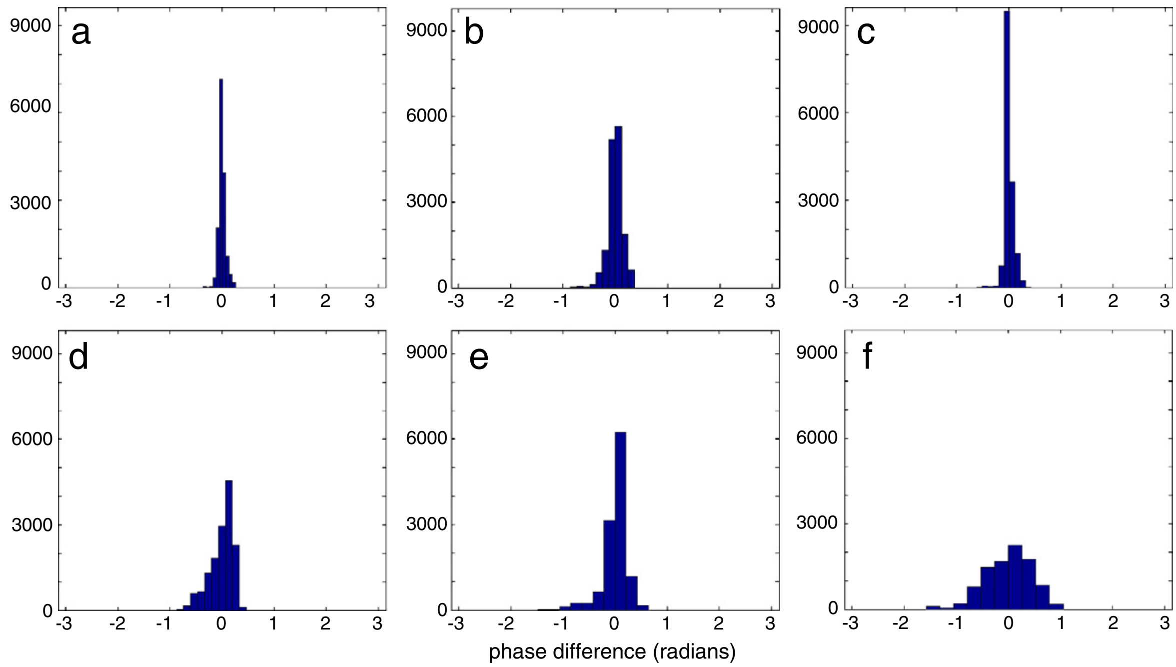

Fig. 5 – Phase difference histograms showing the phase differences between the vertical component of eye movement and the vertical component of target movement for a normal subject (a–c) and an mTBI patient (d–f). Histograms are shown for zero cognitive load (a,d), 1 word (b,e) and 5 words (c,f). Horizontal axes show phase differences from −π to π, and vertical axes show number of time points with a given phase difference.

in these histograms corresponds to the synchronization index γ. The horizontal histograms are typically much sharper than the corresponding vertical ones (i.e., γ closer to 1); this is seen most dramatically in the lower panels of Figs. 4 and 5, which correspond to mTBI subjects. As suggested by the examples shown in these figures, for normal subjects, eye-target phase synchronization in the x-direction was significantly greater than in the y-direction at all cognitive loads; 0 words ($p<0.0001$), 1 word ($p=0.0028$), and 5 words ($p<0.0001$) (Wilcoxon matched-pairs test). A similar result was found for the group of mTBI patients: 0-words ($p<0.0004$), and both 1-word and 5-words ($p<0.0001$). Thus, these results show that horizontal eye-target synchronization is significantly better than vertical for both normal and mTBI subjects. Moreover, the results imply that the detrimental effect of increasing cognitive load on the performance observed in mTBI patients has an even more severe impact in the vertical component.

2.3. *Fatigue effects*

The change in synchronization over time within each trial has different trends for both groups in the different cognitive load cases. In the 0-word task, the normal group shows significant reduction in synchronization between the first and second halves of each trial only in the horizontal direction ($p=0.0457$, Wilcoxon matched-pairs), while the mTBI group shows a significant drop in both directions, horizontal ($p=0.0491$) and vertical ($p=0.0395$). In the 1-word task, neither the vertical nor the horizontal component manifests a noticeable drop for mTBI patients, while normal subjects exhibit a drastic drop in the vertical component ($p=0.0002$). For the 5-word task, neither group showed a significant change in the horizontal component. In the vertical direction, the normal subjects do not exhibit a significant drop; however, the mTBI group exhibits a trend of improvement, which is not quite significant ($p=0.0646$).

2.4. *Comparison with traditional measures*

In order to validate the synchronization analysis results discussed above, it is important to compare them to more traditional approaches. Table 2 shows the velocity error (in deg/s) for normal subjects and mTBI patients. This measure is negatively correlated (often strongly so) with the synchronization index, as shown in Table 3. Thus, subjects with high velocity error have worse performance on SPEM, and therefore a lower synchronization index between eye and target than those with lower velocity error. It is observed that the results for mTBI subjects tend to show a stronger negative correlation than the results of normal subjects. In

Table 2 – Velocity error (in rad/s ± SD) for normal subjects and mTBI patients. N = 12 for mTBI patients, N = 10 for normal subjects.

	0 Words	1 Word	5 Words
Left eye			
Normal	7.42 ± 2.62	6.98 ± 2.19	6.12 ± 1.40
mTBI	8.57 ± 3.36	9.38 ± 3.61	10.64 ± 4.39
Right eye			
Normal	7.81 ± 3.08	7.39 ± 2.55	6.84 ± 1.58
mTBI	9.47 ± 4.43	10.25 ± 4.63	11.45 ± 4.75

Table 3 – Correlation coefficients between synchronization indices and velocity error. Two-tailed p-values are shown in italics; statistically significant values are in bold face.

	0 Words	1 Word	5 Word
Left eye			
Normal	**−0.7043 (*0.0230*)**	−0.6001 (*0.0667*)	−0.2155 (*0.5498*)
mTBI	−0.5550 (*0.0610*)	**−0.7633 (*0.0039*)**	**−0.7410 (*0.0058*)**
Right eye			
Normal	**−0.6969 (*0.0251*)**	−0.1525 (*0.6741*)	−0.4271 (*0.2183*)
mTBI	−0.4769 (*0.1170*)	**−0.8247 (*0.0010*)**	**−0.6536 (*0.0212*)**

addition to velocity error, the number of saccades (Table 4) also shows a strong negative correlation with synchronization index (Table 5), suggesting that increased saccadic eye motions negatively impact a subject's ability to synchronize with the movement of a target. These results indicate that synchronization analysis is at least a comparable method of assessing SPEM performance.

Comparison between subject groups, using traditional measures such as velocity error, show similar results to those presented above using synchronization measures. For example, comparison of velocity error, with a cognitive load of 1 word, between normal and mTBI populations gives $p = 0.0203$ (Mann–Whitney test, U-statistic 141.0), while for a load of 5 words we obtain $p = 0.0003$ (Mann–Whitney test, U-statistic 85.0). In both cases, mTBI subjects showed greater velocity error; $N = 24$ for the mTBI group, with each eye considered as an independent data set; $N = 20$ for the normal group.

3. Discussion

This study investigates and compares the effect of cognitive load on eye-target synchrony of normal and mTBI subjects by applying stochastic phase synchronization techniques. Our findings support the hypothesis that cognitive load is detrimental for eye-target synchrony of mTBI patients over time, but that it improves eye-target synchrony at higher cognitive load (5-words) for normal subjects, at least in the horizontal plane. This supports the idea that the concurrent application of SPEM and word-recall memory tasks may facilitate the activity of the shared frontal network, leading to enhanced eye-target synchrony. Disrupted cortico-cerebellar connections due to mTBI may contribute to the detrimental effects of cognitive load on both word-recall and SPEM. Further studies will require a larger subject pool and comparison with anatomical data, such as diffusion tensor imaging (DTI), which can reveal specific disruptions in cortico-cerebellar fiber tracts. It is possible that SPEM tasks with cognitive load may ultimately be of diagnostic use in the assessment of mTBI subjects, given the clear differences between normal and mTBI subjects, and the decreased within-group variability with cognitive load (Fig. 3).

Table 4 – Number of saccades (± SD) for normal subjects and mTBI patients. N = 12 for mTBI patients, N = 10 for normal subjects.

	0 Words	1 Word	5 Words
Left			
Normal	52.3 ± 28.4	41.1 ± 18.9	34.5 ± 12.4
mTBI	62.8 ± 24.2	57.3 ± 25.4	59.9 ± 18.9
Right eye			
Normal	65.3 ± 41.7	52.2 ± 28.6	40.6 ± 16.5
mTBI	69.1 ± 28.4	66.9 ± 24.2	75.3 ± 43.2

Table 5 – Correlation coefficients between synchronization indices and number of saccades. Two-tailed p-values are shown in italics; statistically significant values are in bold face.

	0 Words	1 Word	5 Words
Left eye			
Normal	−0.4637 (*0.1771*)	−0.3581 (*0.3096*)	−0.4982 (*0.1428*)
mTBI	**−0.7910 (*0.0022*)**	**−0.7718 (*0.0033*)**	−0.3131 (*0.3218*)
Right eye			
Normal	−0.5973 (*0.0682*)	−0.1708 (*0.6371*)	−0.1535 (*0.6721*)
mTBI	−0.1887 (*0.5570*)	**−0.7954 (*0.0020*)**	**−0.6064 (*0.0366*)**

Among the results shown above, we find that subjects perform smooth pursuit eye movement better in the horizontal than the vertical direction. It is known that different neural circuits control horizontal vs. vertical eye movements (Lencer and Trillinberg, 2008); it has been suggested that mammals may perform better in horizontal smooth pursuit since their daily experience typically involves more motion along this direction than along the vertical (Collewijn and Tamminga, 1984). Given these results and previous studies, it would be expected that stronger synchronization between the x-components of eye and target motion than between the y-components should be observed; this is indeed what is found in the data studied here.

A key observation, shown in Fig. 3, is the drop in variability as a function of cognitive load for both normal subjects and mTBI patients. We hypothesize that these results may be explained as follows. One of the hallmarks of mTBI patients is performance variability. This variability is apparent within a single mTBI patient's performance as well as across patients. Within a single patient, performance variability may be due to the disrupted cortico-cortical white matter tract and also to disruption of the cortico-cerebellar white matter tract. Most importantly, the connection between cortico-cortical and cortico-cerebellar regions is not *completely* severed following mild TBI, and therefore not all behavior is affected by the shearing injury. Thus, the mTBI's behavior can become stable at one moment and at the next moment the behavior becomes unstable, just as in young and aged (normal) individuals. However, when a greater cortical load is imposed upon the mTBI patient's disrupted neural network, the behavior just gets worse due to overload of the injured neural circuits. Thus, detrimental (rather than more highly variable) effects remain throughout the whole trial. Therefore, the mTBI's variability becomes smaller despite the deteriorating performance under increased cognitive load. On the other hand, normal subjects are under-challenged during the no-load condition (i.e., the task is too easy and it is more likely that they may become distracted), and therefore their behavior becomes variable due to less activated cortico-cortical and cortico-cerebellar networks. When the normal subjects experience increased cognitive load, their network becomes active because of increased level of attention demanded by the task. This increased attention is reflected in better performance of normal subjects under cognitive loads.

Synchronization analysis thus provides a powerful technique for teasing out the differences in performance between normal and mTBI subjects in an SPEM task with cognitive load. The analysis gives results similar to those obtainable using more traditional methods. However, synchronization analysis also provides additional information not obtainable from traditional approaches, since it allows the separation of eye trajectories into horizontal and vertical components. Since the brain processes horizontal and vertical eye movements through different circuits, it is possible that synchronization analysis may provide a finer tool for parsing performance variability in these populations. We suggest that it may ultimately become a useful addition to the suite of techniques for rapid assessment of mTBI in situations where medical imaging technology is not available.

4. Experimental procedures

4.1. Subjects

Twelve normal subjects and twelve mTBI patients were selected for the study. These two groups were matched in age (normal: 27.9±4.9 years old; mTBI: 29.7±7.3 years old, $p=0.5832$, Mann–Whitney test) and years of education (normal: 16.3±2.1 years; mTBI: 14.8±3.0 years, $p=0.3057$, Mann–Whitney test). Note that years of education data was available only for 10 of the 12 normal subjects, and thus for the comparison of years of education between the two populations, $N=12$ for the mTBI group and $N=10$ for the normal group.

In the selection process of mTBI patients to be included, the conditions required were blunt, isolated mTBI, presence of post-traumatic amnesia, no cranial nerve abnormalities (except those affecting the sense of smell), and non-intoxication. For the mTBI group, the average time since the head injury was 2.2± 1.8 years, ranging from a minimum of 0.1 years to a maximum of 5.4 years. The GCS (Glasgow Coma Scale) score of all mTBI subjects is 15 and the number of head injuries is limited to one.

The criteria for patient exclusion were based on previous mTBI with loss of consciousness for periods longer than 24 h, history of multiple mTBI with loss of consciousness, pregnancy, history of drug or alcohol abuse, pre-injury neurological or psychiatric diagnosis of an axis I or axis II disorder, general anesthesia within two weeks before testing, seizure following trauma, seizure disorders, and pre-injury use of psychotropic medication(s). Normal control subjects, with no history of head injury or head trauma and meeting the non-intoxication criterion, were recruited. All subjects gave written consent approved by the Weill Medical College of Cornell University Institutional Review Board committee.

4.2. Smooth pursuit eye movement and word-recall paradigm

For data acquisition, eye movements were recorded by a human infrared eye tracking system (Eyelink II, SR Research, Canada) with 500 Hz temporal resolution at the Citigroup Biomedical Imaging Center at Weill Medical College of Cornell University. The target visual stimulus, created using a Python program, was displayed on a computer screen 40 cm from the subject. Before testing, an eye chart was used to verify that all subjects had normal or corrected-to-normal vision. Subjects were seated in a darkened room, and their heads stabilized via a bite bar system. Calibration based on 9 points, including center and peripheral, was performed before each session, which ensured that all subjects had a full range of oculomotor movement. If subjects manifested signs of fatigue or discomfort, they were encouraged to pause testing, after which the session was resumed.

During the SPEM task, the subjects tracked a target stimulus, a red circle of 0.2° diameter, which followed a circular trajectory of 10° radius at a rate of 0.4 Hz, in the clockwise direction. Each trial had a duration of 30 s. Prior to synchronization analysis, saccades were removed from the recorded eye position time series if they satisfied the following criteria: $\omega > 0.5$ rad/s (~29 deg/s), $\alpha > 10$ rad/s^2 (~573 deg/s^2). Following identification of a saccade using angular velocity and acceleration criteria, the saccade was deleted if it had a duration of 20 ms$<\Delta t<$240 ms. A longer-duration event, even if it satisfied the velocity and acceleration criteria, was considered too long to be classifiable as a saccade, and was therefore retained in the data set. Following saccade removal, missing values were replaced using linear interpolation.

Cognitive load based on word-recall memory was added to the single SPEM task. This task was performed under two working memory load conditions, one and five words taken from the MRC Psycholinguistic Database, which were read by the experimenter to the participant, and the participant was instructed to remember the words, prior to the onset of the visual tracking task. Words were selected to form a relatively homogenous set by controlling their range with respect to frequency (350–400 on the Kucera–Francis scale), imageability (350–400 on the imageability rating scale), number of syllables (2–3), and familiarity (350–400 on the familiarity rating scale).

4.3. Synchronization analysis

In a previous work (Contreras et al., 2008), synchronization analysis was performed using a geometrical approach, by defining the phase directly as the angle of the time point on the circle, with the center of the target's orbit as reference. An alternative approach used here involves the separation of the horizontal and vertical components of the eye position, followed by calculation of the phase of each of these time series using a Hilbert transform. The synchronization of the x-component with the x-component of the target's motion, and that of the y-component with the corresponding component of the target position, can then be assessed separately. This is of particular interest since it is known that target tracking in the horizontal direction is more accurate than in the vertical direction (Collewijn and Tamminga, 1984), and that these two components of eye motion are controlled by different regions in the cerebellum (Lencer and Trillinberg, 2008).

In order to perform phase synchronization analysis, a Hilbert transform is applied to the time series of the x-component and, separately, to that of the y-component of the eye's position, and also to the components of the position of the target. All analysis was performed using custom-written in-house MATLAB (The MathWorks, Inc., US) code; the actual Hilbert transform itself was calculated using the internal MATLAB "hilbert" function. Specifically, given a time series S (t), its instantaneous phase is extracted by constructing its analytic signal

$$\zeta(t) = S(t) + iSH(t) \quad (1)$$

where

$$SH(t) = (\pi - 1)\int S(\tau) / (t - \tau)d\tau \quad (2)$$

is the Hilbert transform of S(t). Thus, the instantaneous phase of S(t) is defined as

$$\varphi(t) = Arctan(SH(t) / S(t)). \quad (3)$$

The phase difference between eye and target is

$$\Phi(t) = \varphi_r(t)–\varphi_e(t) \quad (4)$$

where $\varphi_r(t)$ is the phase of the target, and $\varphi_e(t)$ that of the eye.

Once the phase difference has been obtained, a synchronization index is obtained from the probability density of the phase differences over time. The histograms in Figs. 4 and 5 show examples of such probability densities. The intensity of the first Fourier mode of this density is given by

$$\gamma^2 = <\cos(\Phi(t))>^2 + <\sin(\Phi(t))>^2 \quad (5)$$

where $<\cos(\Phi(t))>$ and $<\sin(\Phi(t))>$ are time averages. From Eq. (5), the synchronization index γ is defined such that $0 \le \gamma \le 1$, where $\gamma=0$ indicates complete lack of synchronization, while $\gamma=1$ indicates a completely synchronized state. Thus, in Figs. 4 and 5, a sharper histogram peak indicates less variability of phase differences (meaning that the phase difference between eye and target remains relatively constant); this would correspond to a value of γ closer to 1. In contrast, a wider peak indicates more variability in the phase difference (meaning that their eye is tracking the target more poorly, and that the phase difference between eye and target undergoes large variations); this would correspond to a smaller value of γ.

4.4. *Oculomotor data analysis*

As described above in Section 4.2, the x- and y-positions of both eye and target were recorded at 500 Hz temporal resolution and smoothed. Only de-saccaded data were considered for eye velocity error calculation; saccade removal criteria for oculomotor data analysis were essentially identical to those given above in Section 4.2. Eye velocity error is defined as the difference between eye and target velocity, and was calculated in deg/s (Table 2). The number of saccades was also counted (Table 4). Note that eye velocity error data was available for N = 10 normal subjects, and for N = 12 mTBI patients.

4.5. *Statistical analysis*

All statistical evaluations were performed using INSTAT (GraphPad Software, Inc., US); for all tests used, the two-tailed p-value is stated. In all results given, N = 24 in both the normal and the mTBI data sets (considering data from each eye in each subject), unless otherwise stated. Likewise, N = 12 for statistical comparisons between subject populations, unless otherwise stated.

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