Convergence Peak Velocity: An Objective, Non-Invasive, Oculomotor-Based Biomarker for Mild Traumatic Brain Injury (mTBI)/Concussion

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ABSTRACT

Over the past decade, there has been a quest to discover an objective biomarker for detecting the presence of mild traumatic brain injury (mTBI)/concussion.¹ The motivation to do so has come from two primary directions. The first is the military theater related primarily to brain damage from improvised explosive devices (IEDs), and the second is the sports arena related to brain damage from head collisions.² Typically, invasive (e.g., serum levels) and/or costly and complex (e.g., fMRI/DTI) techniques have been proposed.³ While these, and others, may prove to be excellent biomarkers with respect to diagnostic test sensitivity and specificity, they are not too practical and/or rapid in their implementation and diagnostic analysis in many cases such as the battlefield or sports sidelines.

Over a similar time frame, the oculomotor system has received considerable attention, in part due to the constellation of related visual symptoms (e.g., difficulty reading, diplopia, eye tracking problems) reported by individuals with mTBI.² Two primary aspects of the oculomotor system have been extensively studied in this population. The first is conjugate, versional eye movement ability (e.g., fixation, saccades) used to track objects laterally in visual space, such as during visual scanning and reading.² The second, and most relevant here, is disjunctive vergence.

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eye movement ability used to track objects in depth binocularly, as well as to maintain accurate binocular fixation and fusion during sustained activities, in particular reading and other essential near tasks. Together, these two systems work in a coordinated manner to track objects at all distances and directions of gaze in visual space.

During the course of several laboratory investigations over the past decade, one oculomotor parameter in particular has stood out with great potential to be an objective, non-invasive biomarker for the presence of mTBI/concussion: convergence peak velocity (CPV). The CPV dominates the overall vergence response dynamics. There is a lawful relation between the CPV value and its correlated

Figure 1: Mean vergence peak velocity in mTBI versus normals.

Figure 2: Convergence and divergence responses in a control subject (top) and a patient with mTBI (bottom). RE = right eye, V = vergence.
response amplitude: as the response amplitude increases, the related CPV also increases in a non-linear manner. A reduced CPV value lying below this distribution reflects abnormal and impaired neurological control at a low hierarchical level, namely the midbrain. This parameter has been shown to be significantly reduced (~50%, 13 versus 24 degrees/sec for the tested amplitude) in all individuals tested having chronic mTBI/concussion, as compared to normals\textsuperscript{2,5} (Figure 1). This laboratory finding of reduced CPV is consistent with the clinical finding of reduced prism facility in the population, with both reflecting slowed vergence dynamic responsivity. Reduced peak (i.e., maximum) velocity leading to a slower overall vergence response time is evident in Figure 2. Shown here are convergence and divergence responses for both a normal individual and a representative patient with mTBI. The latter response time is approximately twice as long as found in the former (i.e., ~0.6 sec versus 1.3 sec). Furthermore, this reduced CPV is likely due to a reduced pulse component amplitude as part of the overall pulse-step neural controller signal for vergence. This is depicted in Figure 3. On the left panel is shown the vergence step stimulus and related normal pulse-step neural signal (not drawn to scale). In contrast, the pre-training mTBI pulse-step is shown in the middle panel. Note the relative reduction in pulse amplitude, thus responsible for the reduced vergence peak velocity in mTBI. As an aside, also note the more variable neural step component that is responsible for the increased steady-state vergence response variability. It is likely that this reduced pulse component is positively affected and increased by vision therapy per the process of improved temporal neural synchronization of the midbrain’s vergence cells, thus leading to a significantly increased CPV and a faster overall response. That is, as the neural cells fire over a shorter time period and are summated, the peak velocity is increased. This is evidenced in Figure 3 (right panel), as well as in Figure 4 depicting pre/post-training convergence and divergence responses in an individual with

![Figure 3: Neural pulse-step controller signal for vergence in a normal subject and in one with mTBI. Schematic representation of proposed condition and training effects, all as a function of relative time. Arrows show defective pulse (down arrow) and step (up arrow) components in mTBI pre-training. Post-training, the pulse height improves. The pulse height is exaggerated relative to the step for clarity.](image-url)
mTBI. The faster post-training responses are evident. To conceptualize this in more detail, the combination of pre/post-training responses and related velocity profiles are schematically represented in Figure 5. In the lower velocity profiles, note the larger amplitude and more compressed time course in the post-training versus pre-training condition. This is consistent with the aforementioned mechanism of improved neural synchronization of the firing of the midbrain’s vergence cells. Other possible mechanisms include overall reduced neural dynamics and a reduced number and/or strength of vergence-related synapses.

While CPV is similarly reduced in patients with convergence insufficiency (CI) but without mTBI, CI is only present in approximately 5% of the general population. Thus, a “false positive” during such testing would only occur in approximately 1 out of 20 suspected individuals tested (1/20 = 5%), which is highly acceptable per receiver operating characteristics (ROC) analyses and guidelines. The “true positive” rate would be about 95%, which is very high.

Figure 4: Convergence (top) and divergence (bottom) in an mTBI patient before (pre) and after (post) oculomotor-based vision therapy.
Testing could be implemented in at least two different scenarios. In the first, physical targets at two different distances (e.g., 33 cm and 20 cm) could be placed within a portable, video-based system (e.g., the “Right Eye” system) to record horizontal vergence eye movements in free space, along with a microprocessor to analyze and display the eye movement traces and their correlated peak velocities, with all being automated and with direct comparison to normative data. Such a system could be used at a military base for objective vergence assessment pre- and post-deployment, or even in an emergency room facility in the military theater for testing of the injured ambulatory soldiers. Such a compact, wearable device could be employed in a wide range of situations including the military setting, sports sidelines, emergency room, triage medical centers, general hospitals, optometric and medical practices, and sports testing/training facilities, and others.

A practical, objective, non-invasive test system for detecting the presence of an mTBI is not a dream for the distant future. It can be a reality in the clinical world of mTBI, with relatively little effort. Actually, the first proposed scenario already exists in several laboratories\(^4\)\(^-\)\(^7\) (Figure 6), so that testing could be immediate; the second proposed scenario would take a few months of intensive development to become a reality, albeit “virtual”. The technology to do so is readily available for direct application to improve diagnostic capabilities in the mTBI/concussion population, and hence improve their clinical vision care.
REFERENCES


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