**INTRODUCTION**

At the recent annual meeting of the American Academy of Optometry, the topic of mTBI/concussion and its visual sequelae was highly visible. There were several clinical continuing education lectures on its diagnosis and remediation, a research symposium in which the first author was the keynote speaker, another symposium based on the clinical and basic TBI research findings of two prominent Ezell Fellows, and lastly a research symposium on neuroplasticity that included traumatic brain injury. Clinical and research programs of this nature are great to advance the profession of optometry, as well as for rendering the highest quality care in patients with mTBI and related visual problems, which are many, and for whom can be helped by our profession.

A topic that was in the TBI “undercurrent” at the meeting was the search for ‘objective visual system biomarkers’ for mTBI/concussion. This has been, and continues to be, an area of intense interest and activity both by the military and civilian, clinical and research, groups.

Over the past few years, we and other research laboratories have proposed ‘clinical visual system biomarkers’ for the presence of mTBI/concussion, which by their nature are “subjective”, that is they are based on the patient response, and the observation and interpretation of the clinician. Some of these have included:

- the near point of convergence\(^1\)\(^-\)\(^3\)
- the amplitude of accommodation\(^4\),\(^5\)
- the King-Devick saccade test\(^6\)
- the CISS symptom-survey score\(^7\)

These high-yield, predictive tests can help in the diagnosis, prognosis, and treatment of the concussion/mTBI patient, especially in those cases where their history and symptoms may be vague, or questioned in the court of law. However, the quest for the objective visual system biomarker analog(s) continues.

Why an objective biomarker? There are many reasons. First, it does not involve a response that can be altered by the individual. This circumvents the problem of malingering for personal gain. Second, it does not involve any observation or direct response interpretation by the clinician. Third, it can be carefully quantified and used to assess for any natural
recovery, as well as to monitor the progress of some intervention (e.g., vision therapy, near plus spectacles, etc.). Fourth, in many cases, it can be performed readily and quickly by a trained staff member, and thus does not require the presence of a doctor. Lastly, an objectively-based and hence definitive diagnosis of concussion/mTBI helps to reassure the patient and family members as to its reality and presence, with its frequent vague symptoms and at times subtle adverse effects on one’s activities of daily living (ADL).

A few years ago, we published three papers on the topic, one clinically-based, and two laboratory-based, in which we proposed over 50 oculomotor and non-oculomotor-based, vision parameters that could serve as potential objective visual system biomarkers for detecting the presence of mTBI/concussion in our patients. Given the aforementioned optometric meeting findings in mTBI/concussion, and further thoughts over the past few years, we would like to propose what we believe to be more selective, higher-yield, and more specific targeted parameters that could meet the requirements of an objectively-based, visual system biomarker. These include:

- peak convergence velocity
- peak accommodative velocity
- peak pupillary constriction velocity
- peak/average pupillary dilation velocity
- visually-evoked potential (VEP) amplitude with binasal occluders (BNO) specific for those having mTBI and visual motion sensitivity (VMS)
- low luminance VEP amplitude and latency

These tests can each typically be performed in a few minutes, with automated analysis of the data and comparison to related norms. Improvements in technology over the next few years should make this testing easier and more readily available, as well as less costly. Both VEP and pupillometry are currently available for the clinician including their automated analysis.

**Oculomotor Tests**

One of the most robust parameters found in our laboratory studies is peak convergence velocity. Every subject in our testing of nearly 40 adults with mTBI exhibited a significantly reduced peak velocity. The peak, or maximal, velocity occurs at the beginning/initiation of the exponential-like vergence response, with this value being amplitude dependent; the larger the amplitude, the greater the peak velocity. It is typically reduced by approximately 50% of the normative value in these patients, and it significantly increases with vision therapy. Peak vergence velocity cannot be volitionally altered; that is, one cannot try/”will” to make the response slower. Thus, the objectively-based parameter of peak convergence velocity would be optimal.

The aforementioned ideas are also true for accommodative peak velocity. It too was reduced in nearly all mTBI subjects tested, and it significantly increased with vision therapy. Related to the above discussion on vergence, we have also published a detailed case report in a child with convergence insufficiency (CI) but without mTBI demonstrating a similarly reduced convergence peak velocity before vision therapy, and again with a significant increase after successful vision therapy. Thus, we speculate that reduced convergence peak velocity may be an objective biomarker for vergence dysfunction in general. More work is needed in a large sample population (e.g., n=30+) of both children and adults with a diagnosis of CI but without mTBI to evaluate this idea.

Another oculomotor member that has been demonstrated to be excellent for potentially detecting acute concussion is the saccadic system. The specific test device (‘Saccadometer’) is comprised of a headband-mounted, infrared eye movement system with a microcomputer attached to the subject’s waistband for automated display and quantitative analysis. This device has been tested in collegiate boxers (n=12) in the UK immediately before and after their
conventional three-round bouts. No formal testing for concussion was administered nor was it queried. Yet in 75% of them, saccadic latency was significantly increased by 10 to 40 milliseconds, which is relatively large and significant. Interestingly, these values returned back to the pre-boxing, normal baseline in 10 to 14 days. Thus, saccadic latency may provide insight into recovery of brain function. This device is currently available for clinical use. Combining this information with the K-D test may further improve the diagnostic capabilities.

The third and last member of the oculomotor system that shows good promise as an objective visual system biomarker for concussion/mTBI is the pupil, namely its dynamic responsivity. Two recent investigations in the topic have been published.\(^\text{10,11}\) In our study,\(^\text{10}\) the following parameters were found to be consistently significantly reduced in the mTBI population compared to the normal control population:

- peak constriction velocity
- average constriction velocity
- average dilation velocity
- maximum (baseline) pupil diameter
- amplitude of constriction.

**Visually-Evoked Potential (VEP) Tests**

The VEP technique also shows considerable promise in this area. With respect to those with mTBI and VMS, we found in our two laboratory studies\(^\text{12,13}\) that the inclusion of carefully-placed binasal occcluders (BNO) results in a significantly increased VEP amplitude in 90% of the 30 subjects tested. In contrast, in visually-normal individuals, it decreased the VEP amplitude in nearly all cases (n=30). These results confirmed, clarified, and extended an earlier investigation.\(^\text{17}\) Our findings are of particular clinical significance in the diagnosis, as the symptom of VMS in mTBI can be vague, and also poorly understood and poorly comprehended by many, including the patient and some referring doctors. Thus, objective documentation for its presence serves to solidify the diagnosis. In addition, based on our findings and others, BNO is in a highly successful therapeutic intervention for this specific category of mTBI patients.

Related to the above, the VEP technique has also been successful in the objectively-based, **differential diagnosis** of mTBI compared with visually-normal individuals.\(^\text{14}\) With the addition of neutral-density filters (ND=0.5 to 2.5) that reduce target luminance (without affecting its contrast), the VEP amplitude decreased, and its latency increased, significantly greater in those with mTBI (n=19) than in the normal control group (n=20), especially with the most dense ND filter (2.5), especially for the latency parameter.

**CONCLUSIONS**

There are several key vision parameters that have the potential to serve as an objective biomarker for the presence of a concussion/mTBI. An important commonality is the general finding that the response peak velocity is reduced for the near triad, namely for convergence, accommodation, and the pupil. Some of these parameters can presently be assessed objectively in the clinic environment (e.g., pupil). We believe the technology will be forthcoming over the next few years for simple, non-invasive, portable, rapid, and automated clinical assessment of the other proposed parameters (e.g., peak vergence velocity). The proposed tests would cover the spectrum of the concussion/mTBI diagnostic timeframe, that is, the acute (e.g., on the sports sideline, emergency room), subacute (i.e., in either the optometrist or physician’s office several days/weeks later with unresolved visual and non-visual symptoms), and chronic phases (e.g., in the optometrist’s office several months later with persistent visual symptoms and seeking remediation). The diagnosis and treatment of patients with visual problems subsequent to a concussion/mTBI, and TBI in general, will continue to be an area in which the optometric profession will play a major role in the visual rehabilitative process.
REFERENCES


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