Correlation between light sensitivity score, visually evoked signs and symptoms, and VEP in youth following concussion

Preregistration 4/29/21

**HYPOTHESIS:** Increasing light sensitivity will correlate with increased visually evoked signs and symptoms, and with a broadening and enlargement of the P100 peak as captured by an increased PC3 and decreased PC1 coefficient of the VEP PCA model.

**STUDY DESIGN**

Subjects age 11-21 of any biological sex and race/ethnicity will be included who were recruited as part of the Minds Matter concussion research program who sustained a concussion. Recordings that occurred within 1 year of the concussion will be included. Subjects have normal or corrected to normal visual acuity in both eyes. Subjects will have recorded VEP based on ISCEV standards1, signs and symptoms during VEP recording (headache, eye fatigue, etc.), and Post-concussion symptom inventory (PCSI)2 scores recorded. This includes 78 subjects with 140 VEP recording sessions that were recorded from February 2018 – February 2020. An ongoing data pull from February 2020 – April 2021 will be added for the final analysis.

**ANALYSIS**

VEP timeseries data will be fit to our previously described PCA model3.

The dimensionality of the presence/absence of 6 symptoms (eye fatigue, dizziness, headache, nausea, eye pain, other symptom) and 5 signs (eyes slowing, watering, reddening, moving in a circular motion, other sign) evoked by viewing the visual stimulus will be reduced by using Multiple correspondence analysis. The first dimension that in preliminary analysis appears to be representing the presence or absence of signs and symptoms, and the second dimension appears to measure signs and symptoms related to the eyes vs. other signs and symptoms.

Primary outcome measure

The primary outcome measure will be correlation between the PCSI light sensitivity score, visually evoked signs and symptoms (MCA model dimension 1), and PC1 and PC3 of the VEP PCA analysis. The significance of correlation between these components will be determined using ANOVA for a linear mixed effects model.

Secondary outcomes/additional analysis

1. Correlation of visually evoked signs and symptoms (MCA model dimension 1), and PC1 and PC3 of the VEP PCA analysis with migrainous symptoms captured by the sum of PCSI scores for headache, light sensitivity, sound sensitivity, and nausea
2. Correlation of visually evoked signs and symptoms (MCA model dimension 1), and PC1 and PC3 of the VEP PCA analysis with PCSI reduced dimensionality score using polychoric analysis. Only dimensions that meet criteria above random chance will be included.
3. Correlation of visually evoked signs and symptoms (MCA model dimension 1 and 2), and PC1 and PC3 of the VEP PCA analysis with PCSI light sensitivity and PCSI visual problems.
4. Correlation of light sensitivity and MCA with the full 7-dimensional PCA model of the VEP
5. Comparison of PC1 and PC3 to peak analysis on the N75-P100 peak amplitude and N75 and P100 peak latencies to compare to prior work.
6. Since VEP may change and evolve as a function of days post injury, a sub analysis of VEP recordings done at >2 weeks, 2-4 weeks, and >4 weeks will be done separately to measure correlation between the PCSI light sensitivity score, visually evoked signs and symptoms (MCA model dimension 1), and PC1 and PC3 of the VEP PCA analysis using linear regression analysis. The first time point per subject in these time windows will be used to determine if there are differences observed in these time windows.
7. Comparison of subjects with PTH >1 month and those who recovered within 1 month. Subjects with migrainous symptoms (light sensitivity + noise sensitivity and/or nausea) will be separated from those without migrainous symptoms in a sub-analysis.

**REFERENCES**

1. Odom, J. V. *et al.* ISCEV standard for clinical visual evoked potentials: (2016 update). *Doc. Ophthalmol.* **133**, 1–9 (2016).

2. Barlow, K. M. *et al.* Epidemiology of Postconcussion Syndrome in Pediatric Mild Traumatic Brain Injury. *Pediatrics* (2010). doi:10.1542/peds.2009-0925

3. Patterson Gentile, C. *et al.* Developmental Effects on Pattern Visual Evoked Potentials Characterized by Principal Component Analysis. *Transl. Vis. Sci. Technol.* **10**, (2021).