Sex Differences in brain perfusion following mild traumatic brain injury in children

Alessia De Carlo[1,2], Elisabeth Moulaert[1,3], Zheyuan Li[1], Alberto Villagran Asiares[1], Anja Betz[1,3,4], Nico Sollmann[5,6,7,8], Inga Koerte[1,9,10,11]
[1] cBRAIN, Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, LMU University Hospital, LMU Munich, Munich, Germany., [2] Fresenius University of Applied Sciences Munich, Psychology School, Munich, Germany., [3] Graduate School of Systemic Neurosciences (GSN), LMU Munich, Munich, Germany., [4] International Max-Planck Research School for Translational Psychiatry (IMPRS-TP)., [5] Department of Diagnostic and Interventional Radiology, University Hospital Ulm, Ulm, Germany., [6] Department of Nuclear Medicine, University Hospital Ulm, Ulm, Germany., [7] Department of Diagnostic and Interventional Neuroradiology, School of Medicine and Health, Technical University of Munich (TUM) Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany., [8] Technical University of Munich (TUM)-Neuroimaging Center, TUM Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany., [9] German Center for Child and Adolescent Health (DZKJ), Partner Site Munich, Munich, Germany., [10] Psychiatry Neuroimaging Laboratory, Mass General Brigham Academic Medical Centers, Psychiatry Department, Boston, MA, USA., [11] Harvard Medical School, Boston, MA, USA.

Background: Previous studies in adults and rodent models observed reduced cerebral blood flow (CBF) up to 12 months post mild traumatic brain injury (mTBI), suggesting long-term changes (1). This project investigates the differences in global CBF (gCBF) following pediatric mTBI, between or within groups over time.

Methods: The sample included 87 participants, with 36 mTBI patients and 51 typically developing children (TDC). Participants underwent MRI scans acutely after (T1), six months (T6), and twelve months (T12) post-injury. At T12, the drop-out rate was 61 % for mTBI and 53 % for TDC. Type -3 ANOVA and linear mixed-effects models were applied to analyze differences in gCBF within and between groups. Post-hoc tests were conducted to further examine significant differences and timepoints.

Results: The interaction between group and sex overall resulted to be highly significant, $F(1, 27) = 8.51$, $p = .007$, $\eta^2 = .24$. At T1, gCBF in female mTBI patients was significantly reduced in comparison to female TDC, (Mdiff = −15.83, SE = 5.94, $t(49) = -2.66$, $p = .05$). There was also a significant within group difference compared to male mTBI patients, (Mdiff = −23.33, SE = 7.10, $t(46.8) = -3.29$, $p = .01$). There were no significant observations at T6 and T12.

Conclusion: Acutely after mTBI, girls exhibited significantly lower gCBF than boys, suggesting sex-specific changes to perfusion following pediatric brain injury. This is consistent with existing literature having reported reduced regional CBF post-mTBI in female adult patients (1, 2). In rodent models, such effects have previously been linked to gonadal hormones (3). Future studies should investigate the role of hormonal factors in gCBF after mTBI.

References: (1) Churchill et al. (2019) Neurology. (2) Min, D. et al. (2022) Frontiers in Neuroscience. (3) Cai, J. et al. (2015) Neuroscience letters.