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Traumatic Brain Injury Center of Excellence

TBI Hot Topics Bulletin

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STAY INFORMED ABOUT TRAUMATIC BRAIN INJURY (TBI)

Are you a busy health care provider? Not enough time to keep up with research? Stay informed with the *TBI Hot Topics Bulletin*. We track the latest TBI scientific studies, advances, and discoveries most relevant to health care providers.

SCIENTIFIC STUDIES

Therapeutic Effects of Meditation, Yoga, and Mindfulness-Based Interventions for Chronic Symptoms of Mild Traumatic Brain Injury: A Systematic Review and Meta-Analysis

The symptoms of mild traumatic brain injury (mTBI) affect the physical, mental, and emotional domains (e.g., pain, stress, anxiety, depression, and cognitive deficits). Previous studies indicate that meditation, yoga, and mindfulness training can mitigate these symptoms. For example, mindfulness interventions have improved emotional regulation and elicited changes in associated brain regions like the hippocampus, amygdala, prefrontal cortex, and cingulate cortex. In this systematic review, Acabchuk et al. evaluated the effectiveness of meditation, yoga, and mindfulness interventions on mTBI patients. The authors identified 20 studies (total n = 539) with samples of college athletes, civilian adults, and military veterans. Meta-analyses examined the effects on physical health, mental health, cognitive performance, quality of life/self-related processing, and social/occupational outcomes. They found meditation, yoga, and mindfulness interventions improved overall symptoms in mTBI patients but not in controls. There were also significant within-group improvements in physical health, cognitive performance, quality of life, and self-related processing. Fatigue and depression showed the greatest improvements.

Comment

This paper shows that meditation, yoga, and mindfulness training are potential treatments for alleviating mTBI symptoms. While the results are promising, the authors note the lack of randomized controlled trials (RCTs) in their sample. These interventions could prove useful in military populations as stress relief and emotional control may facilitate return-to-duty. More generally, cultivating a mentally healthy force aids in mission readiness.

Acabchuk et al. (2020) *Appl Psychol Health Well Being*, Epub 2 Nov. PMID: 33136346

Reliability and Validity Data to Support the Clinical Utility of the Traumatic Brain Injury Caregiver Quality of Life (TBI-CareQOL)

An important but sometimes overlooked aspect of TBI management is the burden undertaken by caregivers. In this paper, Carlozzi et al. examined the reliability and validity of the Traumatic Brain Injury Caregiver Quality of Life (TBI-CareQOL) outcome measurement system. The TBI-CareQOL consists of a series of self-report questionnaires designed to assess the physical and emotional impact of the caregiver role. The authors administered the TBI-CareQOL to the caregivers of TBI patients (n = 385). Some were caregivers for service members (n = 218), others for civilians (n = 167). Questionnaires were presented by computer-aided testing (CAT), either at home or at an assessment center. They consisted of the following: Caregiver-Specific Anxiety (27-item bank), Caregiver Strain (33-item bank), Feeling Trapped (27-item bank), and Feelings of Loss-Self (30-item bank). Responses were coded on a five-point Likert scale (i.e., 1 = never; 5 = always). The authors also administered several other questionnaires for comparison purposes: PROMIS Sleep-Related Impairment; Neuro-QoL Positive Affect and Well-Being; TBI-QOL Resilience and Grief/Loss; NIH Toolbox Emotional Battery; Rand-12; Caregiver Appraisal Scale; and the Mayo-Portland Adaptability Inventory. As hypothesized, those who cared for lower functioning TBI patients had worse TBI-CareQOL scores. They found the TBI-CareQOL measures exceeded a priori standards for internal reliability. All measures were free from ceiling effects. Only the Feeling Trapped and Grief/Loss measures showed floor effects. The measures also showed strong convergent validity with the item banks for similar constructs.

Comment

The study presents a needed evaluation of the psychometric tools for TBI caregivers. A major limitation is the lack of TBI severity data. Additionally, most of the caregivers were female, and many were in their roles for more than a year. There were also differences between the civilian and service member groups that preclude direct comparison. Further work should explore how TBI severity, post-injury timing, and group-type affect the caregiver experience. Addressing these factors may enhance the quality of life for all parties.

Carlozzi et al. (2020) *Rehabil Psychol*, Epub 12 Dec. PMID: 31829641

Diagnosing Mild Traumatic Brain Injury Using Saliva RNA Compared to Cognitive and Balance Testing

Previous studies have explored TBI biomarkers in blood and cerebral spinal fluid (CSF). A potential new biomarker is non-coding RNA (ncRNA) found in saliva. Altered expression of ncRNAs may reflect post-injury physiological changes mediated by the oropharyngeal cranial nerves. In this study, Hicks et al. examined potential ncRNAs for identifying mTBI cases. Participants (ages 5–66 yrs.) consisted of mTBI patients (n = 251; GCS score above 12; the mTBI occurred ≤ 14 days before testing) and orthopedic controls (n = 287; orthopedic injury; no TBI in the previous 12 weeks). They were divided into training and test sets. Saliva samples were collected at five-time points (< 72 hours, 4–7 days, 8–14 days, 15–30 days, and 31–60 days) and analyzed for ncRNA expression. Training set samples were used to identify ncRNAs that differed between mTBI patients and controls. Several ncRNAs were significantly upregulated in the mTBI group. These candidate ncRNAs were validated in the test set and then used to create predictive models. Other variables such as age, key symptoms, symptom severity, and measures from the Post-Concussion Symptom Scale (PCSS) and ClearEdge Toolkit (i.e., a suite of tests for balance and cognitive assessment) were also included in the models. When applied to the test set, a model with seven ncRNAs, participant age, and chronic headache status correctly identified 76% of mTBI patients and 81% of controls. Another model used four ncRNAs, age, symptom severity, symptom burden, balance, and neurocognitive measures. It identified 81% of mTBI patients and 92% of controls.

Comment

The study shows that salivary ncRNAs can help distinguish between mTBI and orthopedic controls when part of a diagnostic battery. The authors included several other variables in their analyses to help achieve high accuracy. However, it is worth examining ncRNAs alone, as independent biomarkers. Salivary biomarkers are sensitive to acute biomolecular changes, offering a relatively quick and less invasive way of identifying TBI. Accordingly, they may be well-suited for deployed settings and austere environments. More research is needed to explore these possibilities.

Hicks et al. (2020) *Clin Transl Med*, Epub 4 Oct. PMID: 33135344

Comparison of Clinical Outcomes 1- and 5-Years Post-Injury Following Combat Concussion

A challenge in evaluating service members with mTBI/concussion is understanding the impact of long-term outcomes. Most previous studies have relied on data from the acute or subacute clinical time frames. In this study, Mac Donald et al. sought to understand the long-term clinical trajectory of concussion. They followed service members with and without blast concussion (*n* = 347) to time points one- and five-years post-injury. Participants were deployed between 2008 and 2013 with two deployments on average. The sample consisted of four groups: two with a history of concussion (blast and blunt force trauma) and two controls (blast with no blunt trauma and no blast or blunt trauma). Outcome data were obtained via structured interviews, psychiatric evaluations, self-administered questionnaires, and cognitive testing. A cross-sectional analysis found that after five years, neurobehavioral symptoms worsened (relative to predefined baselines) in 66% of patients with blast concussion, 76% of patients with blunt force concussion, and 50% of blast controls (blast with no blunt trauma). However, only 37% of non-blast controls (no blast or blunt trauma) experienced a decline. The concussion groups also showed worse disability and psychiatric scores compared to the controls. However, there were marginal differences in cognitive performance. Ultimately, the data do not show a resolution of symptoms in the five-year time frame. The authors argue the trajectory of recovery can vary considerably among post-deployment mTBI patients.

Comment

The study demonstrates the dynamic nature of recovery from concussion. It also highlights the impact of concussive blast, which needs further research. Longitudinal studies can help anticipate clinical trajectories, potential obstacles, and outcomes. However, the decline observed in some controls is unexplained. Further investigation could include non-deployed military and civilian groups in the analysis. Other limitations include modest sample sizes for some groups (i.e., blunt trauma and blast controls), potential differences in treatment across clinics, limited data on pre-injury health, and the influence of covariates that may impact recovery.

Mac Donald et al. (2020) *Neurology*, Epub 11 Nov. PMID: 33177226

Use of Repetitive Transcranial Magnetic Stimulation in the Treatment of Neuropsychiatric and Neurocognitive Symptoms Associated with Concussion in Military Populations

Repetitive transcranial magnetic stimulation (rTMS) is an FDA-cleared treatment for depression and obsessive-compulsive disorder (OCD). However, it is unknown whether rTMS is effective on TBI-associated depression and posttraumatic stress disorder (PTSD). In this paper, Oberman et al. reviewed the rTMS literature and assessed its efficacy in treating post-concussive symptoms including neuropsychiatric conditions. Unfortunately, the authors found a lack of research on rTMS and concussion. Among the eight relevant studies, sample sizes were low. Results were mixed for depression and PTSD and wholly insignificant for cognitive symptoms. The authors posit that the heterogeneity of symptoms after a concussion may complicate rTMS effectiveness. Also, rTMS protocols (e.g., number of pulses, frequency, etc.) were inconsistent across the studies. It is notable that in the broader literature rTMS studies often exclude participants with a history of seizures. However, none of the reviewed studies indicated that rTMS caused seizures, side-effects, or other adverse events more frequently in concussed patients.

Comment

This paper provides a much-needed state-of-the-science review on rTMS and concussion. The authors found the literature to be sparse and emphasized the need for further research. While rTMS is a proven treatment for depression and OCD, its utility for concussion is unknown. If effective, rTMS could provide valuable non-pharmacological treatment for post-concussive symptoms. This research group is currently preparing a multicenter trial to investigate rTMS treatment on concussed service members.

Oberman et al. (2020) *J Head Trauma Rehabil*, Epub 1 Nov. PMID: 33165152

Smaller Regional Brain Volumes Predict Posttraumatic Stress Disorder at 3 Months After Mild Traumatic Brain Injury

Posttraumatic stress disorder (PTSD) is often associated with TBI. Researchers have documented several risk factors (e.g., IQ, education, history of abuse, etc.) as well as differences in brain structure. PTSD patients appear to have reduced structural volumes and cortical thickness compared to controls. In this study, Stein et al. examined brain volumetrics in mTBI patients with PTSD. This was a retrospective study of the TRACK-TBI cohort (*n* = 421; Glasgow Coma Scale: 13-15; PTSD Checklist: > 33). The authors selected cases with PTSD measures (PCL-5) at three- and six-months post-injury. Structural MRIs were acquired at two weeks post-injury. They analyzed the volumes of eight brain regions: the insula, hippocampus, amygdala, superior frontal cortex, rostral anterior cingulate cortex, caudal anterior cingulate cortex, medial orbitofrontal cortex, and lateral orbitofrontal cortex. Logistic regression assessed the relationship between these volumes and the presence of PTSD at three and six months. Smaller volumes in the superior frontal cortex, rostral anterior cingulate, and caudal anterior cingulate were associated with PTSD at three months. The insula showed a trend but was not significant. The authors used principal components analysis (PCA) to incorporate these areas into a single composite variable. A multivariate model (adjusting for sex, race, education, prior TBI, and early PTSD symptoms) found that this composite predicted PTSD at three months. It did not predict PTSD at six months.

Comment

These findings are important for understanding the relationship between TBI and PTSD. They suggest that regional brain volumes are predictive of the early manifestation (~3 months) of PTSD after mTBI. However, the effect sizes were small. The authors suggest time-from-injury may modulate which variables are most predictive. The paper provides proof-of-principal that MRI volumetrics are predictors of PTSD, but further research is needed to determine their clinical significance.

Stein et al. (2020) *Biol Psychiatry Cogn Neurosci Neuroimaging*, Epub 27 Oct. PMID: 33386283

ABOUT

The *Bulletin* is a product of the Traumatic Brain Injury Center of Excellence (TBICoE) Research Branch and provides a quarterly summary of TBI research and information relevant to health care providers. This issue covers research published from October to December 2020.

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For more information, contact us at 800-870-9244 | dha.TBICoEinfo@mail.mil.