

Bringing attention into higher focus within the traumatic brain injury research agenda

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Traumatic brain injury (TBI) holds a unique position within children's health. It has been clear for decades that TBI is the leading cause of death and disability of children (1,2). However, only recently has the impact of TBI on developing brain gained the attention of the public and lay press due to the attention paid toward injuries in sports such as football, boxing and others. Guidelines for caring for children with mild (3-5) and severe (6) injuries have been assiduously developed from the available literature, yet the proven therapies have remained elusive. Recently, the National Institute of Neurological Disorders and Stroke (NINDS), the European Commission and the Canadian Institutes of Health Research have led (and funded) efforts to address the burden of TBI with the International Initiative for Traumatic Brain Injury Research (InTBIR) with the goal of "working together to improve outcomes and lessen the global burden of TBI by 2020" (7).

To achieve such lofty goals, an honest assessment regarding the state of the field is required. Overall, the field has been hampered by the failure of large interventional studies in both adults and children, with several theories having been offered over to explain these circumstances. In the IMPACT study by Drs. Maas and colleagues, the study team combined already-completed studies into a common database to overcome difficulties with statistical power in an attempt to uncover ways to improve clinical care. In this database of almost 10,000 subjects, they found that inter-center variation was large and the main predictor of patient outcome (8,9). In another effort, Saatman and colleagues argued that neuroimaging findings—such as epidural and subdural hematomas, focal contusions, diffuse injuries—can play important roles in presenting symptoms and

patient outcomes (10). They theorized that the current TBI classification system based solely on the Glasgow Coma Scale (GCS) score is inadequate to fully categorize patients and this mis-classification leads to failed studies. In pediatrics, we have found that an international consortium of pediatric neurotrauma centers have very diverse goals for their medical therapies, including differences related to metabolic support, intracranial hypertension therapies and secondary insults (11). These preliminary efforts have led to three large international studies of TBI—Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI), Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) and the Approaches and Decisions for Acute Pediatric TBI trial (ADAPT Trial)—that are addressing these concerns.

Another important theory regarding the failure of previous studies revolves around selecting the appropriate outcome test for a given population. Over the past decades, it has become recognized that residual sequelae of TBI can range from subtle alterations in cognition to profound psychomotor disability. In addition to the clear deficits rendered by more severe brain trauma, injuries once considered inconsequential are now appreciated to have longer-lasting effects. While ostensibly severe consequences of brain injury such as the inability to perform self-care are obviously associated with monumental individual and societal burdens, more common—though less apparent—changes in function following TBI may have a larger role in the population-level disease burden. The high incidence of mild TBI, coupled with such sequelae, has been demonstrated to confer a significantly larger population-

level burden of disability compared to moderate or severe TBI in children (12).

The lack of standard outcome measures across TBI studies has recently begun to be addressed by the TBI community. NINDS organized several expert panels to identify common data elements of TBI studies, with the desire that eventually combining studies may be revealing (13-16). As a part of this process, a group of outcome experts were empaneled to identify tests from relevant neuropsychological domains that should be performed on children with TBI (17). The group outlined 14 distinct domains, including global outcomes, academics, adaptive living skills, quality of life, physical functioning and TBI-related symptoms, and then identified core tests that should be included within each domain. This has been operationalized by NINDS on their website (<https://commondataelements.ninds.nih.gov/tbi.aspx>) for ongoing use.

Within these domains, the question of attention is included in the TBI-related symptoms domain along with memory difficulties and emotional difficulties. In the most broad sense, deficits in attention are common after TBI (18), but it is less clear which aspects of attention are affected or the optimal methods for investigating the issue (19,20). In this issue of the journal, Königs and colleagues work to distinguish the nature of attentional problems in children who have experienced TBI (21). This retrospective case-control study enrolled children ages 6 to 13 years diagnosed with TBI (case) or non-TBI trauma (control). Participants were assessed with the Attention Network Test (ANT), which the authors note holds an advantage of being able to measure the efficiency of alerting, orienting and executive attention while minimizing the confounding inherent to paper and pencil tests, which are influenced by participants' visumotor limitations. Participants were stratified according to the contemporary TBI severity designations of mild, moderate and severe, with the mild group being additionally stratified according to whether they demonstrated risk factors for complicated TBI (22). Parents and teachers of children who completed the ANT were asked to fill out the child behavior checklist, strength and difficulties questionnaire. Ex-Gaussian analysis was used to distinguish the contribution of extremely slow responses to information processing speed and to adjust for the impact of extremely slow responses when determining information processing speed.

In aggregate, children with TBI had lower full scale IQ, had a longer mean reaction time while completing the ANT, and experienced longer lapses in attention. The relative

difference in performance between alerting, orienting and executive attention tasks were preserved between the control and TBI patients, indicating that TBI patients had no specific deficits in any of these domains relative to non-brain-injured controls. Further, parents of children with TBI were more likely to note attention problems, as well as internalizing and externalizing problems, in their children when compared to parents of the children in the control group. Interestingly, a mediation model demonstrated that lapses in attention accounted for the relation between measured intelligence and parents' perceptions of attention problems. When categories of TBI severity were examined, it was noted that risk-factor negative mild TBI was not associated with perceived or measured deficits in attention.

The study is intriguing in its central finding that lapses in attention, rather than deficits in a particular attention domain, are the main drivers for disparate reaction times between TBI patients and non-TBI controls. The authors contrast their findings with a recent review by Ginstfelt and Emanuelson that highlighted impairments in executive attention following TBI (20). That same review, however, noted that attention span was the most vulnerable domain following traumatic injury, particularly in the first year following injury and beyond one year for those with severe injury.

TBI deficits evolve, if not improve, over time. An important limitation of the current study is the lack of longitudinal follow-up. The mean timespan between the injury and study participation was 1.6 and 1.7 years in controls and TBI patients, respectively. Patterns of post-injury recovery in pediatrics are likely both age and temporally-dependent given the plasticity of the pediatric brain. As previously mentioned, some evidence suggests that the first post-injury year is an important timeframe when assessing TBI-related attention deficits. Whether the same magnitude of difference between the control and TBI population in this study holds as time from injury increases would be interesting to examine. Another obvious limitation to the ANT instrument is its requirement to be performed in Dutch. However, in this way, the test is common with other instruments that have only been validated in selected languages, usually English.

Königs and colleagues have helped clarify the characteristics of attention deficits following pediatric TBI. Their study, along with studies conducted by others that examine how children recover from TBI, must be incorporated into the ongoing work of investigators around the world. Examining whether these findings remain intact longitudinally will be important for guiding therapies and treatments aimed at improving attention in these patients.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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