Diagnosing pediatric mild traumatic brain injury: Current techniques in a vulnerable demographic

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Citation: UBCMJ. 2018: 9.2 (30-31)

Abstract

The Centers for Disease Control and Prevention considers mild traumatic brain injury (mTBI), commonly known as concussion, a genuine public health issue. Emerging research is revealing serious long–term sequelae from repeated concussive blows, yet no single test can definitively diagnose mTBI. Pediatric brains are more sensitive to injury, lending a heightened need for accurate and reliable diagnostic tools. Many tools exist that ostensibly serve as diagnostic tools for mTBI, though most have low diagnostic performance and lack specificity towards the pediatric population. Experimental tools and potential biomarkers are being investigated to improve the sensitivity and specificity of mTBI diagnosis, though they are still in experimental stages and rarely investigated in pediatrics. Research for diagnosing mTBI in the pediatric population presents unique challenges, and is ultimately lacking.

Introduction

Every year, approximately 42 million individuals sustain a mild traumatic brain injury (mTBI), with more than a third of all reported injuries occurring in the pediatric population.[1,2] The Centers for Disease Control and Prevention have viewed mTBI as a serious public health issue for more than a decade, and it has gained widespread public attention following a highly publicized series of studies examining chronic traumatic encephalopathy in NFL players.[3-6] Large meta–analyses have linked mTBI to long–term neurodegenerative diseases such as Alzheimer's, Parkinson's, and amyotrophic lateral sclerosis.[7-10] Despite widespread prevalence and public awareness of the issue, no single test can definitively diagnose or prognosticate recovery of mTBI.[11] The pediatric population was long thought to be less prone to mTBI, as they were considered to have a higher degree of neuroplasticity and "cognitive reserve", which would expedite recovery; however, subsequent research suggests that the pediatric brain is more vulnerable to mTBI.[12,13] The need for an objective diagnostic method is of heightened importance in the pediatric population, and yet, the literature remains scant and conflicting.

Historically, clinical diagnostic tools for mTBI have been developed and validated in adult populations, and some of these have been reformatted for individuals under the age of 18.[14] Definitive diagnosis of mTBI is a key first step to receiving the highest standard of care, and although there are additional factors that make the diagnosis of pediatric mTBI challenging, the largest barrier is simply that there are fewer clinically relevant instruments to work with. A variety of multidimensional diagnostic tools for mTBI exist, the most prominent of which have inherently subjective components, which lend questions surrounding their accuracy. Novel research tools such as magnetic resonance diffusion tensor imaging (MR–DTI) and potential biomarkers such as cerebrovascular functioning and eye movements are being investigated yet remain largely experimental.[15-17]

Sizeable government and research infrastructure is being devoted to the development of valid and reliable diagnostics, yet in the current clinical context, two concerns persist. First, which diagnostic tools are most able to reliably, validly, and accurately diagnose mTBI? Second, which of these, if any, lend the highest degree of clinical utility in the pediatric population?

Current diagnostic tools for mTBI

An overview of some commonly used and experimental diagnostic tools is provided in Table 1. The fifth version of the Sport Concussion Assessment Tool (SCAT5), although imperfect, is widely considered the gold–standard clinical tool and has been developed and refined by an international consortium of experts.[18] The SCAT5 uses a multimodal approach, including tests of neuropsychological functioning, balance, and self–reported symptoms.[19] Despite widespread usage, the previous versions of the SCAT lend only moderate diagnostic utility.[20] The same consortium also released a reformatted Child SCAT5, intended for ages 5-12. Similar neuropsychological tests have been integrated into computer–based programs, including AxonSports, which only tests athletes above age ten, and ImPACT, which offers a pediatric version marketed towards ages 5-11. These computer–based tests are widely used in the context of sport despite yielding an accuracy of only approximately 70%, and providing limited clinical utility due to low validity and reliability.[21]

Prospective biomarkers of mTBI

MR–DTI is an imaging modality that yields parameters indicative of white–matter integrity in the brain.[15] Primary DTI variables characterize the diffusion of water along white–matter tracts with alteration after mTBI indicative of microstructural damage.[15] The literature on MR–DTI in pre–adolescence is scarce and indicates damage in areas other than those seen in adult populations; however, studies on adolescent patients demonstrate findings closer to those found in adults.[22-24] Whereas MR–DTI is an invaluable research tool with which to further our mechanistic understanding of mTBI, current techniques lack the individual–level sensitivity and specificity required for it to reliably be used as a diagnostic tool.[25]

Emerging technologies have spurred the investigation of behavioural biomarkers such as eye movements, as well as physiological biomarkers such as cerebral blood flow and blood proteins, as more objective mTBI diagnostics.[16,17,26] Increased variability of smooth pursuit eye movement has been shown to correlate with MR–DTI markers of mTBI and has a moderate to strong reliability in adults.[17,27,28] However, accurate eye–tracking equipment is expensive and eye movements mature at different rates in childhood, adding specific challenges in the pediatric population that have yet to be fully investigated. Cerebral blood flow decreases following mTBI and can be measured with novel ultrasound and neuroimaging techniques.[16] Ultrasound machines are both relatively portable and quick to administer, though these tools require both the proper equipment and a trained technician. Recently, altered levels of specific blood proteins have been examined as a biomarker of mTBI and combinations of these proteins lend strong sensitivity and specificity for diagnosis.[26,29] However, clinical studies of prospective mTBI biomarkers in pediatrics are sparse. Eye–tracking and blood biomarker research remains largely experimental and have only been investigated in adult populations, and investigations of

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Table 1 | Comparison of established and experimental diagnostic tools for mTBI.

	Diagnostic tool	Time to administer	Validity & reliability	Strengths	Limitations	Pediatric usage
Established	SCAT5[18]	15-20 minutes	Moderate[20]	Multimodal and has established normative scores	Requires training to administer, potential for subjectivity in experimenter scoring	Child SCAT5 for ages 5-12
	AxonSports	10-15 minutes	Low[21]	Easy and fast to administer	Found to be not clinically useful[21]	Only children 10+
	ImPACT	10-15 minutes	Low[21]	Easy and fast to administer	Found to be not clinically useful[21]	Pediatric version for ages 5-11
Experimental	MR–DTI[15]	4-8 minutes (for DTI only)	Undetermined	Can examine neural integrity in vivo	Expensive, impractical, different findings in pediatrics	Yes
	Eye–tracking[17]	<1 minute	Moderate to strong in adults, undetermined in pediatrics[17]	Quick, noninvasive prospective biomarker	Expensive equipment, prone to maturation confounds in pediatrics	Not yet investigated
	Cerebral blood flow[16]	Approx. 5 minutes	Undetermined	Quick, noninvasive prospective biomarker	Expensive equipment, requires technician	Imaging only
	Blood proteins[26]	Approx. 10 minutes	Undetermined	Quick, prospective biomarker	Involves blood draw	Not yet investigated

cerebrovascular alterations in pediatric populations is in early stages.[30]

Discussion

The vast majority of mTBI biomarker research is done in adults and none of the outlined prospective biomarkers have been validated in either adults or children.[14] A primary issue hindering high–quality pediatric mTBI research is that controlling for factors such as selection bias and maturation threats to internal validity are far more challenging than in adult populations. Adult diagnostics are challenged by the heterogeneity of symptoms in mTBI which is further amplified in pediatrics. Baseline testing, followed by post–injury testing to measure intra–individual differences continues to be a research method used to minimize maturation confounds; however, baseline testing is no longer a recommended practice to inform diagnosis.[31]

The injury–prevention organization Parachute Canada provides national guidelines called "Return to Sport"[32] and "Return to Learn"[33] to aid parents, coaches, and teachers of children to safely reintegrate activities following mTBI. However, return to activity guidelines can be best implemented only insofar as there are valid tools to accurately diagnose mTBI. The largest barrier to effective mTBI diagnosis in the pediatric population is simply the incontrovertible fact that we do not have accurate methods of diagnosis in the adult population and thus there are few promising tools to reformat into the pediatric context.

The highest standard of care for all individuals with mTBI can only be provided following a definitive diagnosis, and this is additionally challenging in pediatric mTBI as there are fewer valid and reliable tools available. Widely used computerized tests with pediatric–friendly versions have low validity and reliability and thus provide little clinical utility.[21] The Child SCAT5 is currently the most evidence–based and validated tool for pediatric mTBI diagnosis,[18] although it is still far from a reliable and objective measure. The current gold–standard diagnostic tools provide some degree of clinical utility but often present subjectivity or reliability issues. Emerging technologies show promise in the search for objective biomarkers of mTBI; however, these tools are still in early experimental stages and few are being investigated in pediatrics.

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