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Mild Traumatic Brain Injury Does Not Significantly Affect Midlife Cognitive Functioning Within the General Population: Findings From a Prospective Longitudinal Birth Cohort Study

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Objective: To determine whether differences exist in mid-adulthood cognitive functioning in people with and without history of mild traumatic brain injury (mTBI). **Setting:** Community-based study. **Participants:** People born between April 1, 1972, and March 31, 1973, recruited into the Dunedin Multidisciplinary Health and Development Longitudinal Study, who completed neuropsychological assessments in mid-adulthood. Participants who had experienced a moderate or severe TBI or mTBI in the past 12 months were excluded. **Design:** Longitudinal, prospective, observational study. **Main Measures:** Data were collected on sociodemographic characteristics, medical history, childhood cognition (between 7 and 11 years), and alcohol and substance dependence (from 21 years of age). mTBI history was determined from accident and medical records (from birth to 45 years of age). Participants were classified as having 1 mTBI and more in their lifetime or no mTBI. The Wechsler Adult Intelligence Scale (WAIS-IV) and Trail Making Tests A and B (between 38 and 45 years of age) were used to assess cognitive functioning. *T* tests and effect sizes were used to identify any differences on cognitive functioning domains between the mTBI and no mTBI groups. Regression models explored the relative contribution of number of mTBIs and age of first mTBI and sociodemographic/lifestyle variables on cognitive functioning. **Results:** Of the 885 participants, 518 (58.5%) had experienced at least 1 mTBI over their lifetime, with a mean number of 2.5 mTBIs. The mTBI group had significantly slower processing speed ($P < .01$, $d = 0.23$) in mid-adulthood than the no TBI controls, with a medium

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effect size. However, the relationship no longer remained significant after controlling for childhood cognition, sociodemographic and lifestyle factors. No significant differences were observed for overall intelligence, verbal comprehension, perceptual reasoning, working memory, attention, or cognitive flexibility. Childhood cognition was not linked to likelihood of sustaining mTBI later in life. **Conclusion:** mTBI histories in the general population were not associated with lower cognitive functioning in mid-adulthood once sociodemographic and lifestyle factors were taken into account. **Key words:** *cognitive function*, *concussion*, *mTBI*, *neuropsychology*, *traumatic brain injury*

MILD TRAUMATIC BRAIN INJURY (mTBI) affects 27 million people each year across the globe[1] and is an increasing public concern.[2] Many patients recover naturally in days to weeks following mTBI; however, large prospective observational studies have shown that up to 53% of people can experience persistent symptoms, functional difficulties, and reduced satisfaction with life 1 year post-mTBI if they do not receive access to effective rehabilitation.[3–6]

Evidence suggests that self-reported cognitive symptoms, such as taking longer to think, are most likely to become chronic in the longer term[3] and can impact on people's ability to function in everyday life and perform well at work.[7,8] Evidence from neuropsychological tests shows that mTBI does not appear to impact overall cognition or intelligence but may have a specific impact on certain cognitive domains. For example, a systematic review of neuropsychological outcomes revealed that there were significant differences between mTBI groups and controls on the cognitive domains of working memory, attention, executive functioning, and processing speed but no differences on perceptual organization, verbal comprehension, or motor skills.[9] However, the review integrated data collected days to weeks postinjury to several years postinjury making it difficult to differentiate between acute and more persistent effects. Subsequent reviews have shown that effect sizes on different cognitive domains vary considerably across studies.[10] Reasons for this heterogeneity may include small sample sizes, quality of mTBI data available, representativeness of the mTBI samples, and differences in tests administered.

In the longer term postinjury, a meta-analysis of 21 studies revealed that those who experience an mTBI have nearly twice the risk of developing dementia, including Alzheimer's disease in later life compared with noninjured controls.[11] Most studies exploring the potential impacts of mTBI in older adulthood have focused on athletes who are at high risk of mTBI.[12] For example, in a study of retired elite and community-level rugby players and noncontact sport controls, it was revealed that players who had experienced mTBI over their playing career had poorer complex attention, cognitive flexibility, and executive functioning. There were no differences in overall cognition, memory, physical response time, or psychomotor speed.[13] The cognitive domains identified in retired athletes are similar to those revealed in studies of general population samples conducted within a few years of injury, suggesting that mTBI may have an impact in attentional, processing speed, and executive function domains. However, in the sports context people can also be exposed to multiple mTBIs sustained in close succession over a prolonged period of time. It has been argued that the exposure profile for many sports athletes particularly in contact sports such as rugby and football is distinct to that of the general population. However, within the general population many people are engaged in contact sports and/or are at risk of repetitive mTBI including victims of domestic violence.[14] There is currently a lack of research exploring the impact of mTBI in mid-adulthood (ie, those aged 35-45 years) and in the general population. Consequently, there is a need to explore the impact of mTBI on cognitive outcomes in the general population to determine any similarities and differences between the different contexts.

One of the challenges in studying the impacts of mTBI on cognitive symptoms and functioning is controlling for the complexity of factors that could influence the relationship. Many persistent symptoms and cognitive difficulties reported, such as difficulty remembering things, are not specific to mTBI and may also be influenced by a number of non–injury-related predisposing, perpetuating, and mitigating factors. Non–injury-related factors may include education, social deprivation, financial compensation seeking, preexisting psychological disorders, expectations of recovery, and substance use.[15–18] There are also likely to be a number of injury-related factors that could impact the relationship, such as the number of TBIs experienced over the lifetime and age of first TBI. Yet, the influence of these factors has not been well controlled for in studies to date. Furthermore, current studies have been hindered by a reliance on retrospective data, selection bias, or a focus on specific groups, such as the military or athletes.

An additional complexity is that there may also be a reverse causation relationship between mTBI and cognitive functioning. A study of young men conscripted to the military identified that low overall cognitive function was linked to increased risk of sustaining a subsequent TBI.[19] However, this reverse causation hypothesis requires investigation within a general population sample. One of the strongest predictors of later life cognitive functioning is early life cognitive functioning.[20] Consequently, in order to detect the specific impact of injury on cognition, preinjury

assessments of cognition are needed and yet are rarely prospectively available. The Dunedin Multidisciplinary Health and Development Study, which has systematically assessed injuries and cognition over participants' lifetimes, offers a unique opportunity to determine whether there are any impacts of mTBI on cognitive functioning in midlife while controlling for premorbid cognitive ability and alcohol and substance use. This study aims to determine whether differences exist in cognitive functioning in mid-adulthood between adults with and with no history of mTBI and to explore the impact of age of first injury and number of lifetime TBI.

METHODS

Participants are members of the Dunedin Multidisciplinary Health and Development Study, a longitudinal investigation of health and behavior in a population-representative birth cohort of 1037 individuals (91% of eligible births; 52% male) born between April 1, 1972, and March 31, 1973, in Dunedin, New Zealand.[21] The longitudinal study was established at 3 years of age based on residence in the province.[22] Assessments were conducted at birth and at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, and 38 years, and most recently at 45 years of age, when 94% of the 997 participants still alive took part. Each study member was brought to the research unit for a day of interviews and examinations at each assessment time point. The cohort represents the full range of socioeconomic status (SES) on New Zealand's South Island; health indicators such as body mass index, smoking, physical activity, and number of general practitioner visits closely align with that identified for the New Zealand's population.[23] Study participants were primarily of New Zealand European ethnicity (93% self-identified as White). Written informed consent was obtained from participants at each phase of assessment. The study was approved by the New Zealand's Southern Health and Disability Ethics Committee (reference: 17/STH/25). In New Zealand, the cost of care for any child or adult who experiences an accidental injury is covered by the "no fault" Accident Compensation Corporation reducing any potential impact of financial compensation seeking on outcomes.

Assessments

Sociodemographic characteristics for the sample were extracted from the main participant database. The person's average childhood SES was assessed using the Elley and Irving (1976) scale. This scale categorizes the occupation of both parents/guardians into 1 of 6 groups based on the educational levels and income associated with that occupation using data from the New Zealand census. The scale ranges from 1 = "unskilled laborer" to 6 = "professional." At each assessment between the ages of 3 years and 15 years the highest parent/guardian category was used. The average of SES was taken across all categories from 3 to 15 years of age to reflect the socioeconomic conditions experienced by participants as they grew up.

Alcohol and substance dependence were assessed using the Diagnostic Interview Schedule at 21, 26, 32, 38, and 45 years of age. Responses on this interview were used to classify whether the participant had experienced a period of dependence (using *Diagnostic and Statistical Manual of Mental Disorders* [Third Edition Revised] [*DSM-III-R*] at 21 years of age and *Diagnostic and Statistical Manual of Mental Disorders* [Fourth Edition] [*DSM-IV* criteria] at 26, 32, 38, and 45 years of age). Because of very low rates of use of substances such as cocaine or heroin, only data on alcohol and cannabis use were used in the analysis. Participants were categorized as having a least 1 period of dependence on alcohol or cannabis, or having no lifetime use or occasional use without dependence.

Health status

Health status was determined by the question "In general, would you say your health is" with participants asked to self-report their health on a 5-point scale from 1 = Excellent to 5 = poor.

Cognitive functioning

The Wechsler Intelligence Scale for Children (WISC) was completed at 7, 9, and 11 years of age. The average Full Scale Intelligence Quotient (FSIQ) score of assessments was used to account for early life cognitive functioning to test the hypothesis that low cognitive function in childhood is a risk factor for mTBI.

The Wechsler Adult Intelligence Scale (WAIS-IV) was completed at the age of 38 years and 45 years to measure cognitive functioning across different domains in mid-adulthood. The WAIS-IV consists of 10 different subtests such as describing how 2 words or concepts are similar, arranging blocks in a pattern stated in a visual image, recalling number sequences in forward or backward order, or linking symbols and numbers using a key. Tests are scored for both accuracy and time. Subtest scores as well as Full Scale Intelligence Quotient (FSIQ) scores as well as index scores for processing speed, working memory, perceptual reasoning, and verbal comprehension were calculated using age-related normative data based on combinations of subtest scores.[24] The average scores for each cognitive domain taken from the 2 assessments were used in the analysis to account for potential external variable factors on cognitive performance such as tiredness, recent bereavement, stress, or getting distracted during a task. For the 5.0% of study members who did not complete the WAIS-IV

at both time periods, the single available score was used. These data are referred to as "age 45" data from this point forward.

In addition to the WAIS-IV, the Trail Making Test A was used to assess attention and processing speed, and Test B[25] was used to assess cognitive flexibility (requiring an additional set shifting executive functioning requirement to switch between tasks).[26] The time to complete each trial was recorded. If more than 5 minutes was taken on either trial, the test was stopped.[26] Test scores on each trial (A and B) were averaged between age 38 years and age 45 years assessments to enhance reliability of measurement by accounting for any factors affecting performance on a given day (eg, feeling tired after a poor night's sleep). Raw scores on each portion of the test were converted to *z* scores using age-related normative data.[26]

TBI history

At each assessment, participants were asked a series of structured questions about any accident that they had experienced since the last assessment. This included details of what happened, the injuries that were sustained, age and place of injury, whether they sort medical attention for the injury, and if so, where they went. Before the age of 15 years, the parent/guardian was asked to report all accidents and medical events. From the 16-year assessment upward, the participant was asked about any accidents or medical events that had occurred. In addition, data were extracted from the New Zealand Accident Compensation Corporation and Ministry of Health databases on any accidents or medical events experienced by the study participants. In New Zealand, every person is allocated a unique National Health Index number, which enables identification of government records linked to a particular person over his or her lifetime. Relevant incidents were identified in which there was a risk of TBI identified by 2 researchers independently (99.8% agreement). If there was any doubt or disagreement between the researchers, the incident was retained for further review. Details of these incidents were entered into a database including a description of the accident, where the information was collected from (eg, medical record or self-report), whether the person sought medical attention after the injury, discharge information, diagnostic codes, details of all injuries sustained, age of injury, and whether there was any note of severity of TBI or duration of loss of consciousness. Each potential injury was then reviewed independently by 2 clinicians against the criteria established to determine whether a TBI had occurred (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A685). mTBI was confirmed when the description of the incident indicated that an mTBI was likely, where there was evidence of an external force to the head or the body, and indications of altered consciousness such as feeling dazed or confused or loss of consciousness.[27] Moderate and severe TBIs were classified as injuries where there was a loss of consciousness of more than 30 minutes or where there was evidence of abnormal imaging and/or medical diagnosis of a moderate or severe TBI. Data on TBI history were then extracted and merged with the Dunedin longitudinal assessment data set.

Statistical analysis

Means and SDs or medians and interquartile ranges (dependent on the distribution of each variable) were used to describe the characteristics of the sample and TBI history. Differences in the characteristics and cognitive functioning of those affected by mTBI and those with no mTBI history were determined using χ^2 and *t* test (dependent on whether the data met parametric assumptions). Pearson correlations between each of the variables and variance inflation factors were used to assess collinearity within each regression model. Multiple linear regression models were used to determine relative impact of mTBI variables (eg, number and age of first injury) alongside other variables known to influence cognitive functioning (including childhood cognitive functioning, sex, childhood SES, alcohol and cannabis dependence, and education). Regression models were also used to determine whether childhood cognitive functioning predisposed participants to an increased risk of mTBI in later life. Effect sizes were calculated using Cohen *d*, with $d = 0.1$ defined as a small effect size, $d = 0.2$ medium, and $d = 0.3$ as large.[28] A more conservative level of $P < .01$ was used to determine statistical significance due to multiple comparisons.

RESULTS

Of the 1037 participants from the initial cohort, 40 (3.9%) had died prior to the age 45 assessment. There were an additional 59 (5.7%) who declined or who could not be located, 15 (1.4%) had experienced a moderate to severe TBI, and 17 (1.6%) who did not complete the neuropsychological assessment at either 38 or 45 years of age. A further 21 participants were excluded because of experiencing an mTBI within the past 12 months. There were 885 participants who were included in the analysis (see Fig 1). Attrition analysis was conducted using childhood IQ and SES to determine whether participants in the age 45 data collection were representative of the original cohort. No significant differences in childhood IQ were found between the full cohort, those still alive, or those seen at 45 years of age. However, those who were deceased by the age 45 data collection had significantly lower IQs in childhood than those who were still alive ($t = 2.09$, $P = .04$).

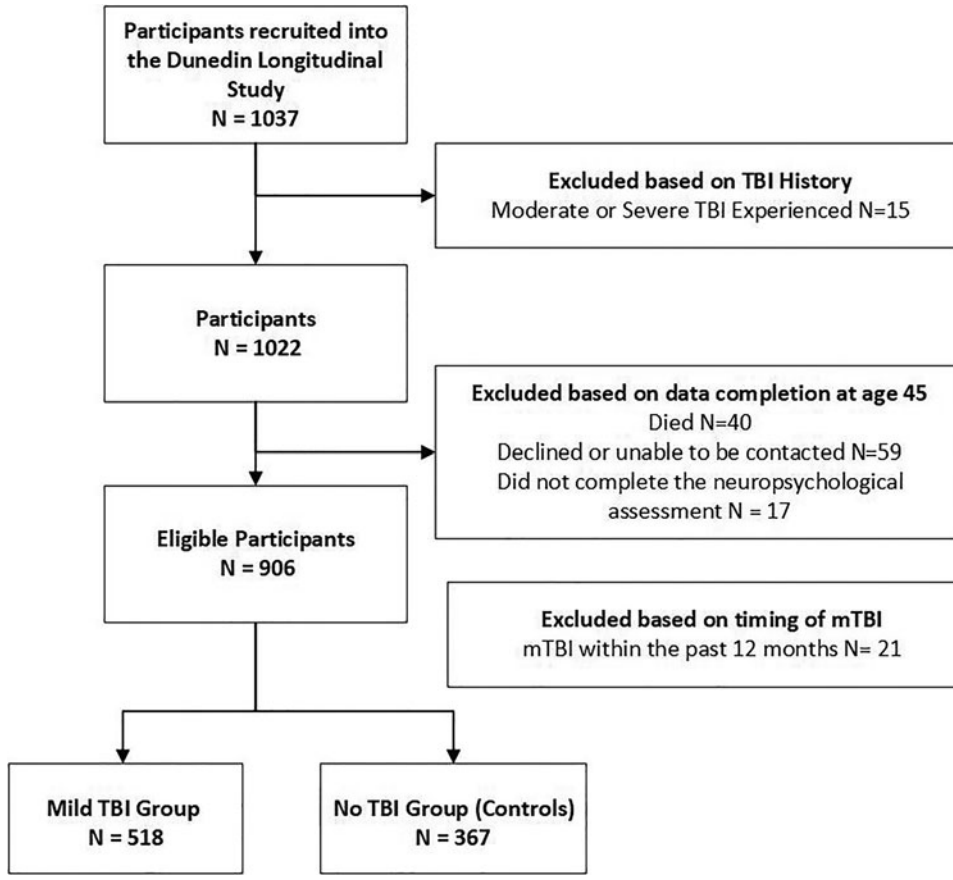

Figure 1. Participant flowchart. mTBI indicates mild traumatic brain injury; TBI, traumatic brain injury.

Characteristics of participants included in the analysis are shown in Table 1. Of these, 518 participants (58.5%) had experienced a least 1 mTBI over their lifetime. Of those who experienced at least 1 mTBI, the mean number of injuries sustained was 2.52 (SD: 19.3). There were 438 (49.5%) participants who experienced at least 1 mTBI before 25 years of age. As shown in Table 1, participants who had experienced at least 1 mTBI in their lifetime were more likely to be male, have lower levels of education, and at least 1 period of alcohol or cannabis dependence.

To test whether participants who had experienced at least 1 mTBI in their lifetime had significantly lower cognitive functioning than those with no TBI history, we compared scores at 45 years of age for each cognitive domain (see Table 2). There was a significant difference between the groups on the WAIS-IV domain of processing speed, with a medium effect size. There were no differences between the groups on overall cognitive functioning, verbal comprehension, perceptual reasoning, working memory, attention, or cognitive flexibility.

To determine whether the number of TBI over the lifetime and age of first mTBI was linked to midlife cognitive functioning, multiple regression was used to test the unadjusted association and adjusted for childhood cognition, sociodemographic factors, and alcohol and substance use as shown in Table 3. All variance inflation factors were around 1. Three or more mTBIs significantly contributed to the regression models on processing speed and cognitive flexibility. However, 3 or more mTBIs no longer remained a significant independent contributor after childhood cognition and sociodemographic and lifestyle factors were taken into account (see Table 3).

As would be expected, childhood IQ significantly contributed to all midlife cognitive functioning across all domains. Regression associated with models showed that older age of first injury was lower perceptual reasoning in midlife but there was no association between age of first injury and the other cognitive domains (see Table 4).

To determine whether lower childhood cognition predisposed individuals to TBI, we conducted a series of regression models between childhood cognitive functioning (IQ) scores and number of TBI by 45 years of age. There was no association between early life cognition and number of TBI experienced (see Table 5). The only childhood factor associated with higher number of lifetime mTBI was sustaining an mTBI prior to 7 years of age.

TABLE 1 *Participant characteristics*

	No history of mTBI ($N = 367$)		At least 1 mTBI ($N = 518$)		Test of difference	*P*
	N	**%**	***N***	**%**		
Sex						
Female	243	66.2	198	38.2	$\chi^2 = 67.3$	<.01
Male	124	33.8	320	61.8		
Highest educational attainment						
School certificate or lower	90	24.5	162	31.3	$\chi^2 = 8.61$	.01
High school or equivalent	142	38.7	211	40.7		
University degree or higher	134	36.5	145	28.0		
Missing	1	<1	0	0.0		
Cannabis use						
No use or occasional use	324	88.3	401	78.6	$\chi^2 = 19.20$	<.01
≥1 period of dependence	39	10.6	114	22.0		
Missing	4	1.1	3	<0.1		
Alcohol use						
Never used or regular drinker	264	71.9	318	61.4	$\chi^2 = 11.73$	<.01
≥1 period of dependence	99	27.0	198	38.2		
Missing	4	1.1	2	<0.1		
Major comorbidity						
No	273	74.4	382	73.7	$\chi^2 = 0.05$	.83
Yes	94	25.6	136	26.3		
Current health status						
Fair/poor	21	5.7	57	11.0	$\chi^2 = 7.86$	.02
Good	126	34.3	158	30.5		
Excellent/very good	220	60.0	303	58.5		
Number of lifetime mTBIs						
No mTBI events	367	100.0	0	0.0	...	...
1 mTBI event	...	...	196	37.8	...	...
2 mTBI events	...	...	141	27.2	...	...
≥3 mTBI events	...	...	181	34.9	...	...
Age at the time of first mTBI, y						
0-4	...	...	158	30.5	...	...
5-9	...	...	98	18.9	...	...
10-14	...	...	95	18.3	...	...
15-19	...	...	65	12.5	...	...
20-24	...	...	22	4.2	...	...
25-29	...	...	12	2.3	...	...
30-34	...	...	15	2.9	...	...
35-39	...	...	24	4.6	...	...
40-45	...	...	29	5.6	...	...
Time since last reported injury in years						
Past 5 y	...	...	109	21.0	...	...
Between 6 and 10 y ago	...	...	61	11.8	...	...
Within 20 y	...	...	64	12.4	...	...
Within 30 y	...	...	96	18.5	...	...
Within 40 y	...	...	134	25.9	...	...
>40 y ago	...	...	54	10.4	...	...
	Mean	**SD**	**Mean**	**SD**		
Highest childhood socioeconomic status (birth to 15 y)	3.9	1.1	3.7	1.4	$t = -1.73$	.08
Average Childhood IQ (WISC IQ: 7, 9, and 11 y)	101.3	13.3	100.5	14.4	$t = -0.90$	.37

Abbreviations: mTBIs, mild traumatic brain injuries; IQ, intelligence quotient; WISC, Wechsler Intelligence Scale for Children.

TABLE 2 *Comparison of average cognitive domain test scores between those with mTBI history and those with no history*

Cognitive domains	No mTBI ($N = 367$) Mean (SD)	At least 1 mTBI ($N = 518$) Mean (SD)	*T* test *P*	Cohen *d* effect size
Full Scale IQ (WAIS-IV)	100.0 (15.1)	98.5 (14.7)	.12	0.1
Verbal Comprehension Index (WAIS-IV)	99.8 (14.6)	98.9 (14.4)	.37	0.06
Perceptual Reasoning Index (WAIS-IV)	100.9 (16.0)	100.1 (15.4)	.47	0.05
Processing Speed Index (WAIS-IV)	100.3 (14.3)	97.0 (14.6)	<.01	0.23
Working Memory Index (WAIS-IV)	99.3 (15.2)	99.5 (14.8)	.88	0.01
Attention and Processing Speed (Trail Making Test A *z* score)	0.1 (1.1)	0.0 (1.2)	.15	0.09
Cognitive Flexibility (Trail Making Test B *z* score)	− 0.1 (1.2)	− 0.3 (1.3)	.07	0.16

Abbreviations: IQ, intelligence quotient; mTBI, mild traumatic brain injury; WAIS-IV, Wechsler Adult Intelligence Scale.

DISCUSSION

This prospective study revealed that there were no significant differences in cognitive functioning between adults with a history of mTBI and controls once childhood cognition and sociodemographic and lifestyle factors were taken into account. Age of first injury was only significantly associated with perceptual reasoning. Early cognitive functioning levels were not found to predispose individuals to an increased risk of mTBI, although experiencing an mTBI before 7 years of age was associated with total number of lifetime TBI. The findings suggest that in the general population, where few people are exposed to the repetitive mTBI observed in sport, there is no evidence of impact of mTBI on cognitive functioning in mid-adulthood.

The prevalence of mTBI found in this sample (with 49.5% of participants experiencing at least 1 mTBI by 25 years of age) is higher than that found in previous studies of 30%.[29] This is likely to reflect differences in injury identification. The current study utilized parent-reported accident records and medical records until 16 years of age. In contrast, the previous study accessed only medical appointments before 16 years of age with self-reported injuries recorded only after 16 years of age. The use of self-reported accident records routinely gathered over participant's lifetimes, in addition to medical records, is a strength of this study. There is evidence that 28% of cases of mTBI do not present to their general practitioner, accident or medical clinic, or hospital postinjury.[30] To be classified as an mTBI case in this analysis, there needed to be sufficient data of a likely mechanism of injury, sufficient force (eg, high speed or height of fall), indication of the head being indicated specifically (eg, lacerations, facial fractures, or bruising) or alterations in level of consciousness (eg, feeling dazed and confused). Despite the higher prevalence, it is likely that some injuries were not identified because of insufficient information being provided within the medical or accident record to meet the inclusion criteria. Underreporting of mTBI may also reflect that New Zealand Accident Compensation Corporation (national compensation provider) medical records became available only from the year 2000 and Ministry of Health data capture only hospital visits following mTBI (and do not include primary care consultations). In addition, some people may have experienced an mTBI while overseas, which would not have been captured in New Zealand medical records. Conversely, there may also be a risk of the study being overinclusive of mTBI events based on the mTBI inclusion criteria. Higher incidence rates of TBI have been found in New Zealand compared with other counties.[30]

There were no differences observed in cognitive functioning in mid-adulthood between mTBI cases and controls after controlling for childhood cognitive, socioeconomic, and lifestyle factors. This finding contrasts with the findings from a previous systematic review, which concluded that there was evidence of effects of mTBI on processing speed, attention, memory, and executive functioning cognitive domains.[9] The difference in findings is likely to reflect that the majority of the current sample (67.2%) experienced their mTBI more than 10 years prior to the age 45 assessment. The findings of the previous review included data obtained from assessments conducted several months postinjury and may therefore be more reflective of the short-term effects of mTBI on cognitive functioning. The findings of this study indicate that impacts of mTBI on cognitive functioning are unlikely to persist in the longer term.

The findings of this study also contrast with studies conducted in the context of sport, in which mTBI and particularly repetitive mTBI have been linked to poorer cognitive functioning.[31] The difference in findings

TABLE 3 *Unadjusted association between number of TBI and cognition in mid-adulthood and adjusted for sociodemographic and lifestyle variables*

	Model 1			Model 2			Model 3			Model 4			Model 5		
	Number of TBI on cognition			Number of TBI on cognition adjusting for childhood IQ			Number of TBI on cognition controlling for sociodemographic factors (SES, education, gender)			Number of TBI on cognition adjusting for alcohol and substance use			Number of TBI adjusting for all factors		
Cognitive outcome	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***
Full Scale IQ (WAIS-IV)															
1 mTBI[a]	−2.24	1.31	.09	−.56	0.84	.50	−.77	1.13	.50	−1.63	1.29	.21	−.13	0.83	.88
2 mTBI[a]	.98	1.47	.50	−.26	0.94	.79	.52	1.26	.68	1.34	1.45	.35	−.03	0.92	.97
≥3 mTBI[a]	−3.10	1.35	.02	−1.86	0.86	.03	−1.74	1.19	.14	−1.84	1.36	.17	−.97	0.88	.27
Childhood IQ	...	...	...	.82	0.02	<.01	...	...					.73	0.03	<.01
Childhood SES							2.71	0.40	<.01				.14	0.31	.65
High school graduate or higher[b]							16.31	1.30	<.01				6.47	1.04	<.01
School certificate[b]							5.84	1.59	<.01				2.18	1.18	.07
Female[c]							−2.05	0.89	.02				−.59	0.66	.38
Alcohol dependence[d]										−2.23	1.10	.04	−2.22	0.69	<.01
Cannabis dependence[e]										−4.52	1.39	<.01	−1.39	0.90	.12
Verbal Comprehension Index (WAIS-IV)															
1 mTBI[a]	−1.73	1.29	.18	−.17	0.96	.86	−.83	1.11	.46	−1.25	1.29	.33	−.18	0.95	.85
2 mTBI[a]	.43	1.45	.77	−.73	1.08	.50	−.63	1.23	.61	.72	1.45	.62	−1.00	1.04	.34
≥3 mTBI[a]	−1.25	1.33	.35	.03	0.99	.98	−.35	1.17	.76	−.47	1.35	.73	.01	1.00	.99
Childhood IQ				.71	0.03	<.01							.57	0.03	<.01
Childhood SES							3.40	0.39	<.01				1.32	0.35	<.01
High school graduate or higher[b]							14.20	1.29	<.01				7.46	1.20	<.01
School certificate[b]							4.02	1.59	.01				1.85	1.37	.18
Female[c]							−3.58	0.87	<.01				−2.49	0.75	<.01
Alcohol dependence[d]										−1.89	1.10	.09	−1.65	0.79	.04
Cannabis dependence[e]										−2.41	1.39	.08	.62	1.03	.55
Perceptual Reasoning Index (WAIS-IV)															
1 mTBI[a]	−1.60	1.39	.25	−.26	1.08	.81	−.64	1.29	.62	−1.07	1.39	.44	−.19	1.09	.86
2 mTBI[a]	1.05	1.56	.50	.11	1.21	.93	.52	1.42	.71	1.34	1.55	.38	.17	1.21	.88
≥3 mTBI[a]	−1.18	1.43	.40	−.08	1.10	.94	−.16	1.35	.91	−.03	1.46	.99	.59	1.16	.61
Childhood IQ				.72	0.03	<.01							.65	0.04	<.01
Childhood SES							2.26	0.45	<.01				.06	0.40	.88
High school graduate or higher[b]							13.25	1.47	<.01				4.93	1.37	<.01
School certificate[b]							3.24	1.81	.07				.58	1.56	.71
Female[c]							−2.74	1.01	.01				−1.47	0.87	.09
Alcohol dependence[d]										−1.78	1.19	.13	−1.89	0.92	.04
Cannabis dependence[e]										−4.26	1.49	<.01	−1.86	1.19	.12

(*continues*)

TABLE 3 *Unadjusted association between number of TBI and cognition in mid-adulthood and adjusted for sociodemographic and lifestyle variables* (Continued)

	Model 1			Model 2			Model 3			Model 4			Model 5		
	Number of TBI on cognition			Number of TBI on cognition adjusting for childhood IQ			Number of TBI on cognition controlling for sociodemographic factors (SES, education, gender)			Number of TBI on cognition adjusting for alcohol and substance use			Number of TBI adjusting for all factors		
Cognitive outcome	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***
Processing Speed Index (WAIS-IV)															
1 mTBI[a]	−3.26	1.28	.01	−2.44	1.13	.03	−.79	1.22	.52	−2.65	1.26	.04	−.47	1.11	.67
2 mTBI[a]	−.74	1.43	.61	−1.73	1.26	.17	.02	1.35	.98	−.29	1.40	.83	−.37	1.23	.76
≥3 mTBI[a]	−5.70	1.31	<.01	−4.99	1.16	<.01	−2.61	1.28	.04	−4.22	1.32	<.01	−1.92	1.18	.10
Childhood IQ				.50	0.03	<.001							.48	0.04	<.01
Childhood SES							.79	0.43	.06				−.89	0.41	.04
High school graduate or higher[b]							12.25	1.40	<.01				4.53	1.39	<.01
School certificate[b]							6.57	1.72	<.01				3.67	1.58	.02
Female[c]							5.10	0.96	<.01				5.84	0.88	<.01
Alcohol dependence[d]										−1.84	1.07	.09	−.98	0.93	.29
Cannabis dependence[e]										−6.08	1.35	<.01	−3.27	1.21	.01
Working Memory Index (WAIS-IV)															
1 mTBI[a]	−.46	1.33	.73	.86	1.07	.42	−.11	1.26	.93	.01	1.33	.99	.42	1.10	.70
2 mTBI[a]	2.85	1.49	.06	1.91	1.20	.11	2.04	1.39	.14	3.06	1.49	.04	1.62	1.21	.18
≥3 mTBI[a]	−1.77	1.37	.20	−.92	1.10	.41	−1.80	1.33	.17	−1.09	1.40	.44	−1.42	1.16	.22
Childhood IQ				.64	0.03	<.01							.59	0.04	<.01
Childhood SES							2.02	0.44	<.01				−.10	0.40	.80
High school graduate or higher[b]							10.94	1.44	<.01				3.17	1.37	.02
School Certificate[b]							3.03	1.78	.09				.37	1.57	.81
Female[c]							−4.07	0.97	<.01				−3.13	0.87	<.01
Alcohol dependence[d]										−1.77	1.14	.12	−1.81	0.92	.05
Cannabis dependence[e]										−2.03	1.44	.16	−.75	1.20	.53

(*continues*)

TABLE 3 *Unadjusted association between number of TBI and cognition in mid-adulthood and adjusted for sociodemographic and lifestyle variables* (Continued)

	Model 1			Model 2			Model 3			Model 4			Model 5		
	Number of TBI on cognition			Number of TBI on cognition adjusting for childhood IQ			Number of TBI on cognition controlling for sociodemographic factors (SES, education, gender)			Number of TBI on cognition adjusting for alcohol and substance use			Number of TBI adjusting for all factors		
Cognitive outcome	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***	*β*	**SE**	***P***
Processing Speed (Trail Making Test A *z* score)															
1 mTBI[a]	−.17	0.10	.09	−.12	0.09	.22	−.07	0.10	.50	−.14	0.10	.15	−.05	0.10	.58
2 mTBI[a]	.01	0.11	.96	−.05	0.11	.62	.03	0.11	.81	.01	0.11	.92	−.01	0.10	.90
≥3 mTBI[a]	−.18	0.10	.08	−.15	0.10	.13	−.05	0.11	.58	−.11	0.10	.29	−.02	0.10	.78
Childhood IQ				.03	0.00	<.01							.03	0.00	<.01
Childhood SES							.06	0.04	.10				−.05	0.04	.13
High school graduate or higher[b]							.63	0.12	<.01				.12	0.12	.32
School certificate[b]							.44	0.14	<.01				.23	0.14	.08
Female[c]							.16	0.08	.05				.19	0.07	.01
Alcohol dependence[d]										−.09	0.08	.32	−.07	0.08	.42
Cannabis dependence[e]										−.36	0.11	<.01	−.28	0.10	.01
Cognitive Flexibility (Trail Making Test B *z* score)															
1 mTBI[a]	−.24	0.11	.03	−.15	0.10	.12	−.10	0.11	.33	−.19	0.11	.08	−.05	0.10	.54
2 mTBI[a]	.08	0.12	.52	.01	0.11	.94	.10	0.12	.41	.12	0.12	.35	.08	0.11	.48
≥3 mTBI[a]	−.30	0.11	<.01	−.23	0.10	.02	−.14	0.11	.23	−.20	0.11	.08	−.09	0.10	.38
Childhood IQ				.04	0.00	<.01							.04	0.00	<.01
Childhood SES							.09	0.04	.01				−.06	0.04	.08
High school graduate or higher[b]							.92	0.12	<.01				.29	0.12	.02
School certificate[b]							.45	0.15	<.01				.23	0.14	.10
Female[c]							.14	0.08	.09				.22	0.08	<.01
Alcohol dependence[d]										−.08	0.09	.36	−.04	0.08	.65
Cannabis dependence[e]										−.39	0.12	<.01	−.20	0.11	.06

Abbreviations: IQ, intelligence quotient; mTBI, mild traumatic brain injury; SES, socioeconomic status; TBI, traumatic brain injury; WAIS-IV, Wechsler Adult Intelligence Scale.
[a]Reference = No TBI events.
[b]Reference = No school certificate.
[c]Reference = Male.
[d]Reference = No alcohol use or dependence.
[e]Reference = No cannabis use or dependence.

TABLE 4 *Determining whether age of first injury influences midlife cognitive functioning*

Outcome	Estimate	SE	*P*	LCI	UCI
Full Scale IQ (WAIS-IV)	−0.09	0.06	.05	−0.22	0.01
Verbal Comprehension Index (WAIS-IV)	−0.08	0.05	.06	−0.21	0.01
Perceptual Reasoning Index (WAIS-IV)	−0.13	0.06	.01	−0.28	−0.05
Processing Speed Index (WAIS-IV)	−0.05	0.06	.27	−0.17	0.05
Working Memory Index (WAIS-IV)	−0.03	0.06	.53	−0.15	0.08
Processing Speed (Trail Making Test A *z* score)	−0.03	0.04	.52	−0.05	0.10
Cognitive Flexibility (Trail Making Test B *z* score)	−0.06	0.09	.21	−0.06	0.28

Abbreviations: IQ, intelligence quotient; LCI, lower confidence interval; UCI, upper confidence interval; WAIS-IV, Wechsler Adult Intelligence Scale.

between this study of the general population and studies in the context of sport may be due to the current sample being less exposed to the repetitive mTBI impacts, sustained in quick succession that can occur during engagement in high-risk sports such as rugby or football. The average number of injuries in our sample was 2.52. Studies in sport have shown that cognitive impacts and structural changes in the brain are more likely observed following multiple (3 or more) mTBI.[32] There were associations between 3 or more mTBIs and processing speed and cognitive flexibility in the initial regression models. However, a linear dose response was not observed and the significant associations did not remain when other factors were taken into account.[12] Furthermore, the current sample was less likely to experience repeated exposure to subconcussive head impacts (where there is an impact to the head but no clinical symptoms). It is likely that there may be other injury-related factors influencing the relationship between mTBI history and later life outcomes, such as whether the person had recovered from a previous injury before another was sustained, symptom burden and type of injury sustained, and the medical advice and treatment that they received following injury. Furthermore, many studies of the impact of mTBI in sport have been based on retrospective designs.[12] The longitudinal prospective design of this cohort and comprehensive life course data enabled the relative contribution of mTBI on cognitive functioning to be explored. The findings from this study highlight the importance of considering the relative impact of mTBI alongside non–injury-related factors such as gender, education, preinjury cognitive functioning, childhood cognitive functioning, and alcohol and cannabis dependence on different cognitive outcomes. There is evidence from previous studies that the impacts of sustaining an mTBI in childhood may impact on behaviors such as increased hyperactivity and risk of conduct disorders.[33] However, limited evidence suggests that there is a lasting impact on cognitive functioning in the longer term.[33,34] The findings from this study that age of first injury was not associated with cognitive functioning in mid-adulthood supports these findings.

TABLE 5 *Influence of childhood IQ, socioeconomic status, and mTBI before 7 years of age on the total number of mTBI experienced over the lifetime*

	β	SE	*P*
Model 1 Childhood IQ on number of mTBI			
Childhood IQ	−.02	0.00	.60
Model 2 Childhood IQ adjusting on number of mTBI for SES			
Childhood IQ	.01	0.00	.80
SES	−.05	0.04	.18
Model 3 Childhood IQ on number of mTBI adjusting for SES and mTBI prior to 7 y of age			
Childhood IQ	.02	0.00	.64
SES	−.05	0.03	.17
mTBI prior to 7 y of age	−.49	0.08	<.07

Abbreviations: IQ, intelligence quotient; mTBI, mild traumatic brain injury; SES, socioeconomic status.

Consequently, the current findings may provide reassurance for parents/guardians that a single childhood injury is unlikely to result in longer-term difficulties with cognitive functioning in later life. In contrast to previous research evidence suggesting a link between low overall cognitive functioning and risk of sustaining a TBI, there was no evidence of an increased predisposition of sustaining an mTBI in later life within this general population sample. However, the analysis considered only Full Scale IQ and did not explore the potential influence of specific domains of cognitive functioning such as working memory or processing speed. The only childhood factor associated with a higher number of lifetime mTBI was sustaining an mTBI before 7 years of age. This supports the finding that sustaining an mTBI increases the risk of sustaining further mTBI.[35]

Key strengths of the study were its prospective longitudinal design, premorbid assessment of cognitive functioning, regularly gathered accident records, and multiple assessments over the participants' lifetimes encompassing injury, lifestyle, and use of neuropsychological measures. However, the structured and focused nature of cognitive testing within a research setting may mask more subtle cognitive issues experienced in the real-world context where there are many demands on a person's attention, distractors in the environment, and the need to multitask. An additional limitation is that the Trail Making Test B is often used as a measure of executive functioning[26]; yet, executive functioning is a complex cognitive domain involving cognitive flexibility, planning and organization, decision making, and behavior regulation. Consequently, only the cognitive flexibility aspect of executive functioning was assessed in this study and other aspects of executive functioning need further investigation. Furthermore, the study did not directly assess for neurodegenerative disorders such as dementia or cognitive decline. A high proportion of the sample identified as being of European ethnicity/White 93% slightly higher than 87% based on population census data for the Dunedin region. Rates of lifetime cannabis dependence in the sample were high. This may reflect differences in definitions and metrics (eg, lifetime dependence vs dependence in past year) but may also reflect strength of the cohort, which is less likely to be affected by healthy volunteer bias due to low attrition rates and its general population sampling approach. However, New Zealand's rates of cannabis use disorder have been found to be higher than in other countries, which may limit generalizability of the findings.[36]

In conclusion, this prospective study revealed that there were no significant differences in cognitive functioning between adults with a history of mTBI and controls once sociodemographic and lifestyle factors were taken into account. The findings offer reassurance to those affected by mTBI in the general population.

REFERENCES

1. James SL, Theadom A, Ellenborgen RG, et al. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2019;18(1):56–87. doi:10.1016/S1474-4422(18)30499-X
2. Maas AIR, Menon DK, Adelson PD, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol*. 2017;16(12):987–1048. doi:10.1016/S1474-4422(17)30371-X
3. Machamer J, Temkin N, Dikmen S, et al. Symptom frequency and persistence in the first year after traumatic brain injury: a TRACK-TBI study. *J Neurotrauma*. 2022;39(5-6):358–370. doi:10.1089/neu.2021.0348
4. Theadom A, Parag V, Dowell T, et al. Persistent problems 1 year after mild traumatic brain injury: a longitudinal population study in New Zealand. *Br J Gen Pract*. 2016;66(642):e16–e23. doi:10.3399/bjgp16×683161
5. Nelson LD, Temkin NR, Dikmen S, et al. Recovery after mild traumatic brain injury in patients presenting to US level I trauma centers: a transforming research and clinical knowledge in traumatic brain injury (TRACK-TBI) study. *JAMA Neurol*. 2019;76(9):1049–1059. doi:10.1001/jamaneurol.2019.1313
6. McMahon P, Hricik A, Yue JK, et al. Symptomatology and functional outcome in mild traumatic brain injury: results from the prospective TRACK-TBI study. *J Neurotrauma*. 2014;31(1):26–33. doi:10.1089/neu.2013.2984
7. Theadom A, Starkey N, Barker-Collo S, et al. Population-based cohort study of the impacts of mild traumatic brain injury in adults four years post-injury. *PLoS One*. 2018;13(1):e0191655. doi:10.1371/journal.pone.0191655
8. Theadom A, Barker-Collo S, Jones K, et al. Work limitations four years following mild traumatic brain injury: a cohort study. *Arch Phys Med Rehabil*. 2017;98(8):1560–1566. doi:10.1016/j.apmr.2017.01.010
9. Frencham KAR, Fox AM, Maybery MT. Neuropsychological studies of mild traumatic brain injury: a meta-analytic review of research. *J Clin Exp Neuropsychol*. 2005;27(3):334–351. doi:10.1080/13803390490520328
10. Karr JE, Areshenkoff CN, Garcia-Barrera MA. The neuropsychological outcomes of concussion: a systematic review of meta-analyses on the cognitive sequelae of mild traumatic brain injury. *Neuropsychol*. 2014;28(3):321–336. doi:10.1037/neu0000037
11. Snowden TM, Hinde AK, Reid HMO, Christie BR. Does mild traumatic brain injury increase the risk for dementia? A systematic review and meta-analysis. *J Alzheimers Dis*. 2020;78(2):757–775. doi:10.3233/JAD-200662
12. Manley G, Gardner AJ, Schneider KJ, et al. A systematic review of potential long-term effects of sport-related concussion. *Br J Sports Med*. 2017;51(12):969–977. doi:10.1136/bjsports-2017-097791
13. Hume P, Theadom A, Lewis GN, et al. A comparison of cognitive function in former rugby union players compared with former

non-contact-sport players and the impact of concussion history. *Sports Med*. 2017;47(6):1209–1220. doi:10.1007/s40279-016-0608-8
14. Valera EM. Increasing our understanding of an overlooked public health epidemic: traumatic brain injuries in women subjected to intimate partner violence. *J Womens Health (Larchmt)*. 2018;27(6):735–736. doi:10.1089/jwh.2017.6838
15. LoBue C, Munro C, Schaffert J, et al. Traumatic brain injury and risk of long-term brain changes, accumulation of pathological markers, and developing dementia: a review. *J Alzheimers Dis*. 2019;70(3):629–654. doi:10.3233/JAD-190028
16. Carroll LJ, Cassidy JD, Peloso PM, et al. Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*. 2004;(43 suppl):84–105. doi:10.1080/16501960410023859
17. Cassidy JD, Boyle E, Carroll LJ. Population-based, inception cohort study of the incidence, course, and prognosis of mild traumatic brain injury after motor vehicle collisions. *Arch Phys Med Rehabil*. 2014;95(3 suppl):S278–S285. doi:10.1016/j.apmr.2013.08.295
18. Rickards TA, Cranston CC, McWhorter J. Persistent postconcussive symptoms: a model of predisposing, precipitating, and perpetuating factors. *Appl Neuropsychol Adult*. 2022;29(2):284–294.
19. Nordström A, Edin BB, Lindström S, Nordström P. Cognitive function and other risk factors for mild traumatic brain injury in young men: nationwide cohort study. *BMJ*. 2013;346:f723. doi:10.1136/bmj.f723
20. Quattropani MC, Sardella A, Morgante F, et al. Impact of cognitive reserve and premorbid IQ on cognitive and functional status in older outpatients. *Brain Sci*. 2021;11(7):824. doi:10.3390/brainsci11070824
21. Poulton R, Guiney H, Ramrakha S, Moffitt TE. The Dunedin study after half a century: reflections on the past, and course for the future. *J R Soc N Z*. 2022;1–20. doi:10.1080/03036758.2022.2114508
22. Poulton R, Moffitt TE, Silva PA. The Dunedin Multidisciplinary Health and Development Study: overview of the first 40 years, with an eye to the future. *Soc Psychiatry Psychiatr Epidemiol*. 2015;50:679–693. doi:10.1007/s00127-015-1048-8
23. Poulton R, Hancox R, Milne B, Baxter J, Scott K, Wilson N. The Dunedin Multidisciplinary Health and Development Study: are the findings consistent with the overall New Zealand population? *N Z Med J*. 2006;119(1235):U2002.
24. Wechsler D. *Wechsler Adult Intelligence Scale: Fourth Edition: Administration and Scoring Manual*. The Psychological Corporation, NCS Pearson, Inc; 2008.
25. Reitan R. Validity of the Trail-Making Test as an indicator of organic brain disease. *Percept Mot Skills*. 1958;8:271–276.
26. Strauss E, Sherman EMS, Spreen O. *A Compendium of Neuropsychological Tests: Administration, Norms and Commentary*. 3rd ed. Oxford University Press; 2006.
27. Menon DK, Schwab K, Wright DW, Maas AI; Demographics and Clinical Assessment Working Group of the International and Interagency Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health. Position statement: definition of traumatic brain injury. *Arch Phys Med Rehabil*. 2010;91(11):1637–1640. doi:10.1016/j.apmr.2010.05.017
28. Funder DC, Ozer DJ. Evaluating effect size in psychological research: sense and nonsense. *Adv Methods Pract Psychol Sci*. 2019;2(2):156–158. doi:10.1177/2515245919847202
29. McKinlay A, Grace RC, Horwood LJ, Fergusson DM, Ridder EM, MacFarlane MR. Prevalence of traumatic brain injury among children, adolescents and young adults: prospective evidence from a birth cohort. *Brain Inj*. 2008;22(2):175–181. doi:10.1080/02699050801888824
30. Feigin VL, Theadom A, Barker-Collo S, et al. Incidence of traumatic brain injury in New Zealand: a population-based study. *Lancet Neurol*. 2013;12(1):53–64. doi:10.1016/S1474-4422(12)70262-4
31. Montenigro PH, Alosco ML, Martin BM, et al. Cumulative head impact exposure predicts later-life depression, apathy, executive dysfunction, and cognitive impairment in former high school and college football players. *J Neurotrauma*. 2017;34(2):328–340. doi:10.1089/neu.2016.4413
32. Ford JH, Giovanello KS, Guskiewicz KM. Episodic memory in former professional football players with a history of concussion: an event-related functional neuroimaging study. *J Neurotrauma*. 2013;30(20):1683–1701. doi:10.1089/neu.2012.2535
33. McKinlay A, Dalrymple-Alford JC, Horwood LJ, Fergusson DM. Long term psychosocial outcomes after mild head injury in early childhood. *J Neurol Neurosurg Psychiatry*. 2002;73(3):281–288. doi:10.1136/jnnp.73.3.281
34. Satz P. Mild head injury in children and adolescents. *Curr Dir Psychol Sci*. 2001;10(3):106–109. doi:10.1111/1467-8721.00127
35. Lasry O, Liu EY, Powell GA, Ruel-Laliberté J, Marcoux J, Buckeridge DL. Epidemiology of recurrent traumatic brain injury in the general population: a systematic review. *Neurology*. 2017;89(21):2198–2209. doi:10.1212/WNL.0000000000004671
36. Shao H, Du H, Gan Q, et al. Trends of the global burden of disease attributable to cannabis use disorder in 204 countries and territories, 1990–2019: results from the disease burden study 2019 [published online ahead of print February 10, 2023]. *Int J Ment Health Addict*. doi:10.1007/s11469-022-00999-4