

The webinar, '**Long-term Cognitive Impairment Following Concussion: Findings from the Canadian Longitudinal Study on Aging**,' will begin shortly.

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We want to acknowledge the heartbreaking news out of BC last week and recognize the painful legacy of residential schools and the importance of honouring the 215 children who never returned home from the Kamloops Indian Residential School.

The National Coordinating Centre of the Canadian Longitudinal Study on Aging (CLSA) is located on the traditional territories of the Mississauga and Haudenosaunee Nations, and within the lands protected by the Dish With One Spoon wampum agreement.

The University of Ottawa is situated on the traditional lands of the Algonquin people. We acknowledge their longstanding relationship with this territory, which remains unceded.

As attendees of this webinar, we want to acknowledge the original inhabitants of the land where we currently have the privilege to research, live and work, wherever that may be.

Long-term Cognitive Impairment Following Concussion: Findings from the Canadian Longitudinal Study on Aging

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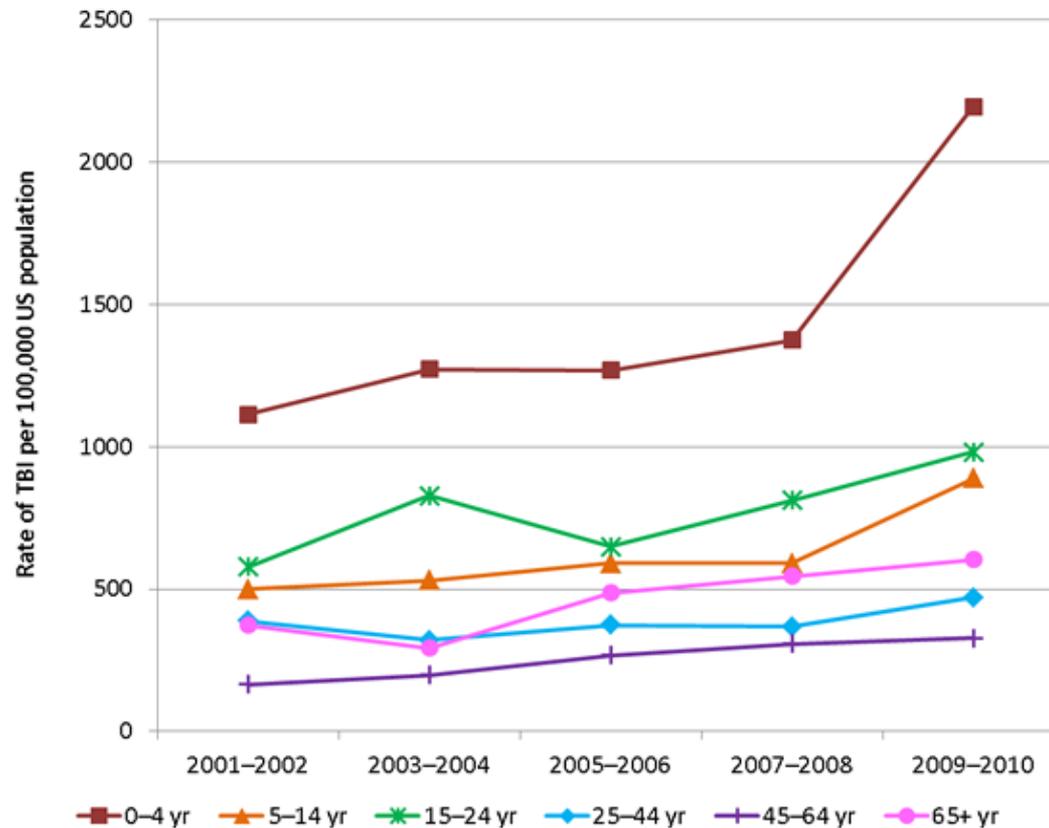
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**May 31, 2021
12-1 PM ET**

Long-term cognitive impairment following concussion: Findings from the Canadian Longitudinal Study on Aging

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TBI Epidemiology



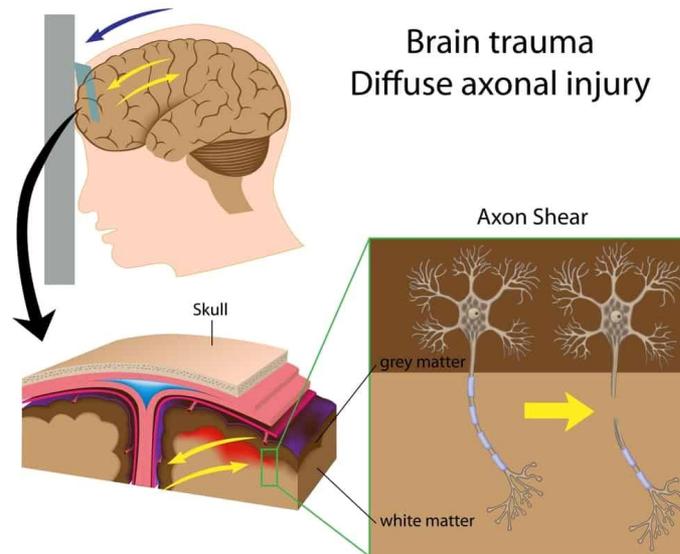
□ Estimated annual incidence of 400 per 100,000 people (Voss, Connolly, Schway, & Scher, 2015)

Mild Traumatic Brain Injury (mTBI)

- **mTBI** is considered following head injury when there is *at least one of* (American Congress on Rehabilitation Medicine, 1993):
 - Loss of consciousness (LOC) < 30 minutes
 - Posttraumatic amnesia < 24 hours
 - Altered mental status
 - Focal neurological deficits
 - Glasgow Coma Scale (Teasdale & Jennett, 1974) Scores are 13 or higher, 30-minutes post
- mTBIs account for approximately 70% of traumatic brain injuries (Voss et al., 2015)

Neuroimaging

- Alterations in frontal areas of the brain have been found in neuroimaging studies acutely after mTBI (McDonald, Saykin, & McAllister, 2012), and also years later (Mac Donald et al., 2017)
 - ▣ More pronounced when **loss of consciousness (LOC)** is experienced (Kraus et al., 2007; Sorg et al., 2014)
 - ▣ LOC thought to occur due to **axonal shearing** (Blyth & Bazarian, 2011; Jang, Kim, & Lee, 2019)



Cognitive Functioning

- Frontal neural circuitry subserves many aspects of cognitive functioning:
 - **Executive functioning** (Stuss, 2011)
 - Response inhibition (Picton et al., 2017), **set-shifting** (Oh et al., 2014)
 - Processes important in **prospective memory (PM)** (Burgess, Gonen-Yaacovi, & Volle, 2011), which can be:
 - **Event-based** – intention is completed in the presence of an external cue
 - **Time-based** – intention is carried out after a set amount of time, or at a specific time

Meta-analyses

- Prevailing view from early metanalyses: deficits remit by 3 months post-head injury (Binder, Rohling, & Larabee, 1997; Frencham, Fox, & Maybery, 2005)
 - Contemporary perspective: metanalyses may have hidden a minority of individuals that exhibit *ongoing impairment years after* (Karr et al., 2014)

Canadian Longitudinal Study on Aging

- The CLSA is a large national, longitudinal comprehensive research platform to examine individuals between the ages of 45 and 85 when recruited, assessing them every 3-years, and for at least 20 years.
 - ▣ Collects a wide variety of data and biological samples to examine health maintenance and the development of disease and disability as people age.

- There are two assessment streams: Tracking (i.e., telephone Ax), and Comprehensive.
 - ▣ We used data from the 30,097 cases in the Comprehensive Cohort
 - ▣ Extensive assessment, including neuropsychological data collected at 11 data collection sites across Canada

- We analyzed baseline data (T1), and second-wave follow-up data (T2)



Primary Measures

- Age
- Sex
- Education
 - ▣ Recoded for international readership/publication
 - ▣ < High school, high school diploma, college diploma, university degree, graduate degree
- mTBI
 - ▣ The Brief Traumatic Brain Injury Screen (BTBIS; Schwab et al., 2007)
 - LOC < 1 min, 1-20 min, or > 20 min
- Depression
 - ▣ Center for Epidemiologic Studies Depression scale (CES-D10; Andresen, Malmgren, Carter, & Patrick, 1994)
 - Score range: 0-30; higher scores = more depressive symptoms
- Testing language
 - ▣ English vs. French

Measures – Continued

- Prospective Memory
 - Miami Prospective Memory Test (MPMT; Lowenstein & Acevado, 2004)
 - **Event-based:** pt to give a \$5 bill to the examiner, and keep a \$10 bill, from an envelope
 - **Time-based:** 15 minutes after MPMT start, pt to ask for an envelope with 5 numbered cards, and to select card number 17
 - Each trial scored 0-3 points for each of:
 - **Intention to perform:** degree that action was performed
 - **Accuracy:** extent that the content of the intention was recalled or substituted
 - **Need for reminders:** reminders given after 4 minutes for time-based trial, or 60 seconds after event-based trial

Measures – Continued

□ Executive Functioning

- **Controlled Oral Word Association Test** (COWAT; Lezak, Howieson, & Loring, 2004)
- **Animal Fluency Test** (AFT; Rosen, 1980)
- **Mental Alternation Test** (MAT; Teng, 1994)
- **Victoria Stroop Test** (Stroop; Regard, 1981)

□ Long-term Memory

- **Rey Auditory Verbal Learning Test** (RAVLT; Rey, 1964)
 - **Immediate Recall** (RAVLT Immediate)
 - **Delayed Recall** (RAVLT Delayed)

Participants

- Exclusion criteria
 - Neurological disease (e.g., Alzheimer's, Multiple Sclerosis, cancer of central nervous system, etc.)
 - Stroke or transient ischemic attack
 - Any brain injury or 'multiple' injuries in the past 12-months
 - Missingness across variables of interest
 - In the case of mTBI:
 - Those who had > 1 brain injury
 - Those who reported > 20 minutes LOC
- Baseline Sample
 - Controls = 13,163
 - LOC < 1 min = 536
 - LOC 1-20 min = 435

Study 1 (Bedard, Taler, & Steffener, 2018)

Study 1 Analyses

- RM ANCOVA to examine group differences on the MPMT; controlling for: age, education, sex, depressive levels, alcohol, and testing language.
 - ▣ Group = between-subjects factor, PM cue type = within-subjects factor
- RM ANCOVA to investigate contribution of executive dysfunction relative to failure of cued content retrieval.
 - ▣ Group = between-subjects factor, failure domain type = within-subjects factor
- Impairment defined as < -2 SD from M of control group time- and event-based PM scores. Kruskal-Wallis to compare impairment rates across groups; Mann-Whitney U tests as follow-up pairwise comparisons.

Table 1

Participant Demographic and Clinical Characteristics

	Controls (n = 13163)	LOC < 1 min (n = 536)	LOC 1-20 min (n = 435)
Age, mean (SD)	61.8 (9.9)	61.0 (9.3)	61.6 (10.14)
Age, range	45-86	45-86	45-85
Sex			
Female (%)	54.0	44.1	44.0
Male (%)	46.0	54.9	55.9
Education			
< High school (%)	2.5	2.2	2.3
High school (%)	7.5	7.5	8.7
College diploma (%)	34.4	34.0	32.4
University degree (%)	29.0	28.2	26.4
Graduate degree (%)	26.6	28.2	30.3
Marital status			
Married (%)	71.6	74.4	73.3
Widowed (%)	7.3	7.3	9.4
Divorced (%)	9.8	6.3	6.0
Separated (%)	2.6	3.2	2.1
Single (%)	8.5	8.8	9.2
Depression, mean (SD)	4.7 (4.3)	4.8 (4.4)	5.3 (4.7)
Alcohol frequency			
Never (%)	9.6	9.0	7.8
< once a month (%)	16.6	19.0	17.9
About once a month (%)	11.2	10.4	11.5
2-3 times a month (%)	22.5	26.9	26.2
Once a week (%)	11.8	11.4	8.5
2-3 a week (%)	10.3	10.1	11.3
4-5 a week (%)	6.7	5.2	4.8
Almost every day (%)	11.3	8.0	12.0

Note. LOC = loss of consciousness.

Table 2

Prospective Memory and Cognitive Test Performance in the Study Samples

Test	Mild Traumatic Brain Injury					
	Control (<i>n</i> = 13163)		LOC < 1 minute (<i>n</i> = 536)		LOC 1-20 minutes (<i>n</i> = 435)	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Prospective memory						
Time-based (0-9)	8.76	0.78	8.69	0.87	8.71	0.88
Event-based (0-9)	8.54	1.27	8.71	0.98	8.52	1.29
Impairment rates						
Time-based (%)	4.6		5.5		7.1	
Event-based (%)	7.2		5.2		6.2	
MPMT Errors						
Intention to perform (0-6)	5.56	1.03	5.58	0.94	5.53	1.08
Reminder (0-6)	5.83	0.49	5.88	0.34	5.82	0.51
Accuracy (0-6)	5.91	0.40	5.93	0.29	5.88	0.46
Executive functioning						
COWAT	40.76	12.42	41.27	11.98	40.94	12.55
Stroop Interference	2.10	0.73	2.07	0.56	2.13	0.88
MAT	27.54	8.30	28.00	8.14	27.69	8.41
Declarative Memory						
RAVLT immediate	6.10	1.86	6.19	1.88	6.05	1.88
RAVLT delayed	4.29	2.15	4.41	2.15	4.14	2.12

Note. LOC = loss of consciousness; MPMT = Miami Prospective Memory Test; COWAT = Controlled Oral Word Association Test; MAT = Mental Alternation Test; RAVLT = Rey Auditory Verbal Learning Test

Study 2 (Bedard, Steffener, & Taler, 2020)

Study 2 Analyses

- MANCOVA used to examine group differences on the neuropsychological tests, controlling for age, education, sex, depressive levels, alcohol frequency, and testing language.
- Impairment to be defined as $Z < -1.5$ below control group age- and education-adjusted mean score on each neuropsychological measure
 - ▣ Impairment rates summed separately for executive functioning and declarative memory; two-test domain impairment identified
 - ▣ Kruskal-Wallis for between group rates of impairment; Mann-Whitney U tests as pairwise comparisons

Table 5

Neuropsychological Test Scores and Impairment Rates Across Study Groups

Test	Control (<i>n</i> = 13163)		Mild Traumatic Brain Injury				<i>p</i> -value
	M	SD	LOC < 1 min (<i>n</i> = 536)		LOC 1-20 min (<i>n</i> = 435)		
	M	SD	M	SD	M	SD	
Declarative memory raw scores							
RAVLT immediate	6.10	1.86	6.19	1.88	6.05	1.88	.29
RAVLT delayed	4.29	2.15	4.41	2.15	4.14	2.12	.14
Impairment rates							
RAVLT immediate (%)	8.4		8.0		13.1		.01
RAVLT delayed (%)	8.4		8.0		13.1		.01
Executive functioning raw scores							
Stroop interference	2.10	0.73	2.07	0.56	2.13	0.87	.52
Mental Alternation Test	27.54	8.30	28.00	8.14	27.70	8.41	.69
COWAT	40.76	12.42	41.27	11.98	40.94	12.55	.42
Animal Fluency Test	20.30	5.56	21.30	5.59	20.41	5.56	.01
Impairment rates							
Stroop Interference (%)	4.0		3.4		6.0		.07
Mental Alternation Test (%)	7.8		9.0		11.4		.01
COWAT (%)	8.4		8.2		13.1		.01
Animal Fluency Test (%)	9.5		6.5		7.8		.07
Two-test impairment							
Declarative memory	8.4		8.0		13.1		.01
Executive functioning	6.5		9.0		9.5		.04

Note. LOC = loss of consciousness; RAVLT = Rey Auditory Verbal Learning Test; COWAT = Controlled Oral Word Association Test; neuropsychological raw scores are presented and rates of impairment based upon scoring 1.5 SD below the control group (*n* = 13163) mean and standard deviations (i.e., Z-scores); *p*-values considered significant (*p* < .05) have been bolded.

Study 3 (Bedard & Taler, 2020)

Study 3 Analyses

- Reliable change index (RCI; Jacobson & Traux, 1991) conducted, by dividing the difference between baseline scores and the follow-up scores by the control group SD of the difference between the two time-point scores
 - Accounts for measurement error and practice effects
 - Improvement: $Z > 1.645$, Decline: $Z < -1.645$
 - Kruskal-Wallis tests to compare between group differences, separately for improvement and decline

Reliable Change Scores (Duff, 2012)

$$\underbrace{(T2 - T1)}_{\text{Each participant}} - \underbrace{(M2 - M1)}_{\text{Comparisons only}} / \text{SED}$$

SED = Standard error of the *difference*

Improvement: $Z > 1.645$, Decline: $Z < - 1.645$

Kruskal-Wallis tests to compare between group differences, separately for improvement and decline

RCI Scores

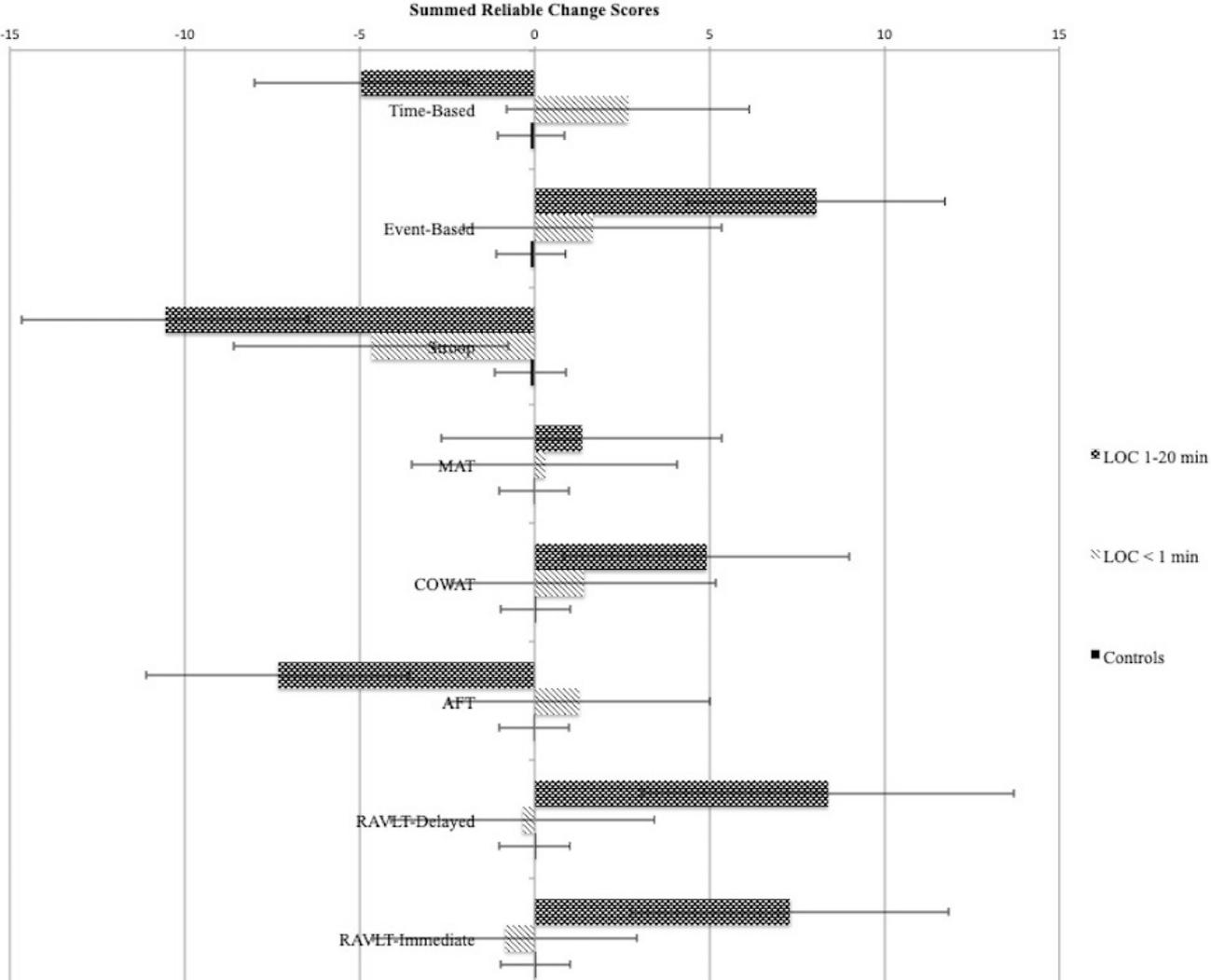


Table 7

Neuropsychological test and impairment rates across study groups

Test, mean (SD)	Mild Traumatic Brain Injury					
	Control (n = 10712)		LOC < 1 min (n = 440)		LOC 1-20 min (n = 350)	
	T1	T2	T1	T2	T1	T2
Declarative memory raw scores						
RAVLT immediate	6.08 (1.84)	6.85 (2.12)	6.14 (1.92)	6.94 (2.23)	6.00 (1.85)	6.84 (2.15)
RAVLT delayed	4.30 (2.12)	4.97 (2.36)	4.28 (2.16)	4.97 (2.48)	4.21 (2.13)	4.89 (2.37)
<u>RCI Deterioration/Improvement</u>						
RAVLT immediate (%)		6.2 / 1.7		5.7 / 1.6		7.1 / 1.7
RAVLT delayed (%)		6.4 / 2.1		5.9 / 1.8		5.1 / 2.0
Executive functioning raw scores						
Stroop interference	2.12 (0.70)	2.10 (0.70)	2.07 (0.50)	2.04 (0.59)	2.19 (1.01)	2.10 (0.52)
Mental Alternation Test	27.62 (8.30)	27.11 (7.36)	27.96 (8.47)	27.03 (7.95)	27.53 (7.94)	26.69 (7.23)
COWAT	40.32 (12.45)	41.13 (12.27)	40.39 (11.97)	41.28 (11.68)	39.83 (12.47)	40.70 (13.02)
Animal Fluency Test	20.32 (5.50)	20.08 (5.13)	20.89 (5.51)	20.60 (5.19)	20.42 (5.10)	20.79 (4.88)
Event-based PM	8.58 (1.19)	8.68 (1.06)	8.68 (1.06)	8.75 (0.92)	8.64 (1.09)	8.69 (0.97)
Time-based PM	8.79 (0.70)	8.70 (0.88)	8.73 (0.73)	8.66 (0.97)	8.77 (0.72)	8.64 (0.96)
<u>RCI Deterioration/Improvement</u>						
Stroop Interference (%)		3.8 / 6.2		3.2 / 5.0		4.6 / 2.6
Mental Alternation Test (%)		5.4 / 2.6		4.8 / 2.5		8.3 / 3.4
COWAT (%)		6.6 / 2.9		5.5 / 3.6		8.6 / 4.3
Animal Fluency Test (%)		4.3 / 4.6		4.3 / 4.3		7.1 / 4.6
Event-based PM (%)		3.8 / 7.3		2.3 / 6.6		2.9 / 6.3
Time-based PM (%)		6.8 / 2.0		5.2 / 1.8		7.4 / 2.6
Global RCI Decline/Improvement						
Two or more tests (%)		6.7 / 6.4		6.6 / 6.1		10.3 / 6.6

Note. LOC = loss of consciousness; RAVLT = Rey Auditory Verbal Learning Test; COWAT = Controlled Oral Word Association Test; RCI = reliable change index; neuropsychological raw scores are presented and RCI rates represent those calculated on age- and education-adjusted test scores. Deterioration, presented before the forward slash is indexed as an RCI value of ≤ -1.645 , and improvement, presented after the forward slash identifies the percentage of RCI values ≥ 1.645 .

General Discussion

- mTBIs are a common occurrence among Canadians, however, our understanding of cognitive difficulties into the long-term has not been well understood
 - ▣ This is particularly the case when LOC is experienced

- mTBI is associated with lower time-based prospective memory functioning. Prospective memory errors were consistent with a breakdown in self-initiated monitoring.
 - ▣ LOC 1-20 minutes were most impaired on time-based
 - ▣ These findings are consistent with reduced structural and functional connectivity in frontal tracts long after mTBI

Discussion Continued

- mTBI is more likely to encounter impairments in verbal memory (encoding and storage/retrieval), and cognitive control/set-shifting
- At a 3-year follow-up window, mTBI is associated with greater rate of cognitive decline, particularly in indices of set-shifting

Conclusions

- A small minority of individuals experience persistent cognitive impairment following mTBI
 - ▣ They may be lost in identifying deficits through grouped mean-level analyses
- mTBI may predispose some individuals to further cognitive decline

Thank you!



Questions?

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Upcoming CLSA Webinar

The next and final CLSA webinar of the season will take place in June and will focus on data linkage.

Details and registration info will be posted to the CLSA website

June 2021

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