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CASE REPORT



## Psychological distress and gender predict cognitive complaint after adult civilian mild traumatic brain injury in pre-morbidly healthy adults

Arielle M. Levy <sup>a</sup>, Michael M. Saling<sup>a</sup> and Jacqueline F. I. Anderson <sup>a,b</sup>

<sup>a</sup>Melbourne School of Psychological Sciences, The University of Melbourne, Melbourne, Australia;

<sup>b</sup>Psychology Department, The Alfred Hospital, Melbourne, Australia

### ABSTRACT

Subjective cognitive symptoms are common after mild traumatic brain injury (mTBI), and are associated with important outcome factors including return to work. This study examined self-reported cognitive symptoms in mTBI and trauma controls (TCs), and explored psychological distress and gender as predictors of these symptoms. Pre-morbidly healthy adults with mTBI ( $n = 68$ ) and general trauma ( $n = 40$ ) were prospectively recruited from inpatient hospital wards and assessed 6–10 weeks post-injury. Primary measures included self-reported cognitive symptoms, post-concussion symptoms, and psychological distress. Groups were matched on all background variables, including objective cognitive performance. Within this context, subjective cognitive symptoms were significantly elevated after mTBI relative to TCs ( $t = 3.396$ ,  $p = .001$ ). In contrast, there was no difference in post-concussion symptoms between groups ( $t = 1.275$ ,  $p = .206$ ). Psychological distress ( $\beta = .536$ ,  $p < .001$ ) and gender ( $\beta = .253$ ,  $p = .012$ ) predicted subjective cognitive symptoms in mTBI, with females and those with higher distress reporting greater symptoms. Unlike general post-concussion symptoms, subjective cognitive symptoms were elevated after mTBI relative to TCs, suggesting that mTBI-specific factors underly this elevation. Females and individuals with high psychological distress are important subgroups to consider for potential intervention following mTBI.



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Gender

Mild traumatic brain injury (mTBI) is the most common type of traumatic brain injury, occurring at a rate of 100–300 hospital-evaluated cases per 100,000 worldwide, not accounting for those who do not present to hospital (Cassidy et al., 2004). Mild TBI is a major public health concern, because of its high incidence, and the failure of a subset of patients to recover successfully (McMahon et al., 2014).

**CONTACT** Arielle M. Levy  [ariellemiriamlevy@gmail.com](mailto:ariellemiriamlevy@gmail.com)  Melbourne School of Psychological Sciences, Redmond Barry Building, The University of Melbourne, Melbourne, VIC 3010, Australia  
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Instances of mTBI often lead to a constellation of subjective cognitive, affective and/or somatic post-concussion symptoms (PCS) in the acute post-injury period (Levin & Diaz-Arrastia, 2015). While many individuals with mTBI make a full recovery in the initial weeks and months after injury, a subgroup of individuals continues to report symptoms in the chronic phase (>3 months) following injury (Cassidy et al., 2014; Machamer et al., 2022). The aetiology of late and persisting symptoms has been a point of debate in the literature (Silverberg & Iverson, 2011).

The cognitive symptom component of PCS, which comprise self-reported deficits in memory, attention, processing speed, and executive function, are very common after mTBI (Clarke et al., 2012). These subjective cognitive symptoms are associated with key outcome factors, including return to work and quality of life (Phillips et al., 2017; Theadom et al., 2017; Voormolen et al., 2019). These symptoms may additionally increase the likelihood of repeated health care presentations, contributing to the substantial economic burden of mTBI (Te Ao et al., 2014).

Despite the importance of subjective cognitive symptoms, these symptoms have received limited direct attention in mTBI research. Rather, most research focuses on post-concussion symptoms generically, with little emphasis on particular domains (Cassidy et al., 2014). Further, the limited research that has addressed subjective cognitive symptomatology as a distinct entity, has typically evaluated cognitive symptoms in terms of a small number of cognitive items that are typically incorporated in generic post-concussion measures (Ngwenya et al., 2018). As these measures only contain three to four cognition-related items, this approach limits the reliability and validity of inferences that can be made about cognitive symptoms specifically (Anderson, 2021). Only a couple of studies have evaluated these symptoms using more comprehensive measures comprised of multiple items for each cognitive construct commonly associated with subjective cognitive impairment after mTBI (i.e., processing speed, attention, memory and executive function; Anderson, 2021; Clarke et al., 2012).

In contrast to generic post-concussion symptoms, which can be reported at similar levels in mTBI and non-mTBI groups (Cassidy et al., 2014; Dean et al., 2012), preliminary findings suggest that subjective cognitive symptoms may be elevated in mTBI relative to controls (de Koning et al., 2016; Ponsford et al., 2011). A recent systematic review and meta-analysis examined this question and found that self-reported cognitive symptoms were elevated after mTBI relative to a combination of healthy and injured controls (Levy et al., 2022). Although this indicates that post-mTBI cognitive symptoms warrant attention, it is not yet clear whether cognitive symptoms are elevated in mTBI patients compared to trauma controls (TCs). Factors associated with general trauma, such as pain (Cnossen et al., 2018) and fatigue (Anderson & Jordan, 2021; Stulemeijer et al., 2007), can contribute to elevated self-reported symptoms. For this

reason, there is a need for research that compares subjective cognitive symptoms between individuals with mTBI and TCs, who have equivalent levels of general trauma-related consequences, in order to control for these potential confounding factors.

Recent studies have also demonstrated that females (Levin et al., 2021) and those with increased psychological distress (Hromas et al., 2021; Stillman et al., 2019) report greater subjective cognitive symptoms after mTBI. However, to date no studies have employed a comprehensive measure of cognitive symptoms to determine whether these findings are specific to mTBI or common to all individuals who have suffered a traumatic injury. Indeed, findings to date suggest that gender and psychological distress may not be associated with self-reported cognitive symptoms in some control groups (Anderson, 2021; Levin et al., 2021). Consequently, the relative specificity of these relationships to mTBI is currently unknown, and our understanding of the mechanisms contributing to the relationships between psychological distress, gender and cognitive symptoms is therefore limited. This is particularly problematic because lack of mechanistic knowledge about the factors contributing to outcome after mTBI deleteriously impacts clinical intervention and management choices for individuals with mTBI.

The primary aims of this study were to comprehensively investigate self-reported cognitive symptoms in pre-morbidly healthy adults with mTBI and TCs. It was hypothesized that approximately 8 weeks after injury: (1) self-reported cognitive symptoms would be greater in the mTBI group than TCs; and (2) subjective cognitive symptoms would be significantly predicted by gender and psychological distress in the mTBI group. A secondary aim of this study was to evaluate whether different cognitive symptom measures have similar utility for evaluating these symptoms in mTBI.

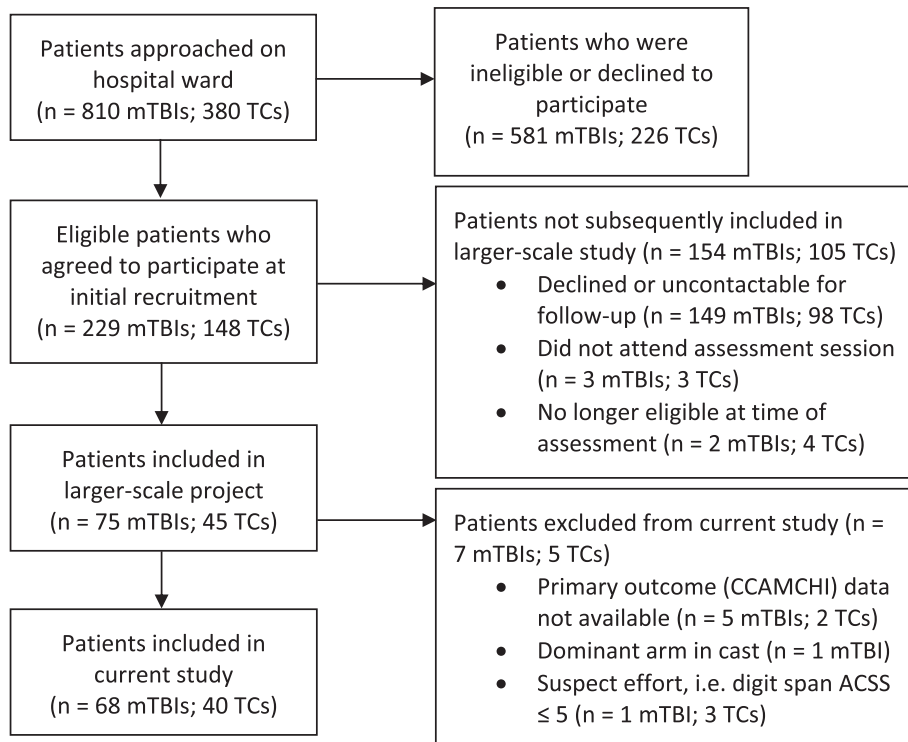
## Methods

### Participants

Study participants were recruited from trauma wards at The Alfred hospital and Royal Melbourne Hospital between December 2016 and January 2020. Potential participants were allocated to either the mTBI or TC group based on the presence or absence of mTBI. The definition of mTBI was based on the World Health Organization (WHO) criteria, i.e., (1) presence of at least one of the following: confusion or disorientation, loss of consciousness  $\leq 30$  min, post-traumatic amnesia  $\leq 24$  h, and/or other transient neurological abnormalities; and (2) Glasgow Coma scale score of 13–15 after 30 min or more post-injury (Carroll et al., 2004). Individuals who had not sustained any impact or injury to the head were assigned to the TC group. Exclusion criteria for both groups included: age  $< 18$  or  $> 60$  years; current or recent mood/anxiety disorder; history of severe psychological

condition; previous moderate-severe head injury; previous neurological history; current or prior intravenous drug use; current or prior heavy alcohol use; or lack of English proficiency. An additional exclusion criterion for the TC group was a history of previous head injury. Further detail on participant recruitment and eligibility has been published previously (Anderson & Cockle, 2021). Participants provided informed consent, and the study was approved by the Human Research Ethics Committees at The Alfred Hospital and Royal Melbourne Hospital.

This study was part of a larger-scale project (Anderson, 2021; Anderson & Cockle, 2021). The current study excluded participants with primary outcome (i.e., CCAMCHI) data unavailable ( $n = 5$  mTBIs, 2 TCs), those who displayed sub-optimal effort ( $n = 1$  mTBI, 3 TCs), and those with their dominant arm in a cast such that it was likely to affect motor performance on the SDMT ( $n = 1$  mTBI; see Figure 1). A flow diagram of participant recruitment is provided in Figure 1.



**Figure 1.** Flow chart of participant recruitment for mild traumatic brain injury (mTBI) and trauma control (TC) patients between December 2016 and January 2020.

## Measures

### Cognitive symptoms – primary measure

Subjective cognitive symptoms were assessed using the Cognitive Complaint After Mild Closed Head Injury (CCAMCHI) scale (Anderson, 2021; Clarke et al.,

2012). The CCAMCHI is a 30-item questionnaire that assesses subjective beliefs about individuals' cognitive abilities in the domains of attention, memory, processing speed, and executive function (Anderson, 2021). Participants with mTBI were asked to rate their current cognitive abilities compared to their abilities prior to their injury. Responses were made on a Likert scale from one (e.g., "much better") to five (e.g., "much worse"). Possible scores ranged from 30 to 150. A score of 90 indicates no change in subjective cognitive abilities; a score above 90 indicates worse cognitive functioning relative to pre-injury; a score below 90 indicates better cognitive functioning relative to pre-injury. The control version of the questionnaire asked participants to rate their current cognitive abilities relative to their abilities 4 weeks ago. The CCAMCHI demonstrated excellent internal consistency ( $\alpha = 0.90$ ) in this sample, which is consistent with previous samples (Clarke et al., 2012).

The CCAMCHI was employed as the primary measure of subjective cognitive symptoms in this study, given that it is: (1) specifically developed for use in mTBI, and thus assesses the key cognitive domains impacted by mTBI (Anderson, 2021); and (2) is a comprehensive, 30-item measure, which is likely to provide higher reliability than cognitive subscales from postconcussion symptom measures, which typically consist of only three to four items (Anderson, 2021). The CCAMCHI is similar in length to other clinically used measures (Rush et al., 1996).

### *Cognitive symptoms – secondary measures*

The A-B Neuropsychological Assessment Schedule (ABNAS; Aldenkamp et al., 1995; Brooks et al., 2001) was employed as a secondary measure of subjective cognitive symptoms in order to explore whether differing measures have similar utility for assessing these symptoms in mTBI. The ABNAS was originally developed to assess subjective cognitive side effects in individuals taking anti-epileptic drugs (Brooks et al., 2001), and has since been employed in other clinical populations (Lamb et al., 2013). The 24-item measure assesses symptoms across the following domains: fatigue, cognitive slowing, memory, concentration, motor coordination, and language. The ABNAS has demonstrated good validity and excellent reliability in clinical and non-clinical samples (Brooks et al., 2001).

The cognitive subscale of the Rivermead Post-Concussion Symptoms Questionnaire (RPQ; King et al., 1995) was also employed as a secondary measure of subjective cognitive symptoms, in order to allow for comparison to previous studies. The cognitive subscale consists of the three cognition-related items from the RPQ: forgetfulness, poor concentration, and taking longer to think (Potter et al., 2006).

### *Post-concussion symptoms*

The total score of the RPQ was employed as a measure of general post-concussion symptoms after injury (King et al., 1995). The 16-item scale assesses the

presence and severity of various cognitive, affective, and somatic symptoms commonly experienced after mTBI. This tool is widely used in mTBI research and shows high reliability (King et al., 1995).

### *Psychological distress*

Symptoms of depression, anxiety, and post-traumatic stress were assessed using the Inventory of Depressive Symptomatology (IDS; 30-item version; Rush et al., 1996), the Beck Anxiety Inventory (BAI; Beck et al., 1988), and the PTSD Checklist for DSM-5 (PCL-5; Weathers et al., 2013). Each of these measures have strong psychometric properties (Beck et al., 1988; Blevins et al., 2015; Rush et al., 1996) and have been used previously in mTBI populations (Levin et al., 2021; Stillman et al., 2019; Suhr & Gunstad, 2002). A psychological distress index was created by converting scores on the PCL-5 to a four-point scale to create equivalence with the IDS and BAI, and then summing scores on the three measures (Anderson & Jordan, 2021). Total possible scores ranged from zero (no symptoms experienced) to 207 (every symptom experienced to an extreme degree).

### *Pain and fatigue*

Pain and fatigue were measured using the Short-Form McGill Pain Questionnaire (SF-MPQ-2; Dworkin et al., 2009) and the Multidimensional Fatigue Inventory (MFI; Smets et al., 1995), respectively. Both measures have been validated for use in clinical populations and have been used previously in TBI research (Anderson, 2020; Lovejoy et al., 2012; Manoli et al., 2020).

### *Objective cognitive performance*

**Premorbid intellectual functioning.** The Weschler Test of Adult Reading (WTAR; Wechsler, 2001) was used to estimate premorbid intellectual abilities. This task requires individuals to read irregularly-spelled words aloud, with the total score being the number of words pronounced correctly. This task has been shown to provide stable estimates of premorbid abilities in controls and in individuals with mTBI (Steward et al., 2017). This is a more accurate method of estimating premorbid intellectual function compared to estimates based on demographic information (Bright & van der Linde, 2020).

**Speed of information processing.** Speed of information processing was assessed using the written version of the Symbol Digit Modalities Test (SDMT; Smith, 1982). This is a timed task that requires individuals to fill in numbers that correspond to specific symbols. This measure is sensitive to changes in processing speed after mTBI (Anderson & Cockle, 2021). The variable of interest on the task was the total number of items completed in 120 s.

**Attention.** The Digit Span subtest from the Weschler Adult Intelligence Scale, Fourth Edition (WAIS-IV) was employed as a measure of attention and working memory (Wechsler, 2008). On this task, individuals are required to repeat digit sets of increasing length in their original order of presentation, reverse order, and ascending order, respectively. Total raw score was used as the variable of interest, with age-scaled scores avoided in order to enable comparison with other cognitive tasks for which age-scaled scores were not available. This measure has good validity and reliability, and is commonly used in mTBI (Wechsler, 2008; Wilde et al., 2010).

**Memory.** Memory was assessed using the Rey Auditory Verbal Learning Test (RAVLT; Schmidt, 1996). On this task, individuals learn a 15-word list over repeated trials and then recall these words after a distraction and delay period. The variable of interest was the total number of items recalled after a 25-minute delay (Trial A7). The RAVLT is commonly used in mTBI research and has good psychometric properties (D'Souza et al., 2019; Wilde et al., 2010).

**Executive functioning.** The Trail Making Test-Part B (TMT-B) completion time (Reitan, 1992) and the Controlled Oral Word Association Test (COWAT) – letters F, A, and S (Benton et al., 1994) were used to assess executive functioning. The TMT-B incorporates various cognitive domains including mental flexibility and set shifting, and the COWAT is a measure of verbal fluency (Strauss et al., 2006). Both tasks are recommended for assessing outcome after TBI (Wilde et al., 2010).

### *Performance validity*

The Digit Span subtest from the WAIS-IV was used as a measure of performance validity (Wechsler, 2008). Suboptimal effort was defined as an age-corrected standard score (ACSS) of five or below, a cutoff which maintains high specificity ( $\geq 90\%$ ) while maximizing sensitivity, including in TBI groups (Babikian & Boone, 2007).

### *Procedure*

Group membership and eligibility were determined through patient interview and hospital records. Individuals who provided consent to be contacted for follow up were subsequently assessed at The Alfred Hospital 6–10 weeks after injury. Measures were completed in the following order: SDMT, WTAR, RAVLT, DS, TMT-B, COWAT-FAS, RPQ, ABNAS, CCAMCHI, MFI, IDS, BAI, PCL-5, and SF-MPQ-2.

### *Statistical analysis*

Statistical assumptions were explored prior to all analyses. Groups were compared using Chi-square tests of independence and Welch two sample t-tests for categorical and continuous data, respectively (Field, 2012). The exception



was the RPQ cognitive subscale, which is a continuous variable but was highly skewed and contained a large number of zero responses. For these reasons, this data was converted into a binary variable (0 = no symptom endorsement; 1 = any degree of symptom endorsement) and analyzed using odds ratios. To assess the relationships between the four symptom variables, Spearman's *rho* correlations were employed. Multiple linear regression was used to examine predictors of cognitive and post-concussion symptoms. These analyses were conducted using the CCAMCHI, due to its large number of mTBI-specific items. Given the small number of females in each group, we additionally calculated bootstrapped confidence intervals for the regression models (Field, 2012). There was no more than one outlier (*z* score > 3.29; Tabachnick & Fidell, 2013), in each group for any variable. When outliers were present analyses were additionally run with Winsorized data; in all cases there were no changes to the results. Small, medium, and large effect sizes were defined as 0.2, 0.5, and 0.8 for Cohen's *d*, and .01, .09, and .25 for  $r^2$ , respectively (Ellis, 2010). Statistical analysis was conducted in R version 3.6.1 (R Core Team, 2019), using the following packages: tidyverse (Wickham et al., 2019), rstatix (Kassambara, 2021), Hmisc (Harrell, 2021), effect size (Ben-Shachar et al., 2020), lm.beta (Behrendt, 2014), confintr (Mayer, 2022), boot (Canty & Ripley, 2021; Davison & Hinkley, 1997), epiR (Stevenson et al., 2022), and DescTools (Signorell, 2023).

## Results

A final sample of 68 mTBI participants (age *M* = 36.8, *SD* = 14.8; 22% female) and 40 TC participants (age *M* = 37.1, *SD* = 12.8; 18% female) was included in the current study. Demographic data and injury characteristics for included participants are presented in Table 1. The groups were well matched on all demographic and injury variables, with no significant between-group differences on any variable.

**Table 1.** Demographic information and injury characteristics.

	mTBI ( <i>n</i> = 68)	TC ( <i>n</i> = 40)	Test statistic <sup>a</sup>	<i>p</i>
Age, mean (SD), range	36.8 (14.8), 18–60	37.1 (12.8), 18–59	−0.095	.925
Gender, <i>n</i> (%)			0.323	.570
Male	53 (77.9%)	33 (82.5%)		
Female	15 (22.5%)	7 (17.5%)		
Years of education, mean (SD)	13.3 (2.4)	13.4 (2.7)	−0.023	.982
Predicted FSIQ, mean (SD)	105.9 (9.2)	106.0 (9.5)	−0.068	.946
Current work status			0.095	.954
Full-time	33 (48.5%)	20 (50%)		
Part-time	11 (16.2%)	7 (17.5%)		
Not working	24 (35.3%)	13 (32.5%)		
Litigant, <i>n</i> (%)	8 (11.8%)	4 (10.0%)	0.079	1.000 <sup>b</sup>
Previous mTBI, <i>n</i> (%)				–
None	51 (75%)	–		
1	12 (17.6%)	–		
> 1	5 (7.4%)	–		
Days since injury, mean (SD), range	60.4 (10.4), 37–84	56.7 (12.0), 39–88	1.643	.105

(Continued)

**Table 1.** Continued.

	mTBI ( <i>n</i> = 68)	TC ( <i>n</i> = 40)	Test statistic <sup>a</sup>	<i>p</i>
Mechanism of injury, <i>n</i> (%)				.680 <sup>b</sup>
Motor vehicle accident	10 (14.7%)	9 (22.5%)		
Motorbike accident	10 (14.7%)	9 (22.5%)		
Cycling accident	22 (32.4%)	9 (22.5%)		
Fall	13 (19.1%)	6 (15.0%)		
Sports	4 (5.9%)	3 (7.5%)		
Other	9 (13.2%)	4 (10.0%)		
Glasgow Coma Scale score, <i>n</i> (%) <sup>c</sup>				–
13	5 (7.4%)	–		
14	14 (20.6%)	–		
15	48 (70.6%)	–		
Loss of consciousness, <i>n</i> (%) <sup>d</sup>				–
None	10 (14.7%)	–		
< 1 min	27 (39.7%)	–		
1–5 mins	20 (29.4%)	–		
5–10 mins	5 (7.4%)	–		
10–20 mins	1 (1.5%)	–		
20–30 mins	4 (5.9%)	–		
Post-traumatic amnesia, <i>n</i> (%)				–
< 1 min	18 (26.5%)	–		
1–5 mins	19 (27.9%)	–		
5–60 mins	12 (17.6%)	–		
1–6 hrs	5 (7.4%)	–		
6–18 hrs	8 (11.8%)	–		
18–24 hrs	6 (8.8%)	–		
Psychological distress, mean (SD) <sup>e</sup>	27.5 (21.2)	22.0 (15.1)		.128
Pain, mean (SD) <sup>f</sup>	1.4 (1.5)	1.3 (1.0)	0.384	.702
Fatigue, mean (SD) <sup>g</sup>	50.6 (15.1)	49.8 (13.4)	0.317	.752

Note: FSIQ = full-scale IQ; mTBI = mild traumatic brain injury; TC = trauma control.

<sup>a</sup>Test statistics are the *t* values for continuous variables (age, education, FSIQ, days since injury, psychological distress, pain, fatigue) and the Chi-squared values for categorical variables (gender, work status, litigation, mechanism of injury).

<sup>b</sup>Based on Chi-squared test with simulated *p*-value (2000 replicates).

<sup>c</sup>GCS score was unknown for one mTBI participant.

<sup>d</sup>Loss of consciousness data was unavailable for one mTBI participant.

<sup>e</sup>Psychological distress data was missing for one mTBI and two TC participants.

<sup>f</sup>Pain data was missing for one mTBI and one TC participant.

<sup>g</sup>Fatigue data was missing for one mTBI participant.

## Cognitive performance

Given that a key focus of this study was to compare subjective cognitive symptom reporting between mTBI and TC participants, groups were first compared on measures of objective cognitive performance. There was no difference in cognitive performance between groups on any cognitive measure (Table 2).

**Table 2.** Group comparisons on cognitive performance measures.

Cognitive domain	Measure	mTBI ( <i>n</i> = 68)	TC ( <i>n</i> = 40)	<i>t</i>	<i>p</i>	Cohen's <i>d</i> [95% CI]
Processing speed	SDMT	67.81 (12.15)	66.65 (13.10)	0.456	.650	0.09 [–0.30, 0.48]
Attention	Digit span	28.91 (4.91)	29.50 (4.72)	–0.616	.539	–0.12 [–0.51, 0.27]
Memory	RAVLT <sup>a</sup>	11.33 (2.61)	10.67 (2.74)	1.220	.226	0.25 [–0.15, 0.64]
Executive function	TMT-B	58.56 (17.32)	59.83 (23.80)	–0.294	.770	–0.06 [–0.45, 0.33]
	COWAT	36.94 (10.18)	39.78 (9.56)	–1.453	.150	–0.28 [–0.68, 0.11]

Note: CI = confidence interval; COWAT = Controlled Oral Word Association Test; mTBI = mild traumatic brain injury; RAVLT = Rey Auditory Verbal Learning Test; SDMT = Symbol Digit Modalities Test; TC = trauma control; TMT-B = Trail Making Test-Part B.

<sup>a</sup>RAVLT data was missing for one mTBI participant and one TC participant.

### Cognitive and post-concussion symptoms

Summary statistics and between-group comparisons for each symptom measure are provided in Table 3. Subjective cognitive symptoms, as assessed by the CCAMCHI, were reported to a significantly greater degree in the mTBI group than the TC group (large effect). On this measure, the mTBI group tended towards reporting worse cognitive functioning relative to before injury (score >90), whereas the TC group reported approximately no change in cognitive functioning (score ~90). There was also a significant difference between groups in cognitive symptom reporting on the RPQ. Due to the binary coding of this variable, this indicates that these symptoms were reported at a higher frequency in the mTBI group than in the TC group (small-medium effect). Of note, this was not a robust finding, given that the confidence interval for the odds ratio verged on including 1.0 (the value that indicates no differences between groups). In contrast, there was no difference between groups in the reporting of cognitive symptoms as assessed by the ABNAS, or in the reporting of general post-concussion symptoms on the RPQ.

**Table 3.** Group comparisons of cognitive and post-concussion symptom measures.

	mTBI ( <i>n</i> = 68) M (SD)	TC ( <i>n</i> = 40) M (SD)	Test statistic <sup>a</sup>	<i>p</i>	Cohen's <i>d</i> [95% CI]	Odds Ratio [95% CI]
CCAMCHI Total	94.6 (7.9)	89.7 (6.7)	3.396	.001	0.65 [0.25, 1.05]	
RPQ Total	12.2 (10.7)	9.6 (9.8)	1.275	.206	0.25 [−0.14, 0.64]	
RPQ Cognitive	2.94 (3.02)	1.64 (2.36)	4.000	.046		2.24 [1.01, 4.97]
ABNAS Total	11.1 (11.6)	9.8 (7.9)	0.665	.507	0.12 [−0.27, 0.51]	

Note: An odds ratio of 1 indicates no difference between groups. ABNAS = A-B Neuropsychological Assessment Schedule; CCAMCHI = Cognitive Complaint After Mild Closed Head Injury; CI = confidence interval; mTBI = mild traumatic brain injury; RPQ = Rivermead Post-Concussion Symptoms Questionnaire; TC = trauma control.

<sup>a</sup>The test statistic provided is the *t* value for all measures except for RPQ Cognitive, for which the Chi-squared value is provided.

Correlations between subjective symptom variables in mTBI and TC groups are provided in Table 4. All four symptom variables were significantly correlated

**Table 4.** Correlations between symptom variables within each group.

	mTBI ( <i>n</i> = 68)		
	RPQ total	RPQ cognitive	ABNAS
CCAMCHI	.62*** [.43, .75]	.66*** [.44, .79]	.76*** [.61, .86]
RPQ total		.84*** [.69, .90]	.78*** [.65, .86]
RPQ cognitive			.75*** [.59, .85]
	TC ( <i>n</i> = 40)		
	RPQ Total	RPQ Cognitive	ABNAS
CCAMCHI	.18 [−.18, .50]	.16 [−.23, .50]	.29 [−.10, .59]
RPQ total		.73*** [.50, .85]	.65*** [.40, .81]
RPQ cognitive			.68*** [.45, .80]

Note. Bootstrapped 95% confidence intervals (BCa method; 9999 replications) are provided in brackets. ABNAS = A-B Neuropsychological Assessment Schedule; CCAMCHI = Cognitive Complaint After Mild Closed Head Injury; mTBI = mild traumatic brain injury; RPQ = Rivermead Post-Concussion Symptoms Questionnaire; TC = trauma control.

\*\*\**p* < .001

with each other in the mTBI group. In the TC group, only responses on the RPQ and the ABNAS were correlated with each other; responses on the CCAMCHI were not correlated with either the ABNAS, the RPQ total score, or the RPQ cognitive subscale.

### *Predictors of cognitive and post-concussion symptoms*

Table 5 provides the results of the regression analyses. Gender and psychological distress were each significant independent predictors of subjective cognitive symptoms in mTBI, with females and those with increased psychological distress reporting greater symptoms (small and medium-large effects, respectively). The overall model was significant,  $R^2_{adj} = .39$ ,  $F(2, 64) = 21.89$ ,  $p < .001$ . In the TC group, neither variable predicted cognitive symptoms, and the overall model was not significant,  $R^2_{adj} = -.06$ ,  $F(2, 35) = 0.02$ ,  $p = .985$ .

Psychological distress was also a significant predictor of general post-concussion symptoms in both the mTBI and TC groups, with medium-large effect sizes. Gender was a significant predictor of post-concussion symptom reporting in the mTBI group, with female gender associated with greater symptoms. Gender was not a significant predictor of cognitive symptoms in the TC group, although estimates of effect size were similar across both groups (small effects). The overall prediction model was significant in both the mTBI group,  $R^2_{adj} = .46$ ,  $F(2, 64) = 28.92$ ,  $p < .001$ , and the TC group,  $R^2_{adj} = .36$ ,  $F(2, 35) = 11.52$ ,  $p < .001$ .

## **Discussion**

Consistent with the hypotheses, this study demonstrated that in the context of equivalent levels of post-concussion symptom reporting and objective cognitive performance between groups, subjective cognitive symptoms were significantly elevated in mTBI participants relative to TCs. This difference in self-reported symptoms was clearly evident on a comprehensive, mTBI-based measure of cognitive symptoms (CCAMCHI). In contrast, findings were less robust when a three-item measure was employed (RPQ-cognitive subscale), and no discrepancy was present when a non-mTBI based measure was employed (ABNAS). This study also found that gender and psychological distress were significantly and independently predictive of self-reported cognitive symptoms in mTBI, with females and those with higher psychological distress reporting greater symptoms. In contrast, neither variable was predictive of cognitive symptom reporting in TCs.

The finding of elevated self-reported cognitive symptoms in mTBI relative to TCs indicates that these symptoms are not simply a result of general trauma. This provides evidence for the specific elevation of cognitive symptoms in mTBI, in contrast with post-concussion symptoms which have been shown to

**Table 5.** Predictors of cognitive and post-concussion symptoms within each group.

Dependent variable	Group	Independent variable	<i>b</i>	SE <i>b</i>	$\beta$	<i>p</i>	Semipartial $r^2$	Bootstrapped 95% CIs <sup>a</sup>
CCAMCHI	mTBI	Psychological distress	0.201	0.037	.536	<.001	.24	<b>0.143, 0.277</b>
		Gender	4.789	1.860	.253	.012	.02	<b>0.515, 9.424</b>
	TC	Psychological distress	0.004	0.085	.008	.967	.00	−0.213, 0.204
		Gender	−0.559	3.250	−.032	.864	.00	−10.019, 8.028
RPQ Total	mTBI	Psychological distress	0.302	0.047	.596	<.001	.37	<b>0.134, 0.419</b>
		Gender	6.244	2.363	.244	.010	.02	<b>0.617, 13.020</b>
	TC	Psychological distress	0.399	0.095	.612	<.001	.18	<b>0.176, 0.559</b>
		Gender	1.028	3.635	.041	.779	.01	−7.741, 8.669

Note. Due to missing psychological distress data (one mTBI participant; two TC participants), sample sizes for regression analyses were  $n = 67$  for the mTBI group and  $n = 40$  for the TC group. Gender was coded as 1 for males and 2 for females. CCAMCHI = Cognitive Complaint After Mild Closed Head Injury; CI = confidence interval; mTBI = mild traumatic brain injury; RPQ = Rivermead Post-Concussion Symptoms Questionnaire; TC = trauma control.

<sup>a</sup>Bootstrapped confidence intervals for the regression coefficients (BCa method; 2000 replicates). Note that when the confidence interval does not include zero (bolded values), this indicates significant results.

be non-specific for post-acute mTBI (Cassidy et al., 2014; Polinder et al., 2018). These findings expand on a recent meta-analysis showing that subjective cognitive symptoms are elevated in mTBI groups relative to combined healthy and injured controls (Levy et al., 2022). Findings are also consistent with a recent study that found elevated self-reported cognitive symptoms in mTBI patients relative to orthopedic TCs specifically (Levin et al., 2021).

The discrepancy in self-reported cognitive symptoms between mTBI and TC groups was found despite equivalent objective cognitive performance between groups, suggesting that the elevation in subjective symptoms in mTBI may not be driven by underlying cognitive deficits in this group. This finding may reflect poor sensitivity of traditional cognitive performance measures in individuals with mTBI (Bigler, 2013), which is an important topic for future research. Nevertheless, current findings align with existing research suggesting that subjective cognitive complaints often do not correspond with objective cognitive performance in mTBI (Anderson, 2021; Stulemeijer et al., 2007). Additionally, both groups in this study consisted of premorbidly healthy individuals, and groups were matched on various potentially confounding factors, including psychological distress, pain, fatigue, and litigation status. This suggests that none of these factors account for the differences in cognitive symptom reporting between groups.

This study also explored gender and psychological distress as predictors of subjective cognitive symptoms in mTBI and TC groups. Increased psychological distress was a significant predictor of greater cognitive symptoms in the mTBI group, but not in TCs. These findings extend those of a recent study which found that self-reported cognitive symptoms were associated with psychological distress in mTBI but not in healthy controls (Anderson, 2021). These findings suggest that it is something unique about the experience of an mTBI, over and above general trauma-related factors, that results in a linear association between psychological distress and subjective cognitive symptoms. One possible explanation for this finding is the hypothesis that symptoms after mTBI are initially attributable primarily to organic causes, and are later maintained by psychological factors such as catastrophizing or symptom preoccupation (Raymont & Fleminger, 2022). This concept has previously been applied to cognitive symptoms in mTBI, where a “subjective cognitive dysfunction loop” is triggered by early objective cognitive deficits, maintained by psychological factors (Kay et al., 1992). These concepts might also explain why there is no relationship between psychological distress and subjective cognitive symptoms in the TC group, as significant early cognitive deficits are not expected in this group.

Similarly, female gender was associated with increased subjective cognitive symptom reporting in the mTBI group, but not in the TC group. This finding suggests that females have a particular vulnerability to cognitive symptoms after mTBI, rather than after trauma more generally. Interestingly, this pattern was seen even when controlling for psychological distress, and therefore

cannot be explained by greater psychological distress in this group (Altemus et al., 2014). Other factors that have been proposed to underlie gender differences in symptom reporting include biological sex differences in symptom perception, or social differences in attention to symptoms or in the willingness to report symptoms (Barsky et al., 2001). Within this framework, it may be possible that if there are limited internal/external cognitive symptom cues (e.g., after general trauma), a gender difference in symptom reporting may be less likely to be seen. That is, gender differences may not have been seen in the TC group because in this population acute cognitive changes do not occur with the same frequency and/or severity that occurs after mTBI (Landre et al., 2006). Further research is necessary to explore these possible explanations.

Consistent with previous research, this study found no difference in the reporting of general post-concussion symptoms after mTBI relative to general trauma (Cassidy et al., 2014; Dean et al., 2012). Additionally, this study found that both psychological distress and gender predicted post-concussion symptom reporting in mTBI participants, a finding that is also consistent with previous literature (Cnossen et al., 2018; Silverberg & Iverson, 2011).

The findings of the current study are clinically relevant given the importance of being able to identify individuals at risk of poor outcome following mTBI. Research has shown that some interventions can be effective at reducing symptoms following mTBI, but that these interventions should directly target those at risk of poor outcome (Ghaffar et al., 2006; Ponsford et al., 2002; Teo et al., 2020). Our findings implicate females and individuals with high psychological distress as subgroups of mTBI patients that particularly warrant clinical attention to determine whether intervention is required.

Our findings also highlight important differences in the relationships between psychological distress, gender, and subjective symptoms in mTBI patients versus TCs. While both psychological distress and gender predicted cognitive symptom reporting in the mTBI group, neither variable predicted self-reported cognitive symptoms in TCs. This suggests that the experience of mTBI may affect which factors underlie cognitive symptom reporting after injury, and may have implications for clinical intervention. Additionally, there was a relationship between subjective cognitive and post-concussion symptoms in mTBI participants but not in TC participants, suggesting that the experience of mTBI may impact the relationships between various symptom types. This raises the possibility that elevated cognitive symptoms in mTBI versus control groups may not necessarily be due to group differences in background variables (e.g., levels of psychological distress). Instead, these differences may be at least in part due to differences in how these factors contribute to cognitive symptom reporting *within* groups. Further research is needed to investigate these possibilities.

The primary cognitive symptom scale used in our study was a comprehensive 30-item scale specifically developed for use after mTBI (Anderson, 2021). When

subjective cognitive symptoms were measured using just three cognitive items from a post-concussion symptom scale (RPQ), findings were less robust, potentially due to the limited reliability of using a small number of items to measure cognitive symptoms (Anderson, 2021). Further, when cognitive symptoms were measured using a scale not developed for mTBI (ABNAS), no elevations in cognitive symptoms were evident relative to TCs. These findings indicate that self-reported cognitive symptoms are not indiscriminately raised after mTBI, and instead cognitive symptom elevation occurs specifically in those domains that are objectively affected by mTBI. Thus, the use of a targeted, mTBI-based measure of cognitive symptoms is crucial when examining these symptoms. Additionally, comprehensive measures of cognitive symptoms may provide a more reliable method for detecting these symptoms after mTBI.

The primary limitation of this study is the modest sample size, particularly in the TC group. Limited sample sizes can result in true effects being missed (Field, 2012). To address this issue, measures of effect size were included for all primary analyses, as these measures are independent of sample size (Sullivan & Feinn, 2012). As recommended, effect size estimates were considered together with tests of statistical significance when interpreting the results of this study (Ellis, 2010). Discrepancies between statistical significance and effect size estimates were found in one instance, and a conservative inferential approach was taken in interpreting these findings. The statistical significance and effect size estimates were otherwise highly consistent, supporting the generalizability of these findings.

## Conclusions

This study examined subjective cognitive symptoms in pre-morbidly healthy adults with mTBI and general trauma approximately 8 weeks after injury. Unlike general post-concussion symptom reporting, cognitive symptoms were found to be greater in individuals with mTBI than in TCs. This suggests that the experience of mTBI, rather than general trauma, is responsible for cognitive symptom elevation in the subacute period after mTBI. Further research is warranted to determine whether neurological and/or psychological factors underlie this mTBI-specific elevation. Nevertheless, these findings suggest mTBI-specific management and intervention may be warranted for individuals with elevated cognitive symptoms. This study also found that in the subacute period following mTBI, both psychological distress and gender were significant predictors of self-reported cognitive symptoms, with females and those with higher psychological distress reporting greater symptoms. In contrast, neither factor was associated with cognitive symptom reporting in TCs. These findings implicate females and individuals with high psychological distress as important subgroups to consider for potential intervention following mTBI. Further research is needed to understand the mTBI-specific mechanisms by which female



gender and greater psychological distress lead to increased subjective cognitive symptoms in this group.

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## ORCID

Arielle M. Levy  <http://orcid.org/0000-0002-5445-6068>

Jacqueline F. I. Anderson  <http://orcid.org/0000-0003-4996-8189>

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