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Original Research

Post-Concussion Symptoms, Cognition and Brain Connectivity in an Australian Undergraduate Population: A Quantitative Electroencephalography Study

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Abstract

Background: An estimated 99 in 100,000 people experience a traumatic brain injury (TBI), with 85% being mild (mTBI) in nature. The Post-Concussion Symptom Scale (PCSS), is a reliable and valid measure of post-mTBI symptoms; however, diagnostic specificity is challenging due to high symptom rates in the general population. Understanding the neurobiological characteristics that distinguish high and low PCSS raters may provide further clarification on this phenomenon. **Aim**: To explore the neurobiological characteristics of post-concussion symptoms through the association between PCSS scores, brain network connectivity (using quantitative electroencephalography; qEEG) and cognition in undergraduates. Hypotheses: high PCSS scorers will have (1) more network dysregulation and (2) more cognitive dysfunction compared to the low PCSS scorers. **Methods**: A sample of 40 undergraduates were divided into high and low PCSS scorers. Brain connectivity was measured using qEEG, and cognition was measured via neuropsychological measures of sustained attention, inhibition, immediate attention, working memory, processing speed and inhibition/switching. **Results**: Contrary to expectations, greater frontoparietal network dysregulation was seen in the low PCSS score group ($p = 0.003$). No significant difference in cognitive dysfunction was detected between high and low PCSS scorers. Post-hoc analysis in participants who had experienced mTBI revealed greater network dysregulation in those reporting a more recent mTBI. **Conclusions**: Measuring post-concussion symptoms alone is not necessarily informative about changes in underlying neural mechanisms. In an exploratory subset analysis, brain network dysregulation appears to be greater in the early post-injury phase compared to later. Further analysis of underlying PCSS constructs and how to measure these in a non-athlete population and clinical samples is warranted.

Keywords: post-concussion symptom scale; post-concussion symptoms; cognition; network connectivity; default mode network; salience network; frontoparietal network

1. Introduction

Globally, mild traumatic brain injury (mTBI) makes up 85% of traumatic brain injuries, equating to approximately 42 million people being injured [1,2]. In Australia, an estimated 99 in 100,000 people experience a traumatic brain injury [3], while global incidence rates are as high as 369 in 100,000 people [4]. Causes of mTBI include motor vehicle accidents, cycling accidents, falls, sports injuries and assaults [5,6]. Symptoms of mTBI can be clustered as cognitive, vestibular, ocular, anxiety/mood, headache/migraines and fatigue [7]. On average, symptoms last two weeks in adults; however, 10–20% develop persistent post-concussion symptoms (PPCS) [8,9]. Although cognitive function is often rapidly regained after mTBI, the literature suggests that in adults with mTBI, 50% have persistent cognitive dysfunction three months after injury [10]. Furthermore, deficits in episodic, immediate, and delayed memory, as well as working memory and executive function were reported at 12 and 24 months post-mTBI [11,12]. While it has been suggested that the cognitive symptoms of mTBI can be longstanding, research investigating the longer term cognitive effects of mTBI is limited [10]. Additionally, a hit to the head may result in sub-concussion [13], where the individual does not display the symptoms of concussion [14]. The cumulative effect of multiple sub-concussions is just as detrimental and may lead to functional and microstructural brain changes [14,15], chronic traumatic encephalopathy [16], dementia-like brain changes such as beta-amyloid and tau accumulation [17,18]. The relationship between sub-concussion-type injuries and the subsequent pathological and behavioural outcomes is not yet well understood [19–22]. While several biopsychosocial factors impact the outcome following mTBI [23], recent research has highlighted that gastrointestinal health is an important factor in injury response regulation [24]. Con-

versely, a neurological injury such as mTBI may lead to dysbiosis of the gut. Although gastrointestinal health is impacted by a myriad of factors [24,25], a factor commonly at play is medication [26–29]. Regardless of the causative factors, persistent symptoms may impact return to premorbid activities and quality of life [30], and hence understanding post-mTBI symptoms was an important focus of this study.

A widely used self-report measure of symptoms following mTBI is the Post-Concussion Symptom Scale (PCSS) [31]. Although it is a reliable and valid measure of PPCS [32,33], the vast and heterogeneous nature of PPCS makes diagnostic specificity challenging. In fact, PPCS-like symptoms are also seen following trauma without brain injury [34], as well as in healthy individuals [35,36]. In a general population sample of 11,759 individuals, 45.1% met criteria for PPCS [37]. Hence, understanding the underlying neurobiological characteristics that distinguish high and low PCSS raters may provide further clarification on this phenomenon. It has been suggested that mTBI does not have a single pathophysiological mechanism but rather a complex interaction of multiple processes leading to both structural and functional changes resulting from both primary and secondary mechanisms of injury [23,38]. Consequently, it has been described as a disease process rather than a single event. Whilst the primary damage occurs at the point of injury, secondary damage may evolve over days, months or sometimes longer [39]. Moreover, altered brain activation has been demonstrated to persist beyond the resolution of clinical symptoms following TBI in athletes, suggesting that being asymptomatic is not a complete indicator of recovery [40–42]. mTBI has also been referred to as "a disorder of brain connectivity" [43], indicating that one potential contributor to post-concussion symptoms is altered brain network activity. In fact, disrupted brain network function has been associated with symptom severity and cognitive function post-mTBI [44].

1.1 Brain Network Function

Altered connectivity in the default mode network (DMN), the salience network (SN) and the frontoparietal network (FPN) have been associated with mTBI and the presence of post-concussion symptoms [45–58]. The DMN is active during rest, playing a key role in internally focused thoughts, and is inhibited when attention needs to be shifted to external stimuli [43]. The integrity of the DMN is fundamental for cognitive functioning, and damage to the cingulum following mTBI, as well as reduced DMN connectivity, are both associated with impaired sustained attention [48]. Decreased connectivity within the DMN was associated with increased post-concussion symptoms six months post-mTBI [59].

Besides altered connectivity within the DMN, alterations in the DMN's interactions with other networks, such as the SN and FPN, were also found following mTBI [57,60]. The SN plays a key role in re-directing attention externally [43] and controlling the activation of the DMN [61]. A dysfunctional interaction between the DMN and SN has been linked to a failure to inhibit the DMN during an externally focused task, which is associated with cognitive deficits following TBI [55,62]. Structural damage within the SN was also related to the failed interaction between these two networks [43], and increased connectivity in both the DMN and SN was associated with cognitive dysfunction [59]. The FPN is thought to have a key role in several cognitive functions including attention, working memory, reasoning, set-shifting [63,64], and novel complex tasks [65]. In the mTBI population, altered FPN connectivity has been associated with a reduction in sustained effort on cognitive tasks and increased cognitive fatigue between three and 24 months post-injury [66]. Additionally, a decreased negative correlation between DMN and FPN activity is among the most common patterns of altered function associated with post-concussion symptoms [67].

1.2 Measures of Network Function

While useful, functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) remain highly expensive and technically challenging, rendering them inaccessible to the general population. Quantitative electroencephalography (qEEG) is a less invasive, cheaper, and more widely accessible, portable technique. Importantly, it offers superior temporal resolution over fMRI and DTI, enabling a direct measure of neural activity compared to the indirect measure offered by fMRI, as well as detecting neural oscillations, which play an important role in communication within the brain [68]. In the mTBI literature, the qEEG measures of coherence, phase and spectral power are commonly explored [69,70]. Coherence is a measure of the correlation of EEG frequency between two electrodes, reflecting the similarity of the activity in underlying brain areas, which is thought to indicate brain network connectivity [69]. Lagged coherence is thought to address the issue of volume conduction in instantaneous coherence [71], and phase is a measure of the temporal synchrony of electrical activity between two brain areas, reflecting the efficiency of data transfer within a neuron cluster, which may impact their synaptic plasticity [72,73]. Spectral analysis refers to the power spectrum of the EEG signal [74].

The utility of EEG brain markers as a measure of functional brain impairment has been demonstrated through studies reporting the correlation of qEEG power, amplitude and coherence with MRI findings in TBI, tumour and stroke [70,75,76]. Measures of amplitude asymmetry, phase and coherence, were distinguished between mTBI and controls with 95% accuracy [70]. Moreover, the severity of brain dysfunction was negatively correlated with cognitive task performance. While qEEG has been validated in the mTBI population, its use for functional network analysis remains sparse. One study reported that brain connectivity findings using DTI were comparable with findings on qEEG

in mTBI [56]. The current study aimed to utilise a novel neuroimaging approach (qEEG network analysis) to better understand the neurobiological characteristics of post-concussion symptoms by exploring the association between PCSS scores, brain network connectivity and cognition in an undergraduate adult sample. This study contributes to developing a deeper understanding of the relationships between these factors in a community sample, which may in turn, enable a more informed approach to mTBI recovery and rehabilitation. We hypothesised that the high PCSS scorers would have (1) more network dysregulation and (2) more cognitive dysfunction compared to the low PCSS scorers.

2. Materials and Methods

2.1 Participants

Ethics approval was provided by the University of Western Australia (UWA)'s Human Research Ethics Committee (2021/ET000033). Undergraduate students enrolled in PSYC1101 at UWA were invited to participate via their instructor (convenience sample). A total of 1047 participants who completed the PCSS [31] were ranked according to their PCSS total score. To identify the required number of candidates for the high and low PCSS score groups, G*Power version 3.1.9.4, (Heinrich-Heine-University, Dusseldorf, Germany) [77] was used. The highest and lowest 8% of scorers were directly invited to participate (n = 84 per group). Data was collected from 40 participants (13 males, 27 females), aged between 17 and 35 years (Mean (M) = 19.68, Standard Deviation (SD) = 3.72) with an average of 12.63 years of education (range = 12–17 years, SD = 1.25); who were divided into high (n = 19) and low (n = 21) PCSS groups. Based on normative data published by Lovell, Iverson [32], participants were high PCSS scorers if their score was >27 (males) and >44 (females), and these scores were considered to be in the 98th percentile. Participants were low scorers if their score was <5 (below the 74th percentile) and considered broadly normal. This method was chosen over a median split approach to avoid increasing type I and type II errors, as discussed in McClelland, Lynch Jr [78]. Volunteer participants received two credits towards their unit mark.

2.2 Materials

2.2.1 Post-Concussion Symptoms

Post-concussion symptoms were measured using the PCSS [31]. This is a 21-item self-report measure assessing symptom severity following concussion on a seven-point Likert scale from 0 (none) to 6 (severe). All items were summed to give a total symptom score, with higher scores indicating a higher symptom burden. Although the psychometric properties of this questionnaire were not reported [79], the test-retest reliability for the questionnaire within the ImPACT test battery was 0.65 [80,81].

2.2.2 Network Function

Brain network connectivity was measured within the default mode, salience and fronto-parietal networks using resting state qEEG. Recording was conducted using a 19-channel Electro-cap (Electro-cap International Inc., Eaton, OH, USA) and a Mitsar amplifier (Mitsar, Ltd., St Petersburg, Russia), whilst quantitative analysis was conducted using NeuroGuide and NeuroNavigator (source localisation) software (Applied Neuroscience, Inc., St. Petersburg, FL, USA), which has been extensively validated in the literature including in a mTBI population [70,82]. For scalp EEG recording, the participant's head circumference was measured and fitted with an appropriately sized Electro-cap, with all electrodes connected using the standard 10–20 placement. Each scalp electrode was prepared by parting the hair and filling it with electroconductive gel (Electro-Gel™, Electro-Cap International Inc, Eaton, OH, USA). EEG activity was recorded from 19 scalp electrodes, and impedance was kept below 10 kΩ, using a linked ears montage. Data were recorded for ten minutes in a resting state (five-minutes eyes open and five-minutes eyes closed). During the eyes closed condition, an eye mask was placed over the participant's eyes to minimise eye movement-related data interruptions. The maximum amount of artifact-free data (minimum of 60 seconds) were selected using NeuroGuide software (Applied Neuroscience, Inc. St. Petersburg, FL, USA). Areas of altered brain network function were identified using low-resolution electromagnetic tomography analysis (LORETA) for source localisation via the NeuroNavigator software (Applied Neuroscience, Inc., St. Petersburg, FL, USA). Each participant's activity was compared to an age and sex-matched normative database (N = 727) to quantify the degree of deviation from normality (z scores). Details regarding the normative database can be accessed at Thatcher, Walker [83] and Thatcher, Walker [84]. The Brodmann areas (BA) comprising each network were preselected by the software program as follows; DMN: bilateral BA 2, 7, 10, 11, 19, 29, 30, 31, 35, 39, 40; SN: bilateral BA 8, 9, 10, 13, 22, 23, 24, 25, 29, 30, 31, 32, 33; FPN: bilateral BA 1, 2, 3, 5, 7, 8, 9, 10, 39, 40, 45, 46.

The degree of brain activation was represented by z scores across all frequencies from 1 to 30 Hz, for each Brodmann area (current source density; CSD), and the degree of connectivity (instantaneous coherence; IC, lagged coherence; LC, and phase difference; PD) between each pair of Brodmann areas, within the networks of interest. The unit of measurement for CSD was microamperes squared per cycle/second. IC and LC are both correlation coefficients, and the closer to 1 the more similar (coherent) the two signals are. PD for raw scores varies from 0 to +/– 180 degrees. For z scores the raw value was squared, and the square root was used as an absolute phase difference which ranged between 0 to +180 degrees. For each network, five measures were calculated including peak z score, mean z

score, z score variance, total number of z scores above +/– 1.96 and the percentage of z scores above +/– 1.96. Z scores of 1.96 or less were considered within normal limits, and z scores above 1.96 indicated brain activity that deviated significantly from the normal range (altered functioning). While a negative z score indicated hypoactivity and a positive z score indicated hyperactivity, this study focused on overall dysregulation, so the direction of deviation (+ or –) was not differentiated in statistical analysis.

2.2.3 Cognitive Function

Sustained Attention and Inhibition. These were measured using the [85] Conners Continuous Performance Test, 3rd Edition (CPT-3; Conners, 2014). This is a computer-based task designed to evaluate sustained attention and inhibition in clinical and research settings [85]. The CPT-3 took 14 minutes to complete and was administered over six-blocks. During each block, the letters of the alphabet are randomly displayed on a screen for 250 ms, with randomised inter-stimulus intervals of 1, 2 or 4 seconds. The participant was required to press the space bar when all letters are displayed, except for the letter 'X'. A short practice trial preceded the experimental task to ensure the participant understood the task. This task provided t scores for response accuracy including detectability (d') and error type (omissions, commissions, perseverations), as well as reaction time statistics (hit reaction time; HRT, HRT standard deviation; HRT SD, variability, HRT block change and HRT interstimulus interval change; HRT ISI change), with higher scores indicating higher levels of inattention and disinhibition. The CPT-3 has been found to have good split-half reliability and test-retest reliability, ranging from 0.05 to 0.92 [85].

Immediate Attention and Working Memory. Verbal and non-verbal measures were used. Immediate attention was measured using the Digit Span forward (DSF), a subtest of the Wechsler Adult Intelligence Scale – 4th edition (WAIS-IV) [86], and Spatial Span Forward (SSF), a subtest of the Wechsler Memory Scale – 4th edition (WMS-IV) [87]. DSF entailed reading strings of increasingly long number sequences to the participant, which they were then asked to repeat. SSF is similar to the Digit Span task; however, no verbal instructions were used. The participant was asked to watch the examiner tap a series of blocks in a particular sequence. They were then asked to recall and mimic that sequence by tapping the blocks. The sequences increased progressively in length and hence, difficulty.

Working Memory was measured using the Digit Span backward (DSB), a subtest of the WAIS-IV, and Spatial Span Backward (SSB), a subtest of the WMS-IV. These involved a similar procedure to DSF and SSF; however, the participant was asked to repeat the sequence in reverse order. The total raw scores for each of the four subtests were converted to z scores, and a higher positive z score indicated better performance [86,88].

Processing Speed and Inhibition/Switching. The Symbol Digit Modalities Test (SDMT; Smith, 2007) is a task that requires attention, visual scanning, fine motor and perceptual speed. In this task participants used a key including nine symbol-digit pairs, to complete a number matching task. Ten practice items were administered and the task was conducted in written and oral formats [89]. The final score was the total number of correct substitutions within a 90-second timeframe, with higher scores indicating better performance. Final scores were converted to z-scores, using norms stratified by age, sex and education [89]. Psychometrically, the SDMT has been shown to have good test-retest reliability (0.08 written, 0.76 oral) and excellent construct validity [90].

The Delis-Kaplan Executive Function System (D-KEFS) Colour-Word Interference subtest [91] was also used. This consisted of four parts: (1) colour naming, (2) word reading, (3) inhibition, and (4) inhibition/ switching. Conditions 1 and 2 were used to measure processing speed, and conditions 3 and 4 measured inhibition and inhibition/switching, respectively. The total raw score was converted to a z score, where a higher positive z score indicated better executive functioning [91].

2.3 Procedure

Participants were emailed an invitation including the participant information form (PIF), participant consent form (PCF) and the COVID screening form. Volunteers booked their testing session online via SONA (Sona Systems Ltd, 1997–2021). Participants attended the Sarich Neuroscience Research Institute. Prior to commencing their face-to-face session, another COVID screen was conducted. Participants were also provided with printed copies of the PIF and PCF and their written and verbal consent was obtained. The testing was administered over three blocks, with block 2 consisting of questionnaires from a wider research project that were not utilised in this study. Block 1 included the demographics questionnaire and the qEEG. Block 3 included the neuropsychological assessment battery (Digit Span, D-KEFS Colour Word Interference Test, Spatial Span, SDMT and CPT-3).

In block 1, participants completed a demographics questionnaire including concussion history, medical history (e.g., epilepsy, seizure disorder, migraines/headaches, sleep disorder, other medical conditions), mental health conditions (depression, anxiety, other psychiatric disorders), developmental history (dyslexia, ADHD (Attention Deficit Hyperactivity Disorder), ASD (Autism Spectrum Disorder)), speech/language delay, other learning/developmental disorders), and medication history, followed by a resting state qEEG.

Next, participants completed blocks 2 and 3. Blocks 2 and 3 were administered in a randomised order via a pre-determined allocation using Research Randomizer (www.randomizer.org) to address order effects. In block 2

Table 1. Cognitive index components.

Cognitive index	Component cognitive measures
Sustained attention index	CPT-3: HRT block change, omissions change by block, and commissions change by block
Inattentiveness index	CPT-3: Detectability, omissions, commissions, HRT, HRT SD, and variability
Immediate attention index	Digit span forward and spatial span forward
Working memory index	Digit span backward and spatial span backward
Processing speed index	SDMT oral and written, DKEFS colour naming and word reading
Inhibitory control index	DKEFS inhibition and inhibition/switching, CPT-3: HRT, commissions, and perseveration measures

Note: CPT-3, Conners Continuous Performance Test, 3rd Edition; HRT, hit reaction time; HRT SD, HRT standard deviation; HRT ISI Change, HRT interstimulus interval change; SDMT, Symbol Digit Modalities Test; DKEFS, Delis-Kaplan Executive Function System; Omissions, rate of missed targets; Commissions, incorrect responses to non-targets; Detectability, ability to discriminate targets (non-X) from non-targets (X); Perseverations, rate of anticipatory; repetitive; or random responses (under 100 milliseconds); Variability, variability of response speed consistency [85].

participants completed the questionnaires using paper and pencil. In block 3, participants completed the neuropsychological testing in the following order: Digit Span, D-KEFS Colour Word Interference Test, Spatial Span, SDMT and CPT-3. The testing session took two hours to complete, and participants were able to withdraw at any time. Individuals received a debrief form which contained educational content about the study, as well as a set of quiz questions to enhance their learning experience.

2.4 Design and Analysis

An observational cross-sectional study design was used. For hypothesis one, the dependent variable was network function with three levels: DMN, SN and FPN. For each network, the functional connectivity was characterised by 5 measures: peak z score, mean z score, z score variance, total number of z scores above +/– 1.96 and the percentage of z scores above +/– 1.96 across instantaneous coherence, lagged coherence, and phase difference. The independent variable was the PCSS group with two levels: high scorers and low scorers. Independent samples *t*-test and Mann-Whitney *U* test analyses were used to measure the difference in brain dysregulation across groups. For some variables, homogeneity of variance was not assumed, and the "equal variances not assumed" *t*-test statistic was interpreted.

For hypothesis two, the dependent variables included six cognitive index scores. Each index score was created by converting the raw cognitive measure scores to z scores using SPSS version 27, IBM Corporation, Armonk, NY, USA (except for SDMT, where z scores were calculated using the manual norms) and then averaging the z scores across the cognitive index components. Table 1 outlines the cognitive measures making up each cognitive index. The independent variable was the PCSS group with two levels: high scorers and low scorers. To evaluate the difference in brain dysregulation across the PCSS groups, independent samples *t*-test and Mann-Whitney *U* tests were applied to normal and non-normally distributed measures, respectively.

A supplementary analysis was conducted to further explore the relationship between time since the last concussion and brain dysregulation (as measured by qEEG). The independent variable was the time since last concussion injury (in months), and the dependent variables included network measures as per hypothesis one. To assess the size and direction of the linear relationship between time since last concussion and brain dysregulation, a bivariate Pearson's product-moment correlation coefficient (r) was calculated across 18 network connectivity measures for which data were normally distributed. In the 42 non-normally distributed brain activity measures, Spearman's rho (r_s) was calculated.

3. Results

3.1 Network Connectivity and Post-Concussion Symptoms

To test the hypothesis that the DMN, SN and FPN are more dysregulated in the high PCSS group compared to the low PCSS group, analyses were conducted on 38 participants (18 high PCSS scorers and 20 low PCSS scorers). Two participants who did not undergo qEEG recording due to technical issues were excluded from all analyses for the first hypothesis. Seventy-seven univariate outliers were detected across all the network connectivity variables (>3 standard deviations from the mean) and managed using winsorisation [92]. Of the 60 brain function variables, 7 were normally distributed, and all other assumptions were met.

3.1.1 Demographic Characteristics

Table 2 shows the descriptive statistics for the demographic variables including reported concussion and medical history, as well as significant differences across the high and low PCSS groups. Participants across groups did not vary significantly on characteristics including age, education, number of concussions and medication intake. However, the high PCSS group had a significantly higher rate of medical and mental health conditions. While the time since last concussion was not significantly different between groups, the low PCSS group had more recent concussions on average (M = 8.5 months, range = 1–18) than the

Table 2. Comparison of Demographic Characteristics Between High and Low PCSS Groups.

	High PCSS score group			Low PCSS score group			Test of group difference			
	n (%)	*M*	*SD*	*n (%)*	*M*	*SD*	*Estimate*	*df*	*p*	
Age	18	18.9	2.4	20	20.3	4.7	151.50		0.41	
Education (years)	18	12.5	1.0	20	12.7	1.5	179.50		1.0	
Sex							2.18	1	0.14	
Male	4			9						
Female	14			11						
Time since last concussion (months)		69.1	72.3		8.5	7.0	1.63	10	0.13	
Total number of concussions		1.3	1.7		0.5	0.9	1.63	24	0.12	
	Yes	No		Yes	No		Chi Square Test			
	n (%)	*n* (%)		n (%)	n (%)		Pearson X^2	*df*	*p*	*(p)*
Concussion history	8 (44.4)	10 (55.6)		4 (20.0)	16 (80.0)		2.62	1	0.11	
Medical condition	10 (62.5)	6 (37.5)		2 (15.4)	11 (84.6)		6.56	1	0.01*	
Mental health condition	10 (58.8)	7 (41.2)		3 (15.8)	16 (84.2)		7.20	1	0.01*	
Learning/developmental disorder	3 (17.6)	14 (82.4)		2 (10.5)	17 (89.5)					0.65
Medication	5 (27.8)	13 (72.2)		5 (25.0)	15 (75.0)					1.0

Note: *, significant difference between the High and Low PCSS score groups; *(p)*, Fisher's Exact Test. Difference tests: For age and education variables, Mann-Whitney *U* Test (*U*); For sex, Chi Square Test (X^2); For time since last concussion and total number of concussions, Independent Samples *t* Test (*t*). Total number of concussions refers to the cumulative number of concussions per participant within each group. For the high PCSS group, medical conditions included migraines (*n* = 4), headache (*n* = 4), sleep disorders (*n* = 3), and other (*n* = 3) including asthma (*n* = 2), Lupus (*n* = 1) and iron deficiency/low blood pressure (*n* = 1). Mental health conditions included depression (*n* = 4), anxiety (*n* = 6), and other (*n* = 3) including anorexia nervosa (*n* = 1), bipolar disorder (*n* = 1) and borderline personality disorder (*n* = 1). Learning/Developmental conditions included dyslexia (*n* = 1), ADHD (*n* = 2), speech/language delay (*n* = 1). For the low PCSS group, medical conditions included migraines (*n* = 1) and other (*n* = 1), Irlens. Mental health conditions included depression (*n* = 2), anxiety (*n* = 2), and other (*n* = 1), PTSD. Learning/Developmental conditions included dyslexia (*n* = 1), and ADHD (*n* = 1).

high PCSS group (*M* = 69.1 months, range = 1–234). Additionally, the standard deviations were very large and were thought to contribute to the determination of no significant difference between groups. Of the subset of participants that had a history of concussion (*n* = 12), eight were in the high PCSS group, and four were in the low PCSS group. The number of concussion injuries reported were one (*n* = 8), three (*n* = 2), four (*n* = 1) and five (*n* = 1). The mechanisms of injury included falls (*n* = 5) and sporting injuries (*n* = 7) for the first injury. Of the four participants who had a second and third injury, mechanisms included falls (*n* = 1), sporting injury (*n* = 2), and hit/assault/other (*n* = 1). The fourth and fifth injuries were sport related. When considering the groups separately, the high PCSS group mechanisms of injury included first injury: falls (*n* = 4) and sporting injuries (*n* = 5), second injury: sports (*n* = 3) and hit/assault (*n* = 1), third injury: sport (*n* = 2), other (*n* = 1), fourth and fifth: sporting injuries. The low PCSS group injury mechanisms included first injury: falls (*n* = 1) and sporting injuries (*n* = 4), second injury: fall (*n* = 1), third injury: fall (*n* = 1).

3.1.2 Network Connectivity Measures

Table 3 shows the descriptive statistics for select network connectivity measures across both groups. Descriptives for the remaining measures can be found in the Appendix Table 9. Independent samples *t*-test was conducted on 7 network function measures, as listed in Table 3. Of these, three reflected statistically significant differences between the two PCSS groups, with brain dysregulation being significantly worse in the low PCSS group for certain measures within the DMN and FPN.

Default Mode Network. The significantly higher measures in the low PCSS group were; DMN IC mean z score with the low PCSS group (*M*: 0.76, *SD*: 0.19) having 0.12 *SD* higher brain dysregulation, 95% Confidence Interval (CI) [–0.22, –0.02], than the high PCSS group (*M*: 0.64, *SD*: 0.11), *t*(36) = –2.45, *p* = 0.019, two-tailed, Hedge's correction = 0.16; and DMN PD peak z score with the low PCSS group (*M*: 4.37, *SD*: 1.65) having 1.05 *SD* higher brain dysregulation, 95% CI [–1.93, –0.16], than the high PCSS group (*M*: 3.32, *SD*: 0.96), *t*(31.14) = –2.42, *p* = 0.022, two-tailed, Glass's delta = 1.65.

Frontal-Parietal Network. The difference in the FPN PD peak z score was also statistically significant with the low PCSS group (*M*: 5.02, *SD*: 2.05) having 1.63 *SD* higher brain dysregulation, 95% CI [–2.67, –0.59], than the high PCSS group (*M*: 3.39, *SD*: 0.90), *t*(26.71) = –3.23, *p* = 0.003, two-tailed, Glass's delta = 2.05. After accounting for multiple comparisons using the Benjamini-Hochberg False Discovery Rate method [93], only the FPN PD peak z score difference remained significant.

Table 3. Independent samples *t*-test for network connectivity (default mode, salience, frontal-parietal).

	High PCSS score group			Low PCSS score group			Independent samples *t*-test			
	n	*M*	*SD*	*n*	*M*	*SD*	*t*	*df*	*p*	*Effect size*
DMN IC mean z score	18	0.6	0.1	20	0.8	0.2	–2.45	36	0.019*	0.16
DMN LC mean z score	18	0.6	0.1	20	0.7	0.2	–1.36	29.20	0.18	
DMN PD mean z score	18	0.6	0.1	20	0.7	0.2	–1.75	31.95	0.09	
DMN PD peak z score	18	3.3	1.0	20	4.4	1.6	–2.42	31.14	0.022*	1.65
SN LC mean z score	18	0.6	0.1	20	0.6	0.2	–1.64	26.84	0.11	
SN PD mean z Score	18	0.6	0.1	20	0.7	0.2	–0.75	36	0.46	
FPN PD peak z score	18	3.4	0.9	20	5.0	2.0	–3.23	26.71	0.003**	2.05

Note: *, significant difference between the High and Low PCSS score groups; **, remained significant after Benjamini-Hochberg correction for multiple comparisons; DMN, Default Mode Network; SN, Salience Network; FPN, Frontal-Parietal Network; IC, instantaneous coherence; LC, lagged coherence; PD, phase difference; CSD, current source density. Effect size is only listed for significant differences.

Table 4. Mann-Whitney U Test analyses of group differences in brain network dysregulation.

	High PCSS score group			Low PCSS score group			Mann-Whitney *U* Test	
	n	*M*	*SD*	*n*	*M*	*SD*	*U*	*p*
DMN IC peak z score	18	3.4	1.2	20	4.3	1.7	126.5	0.12
SN IC peak z score	18	3.4	1.4	20	4.1	1.8	135.5	0.2
SN IC mean z score	18	0.6	0.1	20	0.7	0.2	161	0.59
FPN IC peak z score	18	3.6	1.2	20	5.6	3.3	113	0.051
FPN IC mean z score	18	0.6	0.1	20	0.8	0.2	122	0.09
DMN LC peak z score	18	3.0	1.3	20	3.4	1.6	153	0.44
SN LC peak z score	18	3.1	1.3	20	3.5	1.4	151.5	0.41
FPN LC peak z score	18	3.2	1.3	20	3.6	1.8	156	0.50
FPN LC mean z score	18	0.6	0.1	20	0.6	0.2	122	0.09
SN PD peak z score	18	3.2	0.9	20	3.9	1.3	121	0.09
FPN PD mean z score	18	0.7	0.1	20	0.8	0.3	129	0.14
DMN CSD peak z score	18	2.4	0.8	20	2.4	0.8	174	0.87
DMN CSD mean z score	18	0.9	0.5	20	1.0	0.6	167.5	0.72
SN CSD peak z score	18	2.2	0.6	20	2.5	0.9	149.5	0.38
SN CSD mean z score	18	0.8	0.3	20	1.0	0.6	167	0.72
FPN CSD peak z score	18	2.4	0.9	20	2.4	0.8	160	0.57
FPN CSD mean z score	18	0.9	0.5	20	1.0	0.6	165	0.68

Note: DMN, Default Mode Network; SN, Salience Network; FPN, Frontal-Parietal Network; IC, instantaneous coherence; LC, lagged coherence; PD, phase difference; CSD, current source density.

Mann-Whitney *U* tests were conducted on the remaining network function measures. Select network connectivity measures are listed in Table 4, and the remaining measures can be found in Appendix Table 10. No significant differences in brain dysregulation between the high and low PCSS score groups were detected.

3.2 Network Connectivity and Time Since Last Concussion

Due to the unexpected finding that the low PCSS group had significantly higher network dysregulation, a further exploratory analysis was conducted. It was determined that for those who had experienced a concussion, the time since the last concussion could be a contributing factor. To test the hypothesis that a shorter time since last concussion would be associated with more dysregulated network connectivity, Pearson product moment correlation and Spearman's rank-order correlation were conducted. Data from 12 participants (8 high PCSS scorers and 4 low PCSS scorers) were analysed, and 21 univariate outliers were detected and managed using winsorisation if they were three or more standard deviations away from the mean. Of the 60 brain function measures, 18 were normally distributed, and all other assumptions were met.

As shown in Table 5, there was a negative correlation between time since last concussion and DMN IC peak z score, $r(10) = –0.551$, $p = 0.032$; as well as SN CSD peak z score, $r(10) = –0.523$, $p = 0.041$. However, these correlations did not remain significant after accounting for multiple comparisons using the False Discovery Rate method [93].

Table 5. Pearson product-moment correlations between time since last concussion and network connectivity (for normally distributed measures), N = 12.

Network connectivity measure	*r*	*p*
DMN IC peak z score	–0.551	0.032*
DMN IC z score variance within network	–0.414	0.090
DMN IC number of z scores >1.96 SD	–0.434	0.079
DMN IC percentage z scores >1.96 SD	–0.434	0.079
SN LC peak z score	–0.417	0.089
DMN PD peak z score	–0.372	0.117
DMN PD mean z score	–0.261	0.206
DMN PD z score variance within network	–0.275	0.194
SN PD peak z score	–0.441	0.076
SN PD mean z score	–0.306	0.167
SN PD z score variance within network	–0.344	0.144
DMN CSD peak z score	–0.387	0.107
DMN CSD mean z score	–0.258	0.209
DMN CSD z score variance within network	–0.295	0.176
SN CSD peak z score	–0.523	0.041*
SN CSD mean z score	–0.355	0.129
SN CSD mean z score variance within network	–0.429	0.082
FPN CSD peak z score	–0.464	0.064

Note: *, significant correlation between time since injury and network connectivity; DMN, Default Mode Network; SN, Salience Network; FPN, Frontal-Parietal Network; IC, instantaneous coherence; LC, lagged coherence; PD, phase difference; CSD, current source density.

Table 6. Spearman's rank-order correlations between time since last concussion and network connectivity (for non-normally distributed measures), N = 12.

Network connectivity measure	r_s	*p*
DMN IC mean z score	–0.636	0.026**
SN IC peak z score	–0.828	<0.001**
SN IC mean z score	–0.757	0.004**
SN IC z score variance within network	–0.703	0.011**
SN IC number of z scores >1.96 SD	–0.547	0.065
SN IC percentage z scores >1.96 SD	–0.547	0.065
FPN IC peak z score	–0.702	0.011**
FPN IC mean z score	–0.859	<0.001**
FPN IC z score variance within network	–0.820	0.001**
FPN IC number of z scores >1.96 SD	–0.796	0.002**
FPN IC percentage z scores >1.96 SD	–0.796	0.002**
DMN LC peak z score	–0.626	0.030**
DMN LC mean z score	–0.393	0.206
DMN LC z score variance within network	–0.791	0.002**
DMN LC number of z scores >1.96 SD	–0.726	0.007**
DMN LC percentage z scores >1.96 SD	–0.726	0.007**
SN LC mean z score	–0.571	0.052
SN LC z score variance within network	–0.796	0.002**
SN LC number of z scores >1.96 SD	–0.730	0.007**
SN LC percentage z scores >1.96 SD	–0.730	0.007**
FPN LC peak z score	–0.716	0.009**
FPN LC mean z score	–0.602	0.038*
FPN LC z score variance within network	–0.724	0.008**
FPN LC number of z scores >1.96 SD	–0.731	0.007**
FPN LC percentage z scores >1.96 SD	–0.731	0.007**
DMN PD number of z scores >1.96 SD	–0.617	0.033*
DMN PD percentage z scores >1.96 SD	–0.617	0.033*
SN PD number of z scores >1.96 SD	–0.642	0.024**
SN PD percentage z scores >1.96 SD	–0.642	0.024**
FPN PD peak z score	–0.698	0.012**
FPN PD mean z score	–0.536	0.072
FPN PD z score variance within network	–0.628	0.029**
FPN PD number of z scores >1.96 SD	–0.691	0.013**
FPN PD percentage z scores >1.96 SD	–0.691	0.013**
DMN CSD number of z scores >1.96 SD	–0.486	0.109
DMN CSD percentage z scores >1.96 SD	–0.496	0.101
SN CSD number of z scores >1.96 SD	–0.588	0.045*
SN CSD percentage z scores >1.96 SD	–0.588	0.045*
FPN CSD mean z score	–0.404	0.192
FPN CSD z score variance within network	–0.600	0.039*
FPN CSD number of z scores >1.96 SD	–0.573	0.052
FPN CSD percentage z scores >1.96 SD	–0.573	0.052

Note: *, significant correlation between time since injury and network connectivity; **, remained significant after Benjamini-Hochberg correction for multiple comparisons; DMN, Default Mode Network; SN, Salience Network; FPN, Frontal-Parietal Network; IC, instantaneous coherence; LC, lagged coherence; PD, phase difference; CSD, current source density.

Of the 42 brain activity measures, 32 measures were found to have a statistically significant correlation with time since last concussion, as listed in Table 6. After accounting for multiple comparisons using the False Discovery Rate method [93], 26 correlations remained statistically significant.

Significant negative correlations were found for the following; DMN: instantaneous coherence mean z score, peak z score, and z score variance, as well as lagged coherence number and percentage of z scores >1.96 SD; SN: instantaneous coherence mean z score, z score variance; lagged coherence z score variance, number and percentage of z scores >1.96 SD; phase difference number and percentage of z scores >1.96 SD; FPN: instantaneous coherence peak z score, mean z score, z score variance, number and percentage of z scores >1.96 SD; lagged coherence peak z score, z score variance, number and percentage of z scores >1.96 SD; phase difference peak z score, z score variance, number and percentage of z scores >1.96 SD. Therefore, a more recent concussion injury was associated with a higher degree of dysregulated connectivity within the DMN, SN and FPN.

3.3 Cognitive Function and Post-Concussion Symptoms

To test the hypothesis that cognitive dysfunction is higher in the high PCSS group compared to the low group, independent samples *t*-test analyses were conducted on the

Table 7. Comparison of demographic characteristics between high and low PCSS groups (hypothesis 2).

	High PCSS score group			Low PCSS score group			Test of group difference			
	n (%)	*M*	*SD*	*n (%)*	*M*	*SD*	*Estimate*	*df*	*p*	
Age	19	19.2	2.5	21	20.1	4.6	180.50		0.61	
Education (years)	19	12.6	1.0	21	12.7	1.5	189.00		0.79	
Sex							2.16	1	0.14	
Male	4			9						
Female	15			12						
Time since last concussion (months)		61.9	71.0		7.6	6.4	8.00		0.06	
Total number of concussions		1.4	1.6		0.5	0.9	64.00		0.13	
	Yes	No		Yes	No		Chi Square Test			
	n (%)	*n* (%)		n (%)	n (%)		Pearson X^2	*df*	*p*	*(p)*
Concussion history	9 (47.4)	10 (52.6)		5 (23.8)	16 (76.6)		2.43	1	0.12	
Medical condition	10 (58.8)	7 (41.2)		2 (14.3)	12 (85.7)		6.42	1	0.01*	
Mental health condition	10 (55.6)	8 (44.4)		3 (15.0)	17 (85.0)		6.92	1	0.01*	
Learning/developmental disorder	3 (16.7)	15 (83.3)		2 (10.0)	18 (90.0)					0.65
Medication	5 (26.3)	14 (73.7)		5 (23.8)	16 (76.2)					1.00

Note: *, significant difference between the High and Low PCSS score groups; *(p)*, Fisher's Exact Test. Difference tests: For age; education; time since last concussion and total number of concussions variables, Mann-Whitney U Test (U); For sex, Chi Square Test (X^2). Total number of concussions refers to the cumulative mean number of concussions per participant within each group. For the high PCSS group, medical conditions included migraines ($n = 4$), headache ($n = 4$), sleep disorders ($n = 3$), and other ($n = 3$) including asthma ($n = 2$), Lupus ($n = 1$) and iron deficiency/ low blood pressure ($n = 1$). Mental health conditions included depression ($n = 4$), anxiety ($n = 6$), and other ($n = 3$) including anorexia nervosa ($n = 1$), bipolar disorder ($n = 1$) and borderline personality disorder ($n = 1$). Learning/Developmental conditions included dyslexia ($n = 1$), ADHD ($n = 2$), speech/language delay ($n = 1$). For the low PCSS group, medical conditions included migraines ($n = 1$) and other ($n = 1$), Irlens. Mental health conditions included depression ($n = 2$), anxiety ($n = 2$), and other ($n = 1$), PTSD. Learning/Developmental conditions included dyslexia ($n = 1$), and ADHD ($n = 1$).

Table 8. Independent samples *t*-test analyses of group differences in cognitive function.

Cognitive index	High PCSS score group			Low PCSS score group			Independent samples *t*-test		
	n	*M*	*SD*	*n*	*M*	*SD*	*t*	*df*	*p*
Immediate attention	19	0.00	0.75	21	0.00	0.80	0.00	38	1.00
Processing speed	19	0.29	0.60	21	0.42	0.64	–0.66	38	0.52
Inhibitory control	19	–0.02	0.57	21	0.00	0.46	–0.13	38	0.90
Inattentiveness	19	0.00	0.65	21	0.00	0.50	0.00	36	1.00
Sustained attention	19	48.17	7.45	21	51.3	7.73	0.00	36	1.00
Working memory	19	0.00	1.00	21	0.00	1.00	0.00	38	1.00

full cohort of 40 participants (19 high PCSS scorers and 21 low PCSS scorers). No outliers were detected, and all statistical assumptions were met. Table 7 shows the descriptive statistics for demographic variables including concussion and medical history, as well as the evaluation of significant differences across high and low PCSS groups. Addition of the 2 participants who did not undergo EEG did not change the fundamental characteristics of the populations, as shown in Table 2. Participants across groups did not vary significantly on characteristics such as age, education, number of concussions and medication intake; however, the high PCSS group had a significantly higher rate of medical and mental health conditions.

Table 8 details the descriptive statistics for the cognitive indices across both groups. Independent samples *t*-tests were conducted, and no statistically significant differences in cognitive performance were found between the high and low PCSS groups (results summarised in Table 8).

4. Discussion

The purpose of this study was to gain a better understanding of the neurobiological characteristics of post-concussion symptoms by exploring the association between PCSS scores, brain network connectivity and cognition in a non-clinical sample. The first hypothesis that network dysregulation would be higher in high PCSS scorers compared to low PCSS scorers was not supported. In fact, network dysregulation (FPN and DMN) was significantly higher in low PCSS scorers; however, only the FPN difference remained significant after adjusting for multiple comparisons. The second hypothesis that high PCSS scorers would have more cognitive dysfunction was also not supported. These

findings are not consistent with previous reports that disrupted brain network function is associated with post-mTBI symptom severity and cognitive function [44].

While the finding that low PCSS scorers had more network dysregulation was not anticipated, certain characteristics of this group may offer some explanation for the findings. The low PCSS group had more recent concussions overall, which may have caused them to be more 'interested' in participating in the study and therefore be more engaged with the process. As reflected in the literature [40,41,94], it is possible that individuals will continue to experience network dysfunction after clinical symptom recovery. This appears to be supported by our finding that network dysfunction was present even though clinical symptom ratings were low in the low PCSS group. It is also supportive of the conceptual understanding of sub-concussive injury described in Dioso, Cerillo [13], where functional changes exist in the absence of clinical symptoms. In fact, these findings may provide preliminary support for the mechanisms of sub-concussive functional pathology. Moreover, the high PCSS group had a higher rate of medical conditions, and their PCSS score may have been inflated by their chronic conditions (e.g., mental health challenges), reflecting the fact that it is possible that PCSS symptoms are not specific to concussion and that they might overlap with other conditions, or in fact healthy individuals as reported in the literature [34–36]. While there was no statistically significant difference in the number of participants using prescribed medications between the high and low PCSS groups in this study, the high PCSS group may also have used different types of medication, potentially confounding the results by altering brain network functioning. Considering that medication and chronic conditions are also known to effect gastrointestinal health, which in turn impacts neurological health, exploring the relationship between gastrointestinal health and post-concussion symptom ratings may provide further explanation for the variation between the low and high scorers.

Regarding the lack of significant difference in cognitive dysfunction across the high and low PCSS scorers, it is possible that since the participants were all university students, their attention and processing speed may have been actively trained through their education. Hence, while they may have post-concussion symptoms, they are less likely to display cognitive dysfunction due to higher cognitive reserve. Additionally, this was not a clinical sample, and of those with a reported concussion, most were historical injuries (average time since injury; high group 61.9 months, low group 7.6 months). As indicated in the literature [8], 80–90% of individuals with mTBI would not be expected to have persistent symptoms (e.g., cognitive deficits) at this time point post-mTBI.

The third post-hoc hypothesis was supported, finding that network dysregulation (DMN, SN, FPN) was greater in participants with a more recent mTBI. While this was a non-clinical sample, and participants were not followed up from their injury baseline, the finding that those who had experienced a concussion had significantly less network dysregulation with a greater time since injury, supports the expectation that with time, the functional neurophysiological impacts of concussion are likely to resolve. This was supportive of previous research demonstrating normalisation of network connectivity as time since injury increased when measured at six months post-injury [44]. Although this does not provide a timepoint when normalisation of network function occurs, or what percentage of individuals with mTBI might be expected to have a delayed neurophysiological recovery, and the factors influencing that recovery, it warrants further investigation to inform expectations for neurophysiological recovery from mTBI. Especially since in the present study, the subset of individuals who had experienced concussion was obtained from both high and low PCSS scoring groups, suggesting that symptom score alone was not sufficiently indicative of concussion or recovery status. In fact, it supports previous literature suggesting that neurophysiological dysfunction may be present beyond the point of clinical recovery [40].

While the findings are intriguing, the study was limited by a small sample size with limited power to detect significant differences, especially considering the very large number of variables measured and the highly varied time since injury. The large standard deviation for time since last concussion makes the conclusion challenging. With a larger sample, future research would benefit from separating the groups into acute and chronic mTBI or analysing data from participants with a narrower timeline post mTBI. Additionally, university students may be engaged in a higher level of cognitive activity than the general population. Considering the functional networks measured are closely aligned with cognitive functioning, participants in this study may have had a higher level of compensation than the general population, which may have skewed the results resulting in less cognitive dysfunction. Additionally, the neuropsychological measures used may have been too 'simplistic' to capture mild deficits in individuals with higher cognitive performance. Selecting a more comprehensive neuropsychological battery which is catered to higher functioning individuals, particularly in the domain of executive functioning, may have provided a better understanding of participants' cognition. Selection bias was also a limitation since volunteers may have been particularly invested in the study due to an interest in the topic of research. Importantly, this study was not conducted in a clinical population, and concussion history was determined by self-report. Additionally, this study had a majority female sample (68%), and analyses to determine the impact of covariates such as sex and mechanism of injury were not conducted due to the limited sample size. Moreover, confounding variables such as medication and medical history were not controlled for in the statistical analyses conducted. Although more thor-

Table 9. Descriptive statistics for network connectivity on QEEG (DMN, SN, FPN).

	High PCSS score group			Low PCSS score group		
	n	*M*	*SD*	*n*	*M*	*SD*
DMN IC Z Score Variance Within Network	18	0.2	0.1	20	0.4	0.3
DMN IC Number of Z scores >1.96 SD	18	121.6	105.6	20	336.1	392.6
DMN IC Percentage Z scores >1.96 SD	18	1.8	1.5	20	4.8	5.7
SN IC Z Score Variance Within Network	18	0.2	0.1	20	0.3	0.2
SN IC Number of Z scores >1.96 SD	18	153.1	183.7	20	293.2	337.1
SN IC Percentage Z scores >1.96 SD	18	1.6	1.9	20	3.0	3.5
FPN IC Z Score Variance Within Network	18	0.2	0.1	20	0.4	0.3
FPN IC Number of Z scores >1.96 SD	18	170.2	156.1	20	469.6	551.3
FPN IC Percentage Z scores >1.96 SD	18	2.1	1.9	20	5.7	6.7
DMN LC Z Score Variance Within Network	18	0.2	0.1	20	0.3	0.2
DMN LC Number of Z scores >1.96 SD	18	131.9	175.7	20	217.5	294.9
DMN LC Percentage Z scores >1.96 SD	18	1.9	2.5	20	3.1	4.3
SN LC Z Score Variance Within Network	18	0.2	0.1	20	0.3	0.2
SN LC Number of Z scores >1.96 SD	18	152.2	172.2	20	245.2	325.8
SN LC Percentage Z scores >1.96 SD	18	1.6	1.8	20	2.5	3.3
FPN LC Z Score Variance Within Network	18	0.2	0.1	20	0.3	0.2
FPN LC Number of Z scores >1.96 SD	18	127.3	177.7	20	228.5	262.5
FPN LC Percentage Z scores >1.96 SD	18	1.5	2.1	20	2.8	3.2
DMN PD Z Score Variance Within Network	18	0.2	0.1	20	0.3	0.2
DMN PD Number of Z scores >1.96 SD	18	98.7	88.7	20	294.9	359.2
DMN PD Percentage Z scores >1.96 SD	18	1.4	1.3	20	4.3	5.2
SN PD Z Score Variance Within Network	18	0.2	0.1	20	0.3	0.1
SN PD Number of Z scores >1.96 SD	18	145.2	144.7	20	264.6	294.4
SN PD Percentage Z scores >1.96 SD	18	1.5	1.5	20	2.7	3.0
FPN PD Z Score Variance Within Network	18	0.3	0.1	20	0.4	0.3
FPN PD Number of Z scores >1.96 SD	18	184.4	187.1	20	499.4	607.9
FPN PD Percentage Z scores >1.96 SD	18	2.2	2.3	20	6.0	7.3
DMN CSD Z Score Variance Within Network	18	0.3	0.1	20	0.3	0.1
DMN CSD Number of Z scores >1.96 SD	18	18.2	23.3	20	60.9	98.5
DMN CSD Percentage Z scores >1.96 SD	18	8.2	16.8	20	9.2	14.9
SN CSD Z Score Variance Within Network	18	0.3	0.2	20	0.3	0.1
SN CSD Number of Z scores >1.96 SD	18	26.2	39.6	20	68.1	102.6
SN CSD Percentage Z scores >1.96 SD	18	3.1	4.7	20	8.1	12.2
FPN CSD Z Score Variance Within Network	18	0.3	0.2	20	0.2	0.1
FPN CSD Number of Z scores >1.96 SD	18	5.9	6.4	20	56.9	87.8
FPN CSD Percentage Z scores >1.96 SD	18	0.8	0.9	20	7.9	12.2

Note: DMN, Default Mode Network; SN, Salience Network; FPN, Frontal-Parietal Network; IC, instantaneous coherence; LC, lagged coherence; PD, phase difference; CSD, current source density; QEEG, Quantitative Electroencephalogram.

ough inclusion criteria such as recruiting confirmed mTBI cases based on neuroimaging or a biological biomarker, would be beneficial, they were beyond the scope of this study. Future research into concussion samples would benefit from a clearly differentiated concussion sample. Furthermore, participant recruitment for this study was significantly impacted by the COVID-19 pandemic. It would be ideal to recruit many more participants so that stratification of the sample by mechanism of injury can be used in statistical analysis, ensuring specificity in our understanding of mTBI. While categorising the participants by injury mechanism would be ideal, it was considered that further dividing a subset sample of 12 participants for statistical analysis would reduce the power of the analyses relating to this subset of participants. Participant recruitment is challenging in this field of research and particularly in a sparsely populated location such as Western Australia, with the additional restrictions of a pandemic. The authors believe that appropriate caution was used in the selection of statistical analyses, interpretation of findings and transparency of the study limitations.

Future research may improve the generalisability of the findings by recruiting a non-university sample to reduce potential cohort effects relating to undergraduate stu-

dents. Having a larger sample would allow for further stratification of time since injury, mechanism of injury, sex and PCSS symptom scores which would enable a broader understanding of the relationships suggested in this study. Controlling for confounding variables such as medication intake, medical history and gastrointestinal health would also be important in future studies. Considering that participants with a history of concussion were several months to years post-injury on average, conducting the study in a clinical sample during various stages of recovery (acute, subacute, chronic), as well as exploring repeated concussion and sub-concussion would further improve the understanding of brain network and cognitive function following mTBI. Using concussion diagnostic criteria or at least medically diagnosed concussion inclusion criteria would be more reliable than self-report in future studies. Lastly, analysing the relationships between post-concussion symptoms and other conditions would further enhance our understanding of the specificity of the PCSS, particularly as it relates to the large proportion of the normal population who meet the criteria for PPCS.

5. Conclusions

In conclusion, the present study highlighted that in a sample of undergraduate students, preliminary findings suggest that brain network dysregulation appears to be greater in the early post-injury phase compared to later. Additionally, the PCSS does not relate to network connectivity and cognition. This suggests that measuring post-concussion symptoms using the PCSS does not necessarily inform us about alterations in underlying neural mechanisms. That is, higher PCSS scores do not necessarily indicate more dysfunction in network connectivity or cognition. In fact, the finding that the low PCSS group had more network dysfunction provides a possible explanation for the mechanisms of sub-concussive injury. Moreover, the high PCSS group had a higher number of medical and mental health conditions, suggesting that PCSS scores may be influenced by other health-related conditions and are not specifically measuring concussion-related symptoms. Additionally, non-specific symptoms like fatigue, dizziness and sleep quality may be influenced by medication or general daily activities that are unrelated to the concussion injury. The PCSS involves rating of non-specific symptoms; it does not consider confounding factors such as medication intake or other possible reasons for the symptoms, e.g., hormonal fluctuations or activity levels and bases the post-concussion symptom score on a single timepoint rather than the entire time-period since the concussion injury. This means that the PCSS score is likely confounded by a multitude of variables that are clouding the assessment of concussion recovery, especially in the non-acute phase. While the PCSS was developed for the athlete population, it seems that administering it to the general population may bring more complexities to post-concussion recovery that are not captured by this scale. Considering its widespread use, the measurement of post-concussion symptoms in the general population requires further investigation, particularly the underlying PCSS constructs in a non-sporting population. Furthermore, further investigation in clinical samples is warranted.

Table 10. Mann-Whitney U Test analyses of group differences in brain network dysregulation.

	U	*p*
DMN IC Z Score Variance Within Network	118.5	0.07
DMN IC Number of Z scores >1.96 SD	121	0.09
DMN IC Percentage Z scores >1.96 SD	121	0.09
SN IC Z Score Variance Within Network	143.5	0.29
SN IC Number of Z scores >1.96 SD	132	0.17
SN IC Percentage Z scores >1.96 SD	132	0.17
FPN IC Z Score Variance Within Network	113.5	0.052
FPN IC Number of Z scores >1.96 SD	116	0.06
FPN IC Percentage Z scores >1.96 SD	116	0.06
DMN LC Z Score Variance Within Network	161	0.59
DMN LC Number of Z scores >1.96 SD	147.5	0.35
DMN LC Percentage Z scores >1.96 SD	147.5	0.35
SN LC Z Score Variance Within Network	158.5	0.53
SN LC Number of Z scores >1.96 SD	158	0.53
SN LC Percentage Z scores >1.96 SD	158	0.53
FPN LC Z Score Variance Within Network	149.5	0.38
FPN LC Number of Z scores >1.96 SD	133	0.18
FPN LC Percentage Z scores >1.96 SD	133	0.18
DMN PD Z Score Variance Within Network	127.5	0.13
DMN PD Number of Z scores >1.96 SD	119.5	0.08
DMN PD Percentage Z scores >1.96 SD	119.5	0.08
SN PD Z Score Variance Within Network	153	0.44
SN PD Number of Z scores >1.96 SD	148	0.36
SN PD Percentage Z scores >1.96 SD	148	0.36
FPN PD Z Score Variance Within Network	119.5	0.08
FPN PD Number of Z scores >1.96 SD	116	0.06
FPN PD Percentage Z scores >1.96 SD	116	0.06
DMN CSD Z Score Variance Within Network	177	0.94
DMN CSD Number of Z scores >1.96 SD	160	0.57
DMN CSD Percentage Z scores >1.96 SD	172	0.83
SN CSD Z Score Variance Within Network	180	1.0
SN CSD Number of Z scores >1.96 SD	154.5	0.46
SN CSD Percentage Z scores >1.96 SD	154.5	0.46
FPN CSD Z Score Variance Within Network	168	0.74
FPN CSD Number of Z scores >1.96 SD	133.5	0.18
FPN CSD Percentage Z scores >1.96 SD	133.5	0.18

Note: DMN, Default Mode Network; SN, Salience Network; FPN, Frontal-Parietal Network; IC, instantaneous coherence; LC, lagged coherence; PD, phase difference; CSD, current source density.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

FB, CP, MF and JB designed the research study. FB performed the research, supervised by CP, MF and JB. SM developed extensive code for data extraction and processing. FB and SH analyzed the data in consultation with CP, MF and JB. FB, CP, MF, JB wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Ethics approval was provided by the University of Western Australia (UWA)'s Human Research Ethics Committee (2021/ET000033). Participants provided written consent.

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Conflict of Interest

The authors declare no conflict of interest.

Appendix

See Tables 9,10.

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