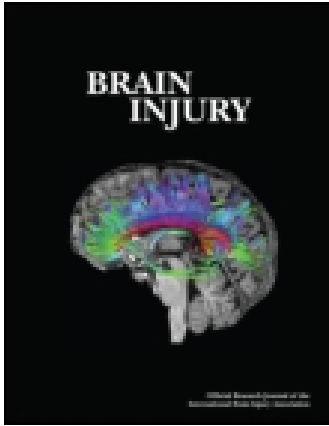


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Brain Injury

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/ibij20>

Long-term working memory deficits after concussion: Electrophysiological evidence

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Published online: 10 Jun 2013.

To cite this article: Lana J. Ozen, Roxane J. Itier, Frank F. Preston & Myra A. Fernandes (2013) Long-term working memory deficits after concussion: Electrophysiological evidence, *Brain Injury*, 27:11, 1244-1255

To link to this article: <http://dx.doi.org/10.3109/02699052.2013.804207>

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ORIGINAL ARTICLE

Long-term working memory deficits after concussion: Electrophysiological evidence

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Abstract

Background: Persistent complaints of lingering memory and concentration difficulties are common following a concussion, although the brain basis of these is unknown. Some suggest abnormalities can be found on the P300 event-related potential component, recorded using electroencephalography (EEG), despite unobservable cognitive impairments.

Objective: To examine the P300 and cognitive performance following a remote concussion during an *n*-back task that varies in working memory load.

Research design: Seventeen participants with a remote concussion and 17 controls performed a visual *n*-back task in which working memory demands were systematically increased by manipulating cognitive load. Participants also completed neuropsychological and self-report measures.

Results: The concussion group showed a decrease in P300 amplitude compared to controls that was independent of working memory load on the *n*-back task. While no performance differences were observed between groups, P300 amplitude was negatively correlated with response times at higher loads in both groups.

Conclusion: High functioning young adults with a remote concussion may have inefficient recruitment of processing resources for target identification, evident by the attenuated P300. The negative correlations between response time and P300 amplitude suggest that the time necessary to accurately respond to targets increases as the efficiency of allocating processing resources decreases during highly demanding working memory tasks.

Keywords

Attention, event-related potential, mild traumatic brain injury, *n*-back task, P300

History

Received 21 December 2012

Revised 9 April 2013

Accepted 7 May 2013

Published online 22 July 2013

Introduction

An estimated 1.7 million people sustain a traumatic brain injury (TBI) worldwide each year [1]. Approximately 80% of TBIs have been classified as concussions (i.e. mild TBIs) in the US over a recent 25-year period [2]. Young adults, 15–24 years of age, have one of the highest incidences of TBI [3] and are often not admitted to the hospital after a concussion [4]. As a result, concussion prevalence, especially among young adults, is even higher than most reported rates based on hospital admissions [5]. Although mild in severity, it is well known that concussions may result in acute cognitive deficits when measured within 3 months of injury. However, there is little evidence for residual neuropsychological impairment beyond 3 months [6–8].

Recent evidence suggests concussion-related impairments can persist well beyond 6 months when assessed by more complex cognitive tasks [9–12] and electrophysiological measures [9, 13–16]. To date, however, the precise cognitive domains and neural processes most vulnerable to the long-term effects of concussion are unknown. Moreover, few studies have attempted to specify the long-term effects of

concussion by manipulating task complexity within a single cognitive domain (e.g. working memory) while also measuring brain activity correlates. The goal of the present study was to examine the residual effects of concussion in young adults (mean age of 20 years old), at least 6 months post-injury, on both cognitive and neural processes. Accordingly, a task was implemented in which working memory complexity was manipulated across four conditions while recording event-related potentials (ERPs).

Working memory is a type of short-term memory in the order of seconds and is defined by Repovs and Baddeley ([17], p.17) as:

The ability to maintain and manipulate information in the process of guiding and executing cognitive tasks... [Working memory is] a multi-component system guided by an executive component consisting of a number of processes that provide attentional control over other components of working memory as well as other cognitive abilities.

Some studies have shown that, at least 6 months after concussion, performance is unaffected during simple selective attention tasks; however, both accuracy decrements [9, 12] and response slowing [10–12] have been documented using relatively more complex measures of working memory.

In other words, while individuals with a remote concussion may effortlessly complete a single task that requires relatively few attentional resources, they may experience difficulties when significant attentional control is required, such as performing a complex set of working memory operations (e.g. under dual task conditions).

A small number of studies have also provided support for long-term changes in functional brain activity after concussion by recording EEG and measuring the classic P300 ERP component. The P300 is thought to reflect a basic cognitive process by which incoming information is categorized and has also been linked to processes involved in updating the context of working memory [18, 19]. Typically observed using the oddball paradigm, whereby participants are required to identify infrequent targets among frequent non-targets, an increase in P300 amplitude is recorded when the target sequence probability decreases. This has been suggested to reflect that more cognitive resources are engaged in the active processing of infrequent target stimuli compared to the frequent stimuli. Individuals with a history of only one concussion [9, 13, 14, 16] and those who sustained multiple concussions [20–22] at least 6 months in their past show an attenuation of P300 amplitude during accurate target detection with no measurable performance deficits on standard oddball tasks compared to non-head-injured controls. These results suggest long-term inefficiencies in cognitive resource allocation or fewer processing resources available for target classification long after concussion [23] and emphasize the utility of using the ERP technique to detect residual neural changes post-concussion, even in the absence of observable cognitive impairment.

Results from two studies show that, while oddball tasks are useful in revealing changes in functional brain activity long after concussion, dual-tasks have been successful at identifying cognitive deficits, in addition to neural changes [9,16]. In both studies, decreases in P300 amplitude were recorded with no performance decrements on an oddball task at least 1 year post-injury, but, when participants were required to concurrently perform the oddball task with a working memory task, accuracy decrements were observed in addition to P300 changes. The authors suggested that, while a limited or inefficient pool of processing resources may be sufficient to enable performance for concussion participants during simple oddball detection, performance suffers when dual-task demands exceed available processing capacity (i.e. by increasing working memory demand) [9].

From the extant literature, it is unclear how high the demand on working memory processes must be in order to detect cognitive impairment and associated changes in brain activity long after concussion. As a result, the present study systematically varied working memory demand across four conditions of a well-known *n*-back task [18], while recording the classic P300 ERP component, in addition to recording traditional accuracy and response time measures. In a typical *n*-back task, participants are required to identify a stimulus as a target if it matches a pre-specified infrequent stimulus (0 letters previous; a standard oddball task) or if it matches an infrequent stimulus presented 1 letter previous, 2 letters previous or 3 letters previous. In order to systematically vary working memory demands, this study used a visual

n-back task to letters consisting of four loads (0-, 1-, 2- and 3-back).

Similar to standard findings in healthy controls on the classic oddball tasks [23], P300 amplitude has been shown to be larger for infrequent match targets compared to frequent non-match stimuli on all working memory loads of the *n*-back task, conceptualized as more effort or processing resources required to identify the match targets [24, 25]. The *n*-back task is unique in that P300 amplitude can also be measured as a function of working memory load and an inverse relationship between the two has been found. Particularly, as working memory load increases from 0–3-back loads, P300 amplitude decreases [24, 25]. It has been posited that this inverse relationship between P300 amplitude and working memory load is a result of dual-task demands, with attentional resources being reallocated from the demands of matching sub-task (i.e. oddball selection) to the increasing demands of the working memory sub-task (i.e. storage, encoding, manipulating and searching) [24, 25].

The current study hypothesized that concussion participants would show an overall decrease in P300 amplitude compared to controls for accurate identification of targets, in line with previous studies suggesting that concussion participants have fewer attentional resources available for accurate detection, at least on an oddball task [9, 13, 14, 16]. Additionally, it was expected that both groups would show typical decreases in P300 as a function of working memory load, but that group differences may emerge at higher loads. It was specifically predicted that, as working memory load increased, concussion participants may show larger decreases in P300 amplitude compared to controls due to inefficient attentional resource allocation.

Previous reports in the acute phase of a concussion showed no group differences in performance accuracy on the *n*-back task [26, 27]; none were expected here either. If differences in response times emerged, they were expected to be longer in the concussion group only during moderate-to-high *n*-back loads based on past reports of slowing on complex measures of working memory long after concussion [10–12]. In line with previous research [6–8], one did not expect to find group differences on standard neuropsychological or self-report measures. If supported, the findings would provide electrophysiological evidence for reduced working memory efficiency, long after concussion, which cannot be detected using standard accuracy and response time measures.

Methods

Classification of TBI

Participants were recruited through the University of Waterloo's online research group or by flyers posted around campus. Participants were paid \$20 or received course credits and provided signed consent as approved by the Research Ethics Board of the University of Waterloo before testing began.

The severity, cause and time elapsed since the concussion, as well as demographic/health-related information, were all determined prior to participation. If inclusion criteria were met, the researcher and participant set up a study time (see Figure 1). Participants were informed if they did not meet the

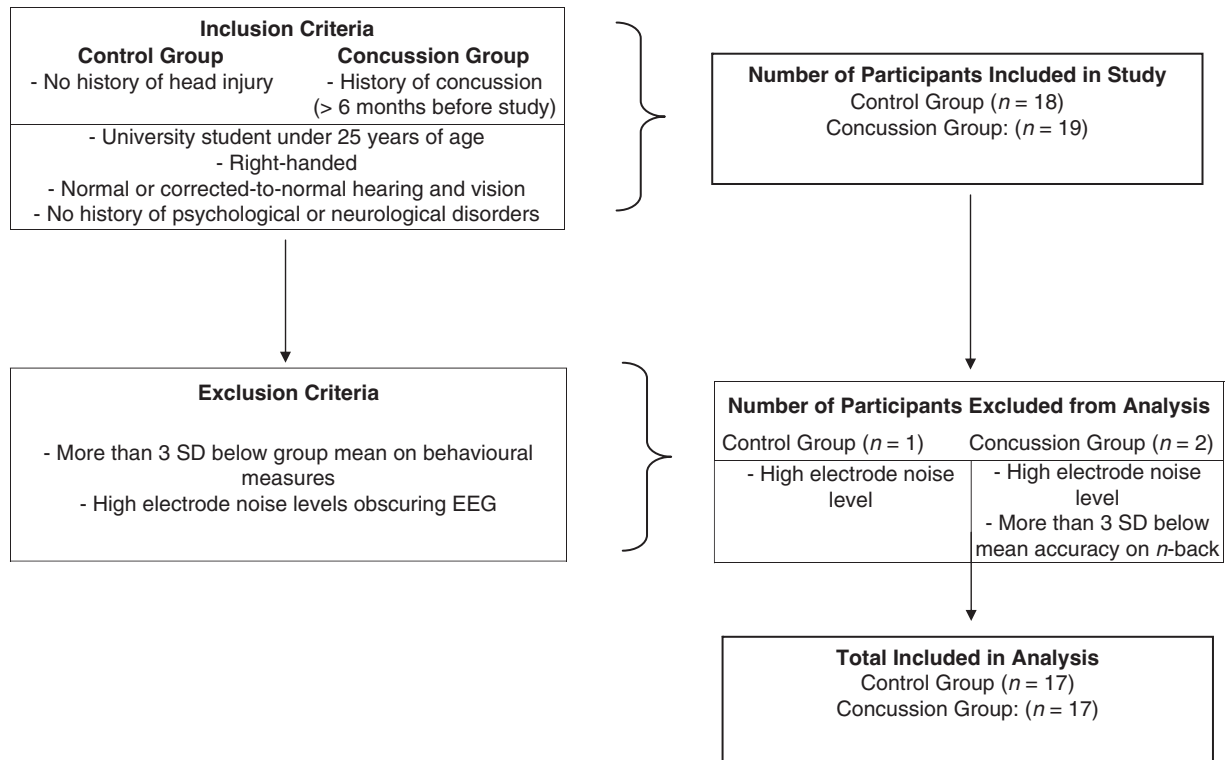


Figure 1. Inclusion and exclusion criteria.

inclusion criteria and were thanked for their interest. A demographic/health questionnaire was administered to each participant at the beginning of the study to confirm head injury status and to document further details about the concussion (e.g. time since injury, loss of consciousness duration, etc.).

A concussion, by definition, is a mild traumatic brain injury [28] and was defined in the current study as any strike to the head or any acceleration/deceleration force (i.e. whiplash) that resulted in a loss of consciousness (LOC) lasting no longer than 30 minutes and/or memory loss (brief amnesia), not exceeding 24 hours [29]. Participants could also report experiencing confusion (inability to focus attention) and/or disorientation (loss of physical bearings), all not exceeding 24 hours [29], in addition to LOC and memory loss (see Table I). This study only included participants in the concussion group if they fit the above criteria for concussion and if it was sustained at least 6 months prior to testing. All participants in the concussion group who completed the study happened to be at least 1 year post-injury. To be included in the control group, participants must have indicated that they had never, to their knowledge, sustained any type of head injury or hit to the head in their past.

Participants

A total of 37 individuals met inclusion criteria and completed the study, although data from three participants were removed from data analyses as they did not meet the exclusion criteria (see Figure 1). Thus, data from a total of 34 participants were analysed: 17 control participants (nine female) and 17 concussion participants (six female). Twenty-four participants were recruited for credit (14 controls and 10 concussion participants) and 10 for pay (three controls and seven

concussion participants). Mean group age and education significantly differed (see Table II). While it was not expected that a 1 year difference between groups, in age and education, would affect the cognitive task performance and ERP findings, additional correlations were conducted to ensure this difference did not affect the main dependent variables (see results section).

All procedures were performed in compliance with the University of Waterloo's ethics guidelines for human research and were approved by the University's Office of Research Ethics.

N-Back task

Stimuli

A classic letter variant of the n -back task was used [30]. Participants were presented with letters on the computer screen, one at a time, using Presentation software (Neurobehavioral Systems, <http://www.neurobs.com>), which also recorded behavioural responses from a mouse click. Only orthographically distinct uppercase consonants were used in this experiment (B, C, D, F, G, H, J, K, M, Q, R, S, T, V, X, Z [31]). Participants sat 27'' from a 17'' CRT monitor with a refresh rate of 60 Hz. The white-coloured letters were presented on a black background in 100-point font. Each trial started with the presentation of a fixation cross lasting 250 milliseconds, then a black screen for 150 milliseconds, followed by the letter stimulus for 500 milliseconds and ending with a final black screen for a randomized inter-stimulus interval of 1800–2200 milliseconds.

Procedure

There were four n -back conditions (0-back, 1-back, 2-back and 3-back) that varied in working memory load. Each load

Table I. Demographic and head injury details for concussion participants.

Gender	Age	Education	TSI	LOC	PTA	Conf	Disorien	Cause of injury
M	22	16	5.5	<1 min	0.5 h	0.5 h	5 min	Playing—Hit back of head on floor
M*	18	13	1.5	<1 min	1 h	0.5 h	5 min	Floor hockey—hit head on floor
			3	<1 min	—	—	—	Basketball—elbow to head
F	22	16	1.33	<1 min	<5 min	2 h	1 week	Hockey—hit head on boards
F*	20	15	3.33	<1 min	No	24 h	0.5 h	Rugby—kicked in head
			4	No	No	No	No	2 separate accidental hits
F	22	16	8	<1 min	<5 h	<5 h	<5 h	Jumped—hit head on ceiling
M*	21	16	4.42	<1 min	No	3–4 h	1.5 h	Hit by car—head hit windshield
			10	<1 min	No	No	No	Boating—hit in head by boom
F*	22	17	9	No	No	No	No	Soccer—hit in head 2× same game
			1	No	<5 min	<5 min	No	Soccer—head-to-head hit
M	22	16	12	<1 min	No	No	No	Skiing—Fell and hit head
M	22	16	15	1 >5 min	2 h	1 h	No	Playing—Hit back of head on floor
F*	20	14	5	No	No	No	48 h	Horse reared up and hit front head
			4	No	No	No	No	Biking—fell and hit head
M*	19	14	5	<1 min	No	10 min	1 h	Hockey—hit head on ice
			Multiple	No	—	—	—	Hockey—about 10 hits—no LOC
M*	21	15	5	<1 min	No	No	No	Fainted—hit back of head
			Multiple	No	—	—	—	Sports' hits over time—no LOC
M	21	16	10	—	5 h	24 h	24 h	Rugby—hit in head 3× same game
M	18	13	1.67	<1 min	No	No	No	Hockey—head hit boards, then ice
M	21	14	4	<1 min	No	No	2 h	Biking—fell off cliff, head hit rock
M	22	16	7	<1 min	No	<1 min	4–5 hours	Snowboarding—fell and hit head
F	22	16	5	<1 min	0.5 min	0.5 hour	0.5 hour	Fell off cliff, hit head on rock

F, Female; M, Male; TSI, Time since injury in years; LOC, Duration of loss of consciousness; PTA, Post-traumatic amnesia; Conf, Length of Confusion; Disorien, Length of Disorientation.

*Participant experienced more than one hit to the head. — participants did not answer/could not recall. It is important to note that, while some participants' reported more than one hit to the head, most of the hits were not severe enough to be classified as a mild TBI/concussion according to the criteria (i.e. they answered no to or could not recall experiencing LOC, PTA, confusion and disorientation).

Table II. Demographics for control and concussion participants.

	Control (n = 17)	Concussion (n = 17)	t/χ^2 -value (df)	p-value
Female	9 (53%)	6 (35%)	1.07 (1)	0.30
Age	19.71 (1.21)	20.88 (1.41)	-2.61 (1)	0.01
Years of education	14.29 (1.26)	15.24 (1.20)	-2.23 (1)	0.03

Number of females (%) and mean age and years of education (SD) for each group. Group means compared using Independent-Samples *t*-tests; proportions compared using Chi-Square test.

condition consisted of 75 trials: 25 match stimuli and 50 non-match stimuli (15 of which were distracters). Distracters were added to each load condition to ensure that participants were not merely identifying matches regardless of the condition. Every participant completed three fixed-order blocks, each block consisting of four different *n*-back load conditions (i.e. *Block One*: 1-back, 0-back, 2-back, 3-back; *Block Two*: 0-back, 2-back, 1-back, 3-back; *Block Three*: 1-back, 3-back, 0-back, 2-back). Participants were instructed to make a left click for match targets (match condition) and a right button click for all letters that did not match the target (non-match condition), depending on *n*-back load. Participants were informed that all responses had to be made prior to completion of each trial. Specifically, in the lowest load 0-back condition, participants were informed that the letter 'W' was the target. In the low load 1-back condition, a target was to be identified when letter on the screen matched the one shown immediately before it. In the moderate load 2-back and highest load 3-back conditions, the letter on the screen was to be identified as a target if it matched the letter shown two or three trials previous, respectively (see Figure 2 for example of

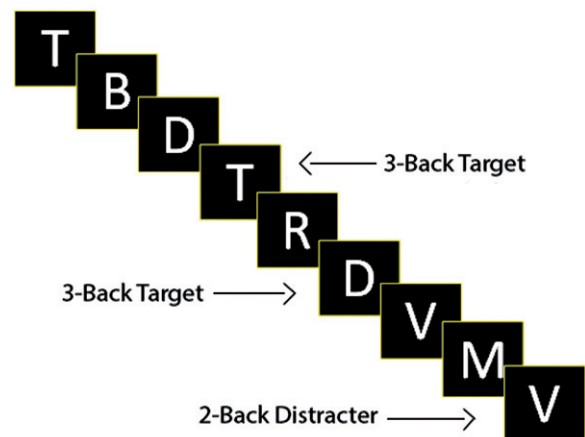


Figure 2. Schematic representation of the 3-back load condition of the *n*-back task.

3-back load). Responses made after the completion of the trial and, thus, made during the subsequent trial were coded as incorrect.

The *n*-back task started with a practice session, in which all participants completed the 0-, 1-, 2- and 3-back loads, in that order. Prior to each condition, the experimenter read aloud the instructions on the screen. Practice for each load condition took ~1 minute to complete. For each, participants were asked to respond to six target and 14 non-target stimuli. In the experimental session, participants completed each of the four *n*-back loads three times, presented in the three fixed-ordered blocks. While the order of the *n*-back loads within each block was fixed, as listed above, the order of the blocks was counterbalanced across participants to avoid practice effects

(e.g. block three, block one, block two). Participants were told that the *n*-back loads would be presented in a random order. Participants were notified when they were one-, two- and three-thirds through the experiment. They were also encouraged to take breaks if necessary in between conditions. The experimental session took ~45 minutes to complete, plus breaks varying in length between loads/blocks depending on participant.

Neuropsychological tests

Individual working memory span was assessed using the Digit Span Forward and Backward tasks [32]. The Trail Making A and B tests [33] were used to examine processing speed and cognitive flexibility, respectively. Processing speed and paired and free recall were measured using the Digit-Symbol Substitution task [32].

Self-report scales

All participants completed a demographic/health form, Beck Depression Inventory (BDI [34]), State-Trait Anxiety Inventory (STAI [35]), the Attention-Related Cognitive Errors Scale (ARCES) and the Memory Failures Scale (MFS) [36]. The latter two scales are composed of 12 questions asking participants to respond by choosing one of five responses on a Likert scale ranging from 'Never' to 'Very Often'. The scales were originally developed by selecting items from the Cognitive Failures Scale [37], Reason's diary studies [38], in which participants recorded descriptions of slips of action in their daily lives, and from the authors' own experiences, based on personal diaries of attention and memory lapses. All participants also completed the Rivermead Post-Concussion Symptom Checklist [39], a questionnaire used to determine existence and severity of post-concussive symptoms participants may be experiencing. Control participants also filled out this checklist and were told that these are symptoms they may or may not experience in daily life. They were asked to report how often, if ever, they experienced any of the classic concussion symptoms.

Experimental procedure

The experiment began with the participant reading the information letter and signing the consent form. The researcher then asked the participant questions from the Demographic and Head Injury questionnaire, after which participants completed the Digit-Substitution task, followed by the Trail Making and the Digit Span Forward and Backward Tasks. Next, the participant completed the self-report questionnaires in the following order: ARCES, MFS, BDI, STAI and finally the Rivermead Post-Concussion Inventory. Participants were then fitted with an electrode cap and appropriately prepped for EEG recording. The experimenter sat beside the participant during the *n*-back task to ensure condition-specific instructions were followed and monitor EEG recordings on a computer screen (e.g. frequency and timing of blinks). Following completion of the task and electrode removal, participants received a feedback letter. The total duration of the study was 2 hours, for which participants received two course participation credits or \$20 remuneration.

EEG recording and data analysis

EEG data were recorded using 64 Ag/AgCl active electrodes (BioSemi Active Two system, The Netherlands; <http://www.biosemi.com>) mounted on a flexible cap according to the extended international 10/20 system. A Common Mode Sense (CMS) active electrode and Driven Right Leg (DRL) passive electrode serving as ground were used. Eight additional electrodes were used: four electrodes recorded horizontal and vertical eye movements and were placed at the outer canthus and under the centre of each eye; two additional electrodes were placed on the posterior part of the cap on the left and right sides (CB1 and CB2, respectively) and two more electrodes were placed on the left and right mastoids (TP9 and TP10). EEG was digitized at a sampling rate of 512 Hz.

The data were processed using the EEGLab toolbox [40] and ERPLAB toolbox (<http://erpinfo.org/erplab>) implemented in Matlab (Mathworks, Inc.). Only correct-response trials were analysed. EEG was epoched offline using a 100 millisecond pre-stimulus baseline until 600 milliseconds after letter stimulus onset. Then, trials were digitally band-pass filtered (0.01–30 Hz) and average referenced. Trials containing large artifacts were manually removed through visual inspection. Ocular artifacts were removed using independent component analysis (ICA) decomposition as implemented in EEGLab.

Data analysis

For each *n*-back load, there were 75 possible match responses (25×3 blocks) and 150 possible non-match responses (50×3 blocks).

ERP data

On average, 59.17 (SD = 4.17; range = 30–75) trials were kept for correct match responses in each *n*-back load and 139.73 (SD = 3.97; range = 118–150) were kept for correct non-match responses in each *n*-back load for each participant. Trials were averaged for each group according to *N*-back Load (0–3-back) and Stimulus Type (match or non-match). P300 peak amplitude and latencies were measured at the maximum positivity between 300–400 milliseconds after stimulus onset at central-parietal (CPz) and parietal (Pz) electrodes, the midline electrodes where P300 was largest when averaged across participants in each group. For match responses, each participant's average P300 *peak* amplitude was visually inspected and confirmed to reach a maximum during the 300–400 millisecond window in every *n*-back load condition. Observing clear peaks was not always possible for non-match responses. Thus, this study also calculated the *mean* amplitude between 300–400 milliseconds window for each groups' match and non-match responses in every *n*-back condition.

For ERP analysis, three separate repeated-measures analyses of variance (ANOVAs) were conducted with *N*-back Load (4), Stimulus Type (2) and Electrode (2) as the within-subject factors and Group (2) as the between-subject factor to examine P300 peak amplitude, mean amplitude and latency.

Behavioural data

Hit rates were calculated for each load by dividing each participant's number of accurate match responses and accurate non-match responses by the total possible number of accurate responses for each stimulus type. Median response times were also calculated for each participant for both accurate matches and non-matches in each n -back load.

To analyse hit rate and response time data, two repeated-measures ANOVAs were conducted with N -back Load (4) and Stimulus Type (2) as the within-subject factors and Group (2) as the between-subject factor.

All ANOVAs used Greenhouse-Geisser adjusted degrees of freedom and planned contrasts used Bonferroni corrections for follow-up analyses.

For neuropsychological and self-report data, independent-samples t -tests were conducted to examine differences between groups.

Results

Behavioural data

Hit rate

A significant main effect of Stimulus Type, $F(1, 32) = 206.91$, $p < 0.001$, revealed that participants had higher hit rates in the non-match condition compared to the match condition, regardless of Group. There was also a main effect of N -back Load, $F(3, 96) = 156.85$, $p < 0.001$ (see Figure 3), due to the 0-back condition yielding larger hit rates than 1-back, 2-back and 3-back conditions (all comparisons at $p < 0.01$). A significant Stimulus Type \times N -back Load interaction, $F(3, 96) = 102.53$, $p < 0.001$, was followed up with separate one-way ANOVAs that showed larger effects of load for the match condition, $F(3, 132) = 112.37$, $p < 0.001$, $\eta^2 = 0.72$, compared to the non-match condition, $F(3, 132) = 58.11$, $p < 0.001$, $\eta^2 = 0.57$. There was no effect of Group and Group did not interact with N -back Load or Stimulus Type.

Response times

A significant main effect of Stimulus Type showed that, regardless of Group, response times, were significantly longer for matches than non-matches, $F(1, 32) = 6.00$, $p < 0.05$. There was also a significant main effect of N -back Load, $F(3, 30) = 32.29$, $p < 0.001$, such that participants took longer to respond accurately in the 2-back compared to 0-back condition, $t(132) = -3.16$, $p < 0.01$, and the 3-back compared to the 0-back condition, $t(132) = -6.33$, $p < 0.001$, but not the 1-back compared to 0-back condition, $t(132) = -1.20$, $p > 0.20$ (see Figure 4). The main effect of Group was non-significant, $F(3, 30) = 1.83$, $p > 0.10$, as were interactions between group and the other factors.

Neuropsychological and self-report measures

There were no significant group differences on any neuropsychological task or self-report measure (see Table III).

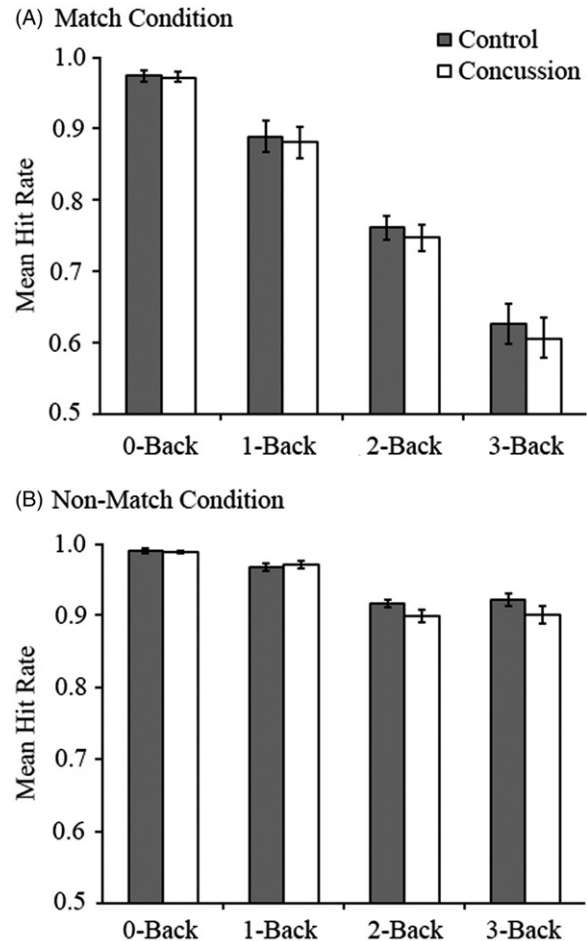


Figure 3. Top graph: Mean hit rate for control and concussion participants in each n -back load of the match condition. Bottom graph: Mean hit rate for control and concussion participants in each n -back load of the non-match condition. Error bars represent standard error of respective means.

Electrophysiological data

P300 amplitude

A significant main effect of Stimulus Type revealed that participants had higher peak P300 amplitudes for match compared to non-match trials, $F(1, 32) = 398.27$, $p < 0.001$ (see Table IV, Figure 5). There was also a main effect of Group such that concussion participants had significantly lower peak P300 amplitudes compared to controls, $F(1, 32) = 4.79$, $p < 0.05$. These results were qualified by a Stimulus Type \times Group interaction, $F(1, 32) = 7.30$, $p < 0.02$, which showed that concussion participants had significantly lower P300 peak amplitudes only for match trials, $t(32) = 2.48$, $p < 0.05$ (see Figure 6), but showed no difference relative to controls on non-match trials, $t(32) = 1.64$, $p > 0.10$ (see Figure 5). Group did not interact with any other variables.

There was a main effect of electrode, $F(1, 32) = 25.07$, $p < 0.001$, with higher average P300 peak amplitude recorded from Pz compared to CPz. The main effect of N -back Load was significant, $F(3, 96) = 16.97$, $p < 0.001$, and planned contrasts of interest revealed significantly smaller P300 amplitudes in the 2-back relative to the 0-back condition, $t(132) = 1.94$, $p = 0.05$, as well as in the 3-back relative to the

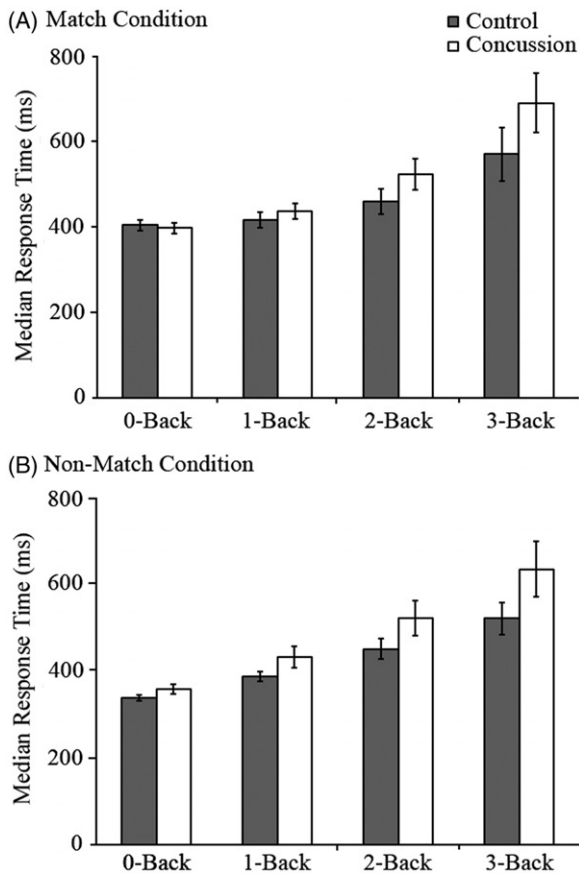


Figure 4. Top graph: Median response time for control and concussion participants in each n -back load of the match condition. Bottom graph: Median response time for control and concussion participants in each n -back load of the non-match condition. Error bars represent standard error of respective means.

Table III. Means with corresponding t -values and p -values for neuropsychological task and self-report questionnaires.

Task/questionnaire	Control	Concussion	t -value	p -value
Digit-Symbol (DS)	93.1 (13.3)	86.1 (17.3)	1.33	0.19
DS Assisted Recall	7.7 (1.8)	6.8 (2.6)	1.05	0.30
DS Free Recall	8.1 (0.9)	7.5 (1.4)	1.36	0.18
Digit Span Forward	8.9 (1.7)	9.5 (2.4)	-0.84	0.41
Digit Span Backward	8.2 (2.2)	8.8 (1.7)	-0.87	0.39
Trail Making A	15.9 (5.0)	17.0 (6.0)	-0.58	0.57
Trail Making B	38.6 (9.1)	37.9 (17.9)	0.15	0.89
Trail Making Errors B	0.8 (1.6)	0.3 (1.0)	1.17	0.25
ARCES	30.8 (5.0)	33.2 (7.5)	-1.13	0.27
MFS	27.9 (3.8)	30.1 (5.7)	-1.35	0.19
BDI	6.4 (4.1)	8.5 (5.3)	-1.27	0.21
STAI_State	29.5 (7.3)	30.8 (7.2)	-0.52	0.61
STAI_Trait	34.7 (7.8)	34.7 (7.8)	0.00	1.00
Rivermead Checklist	10.6 (6.0)	12.3 (8.5)	-0.64	0.53

ARCES, Attention-related Cognitive Error Scale; MFS, Memory Failures Scale; BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory.

Standard deviations in parentheses.

0-back condition, $t(132) = 3.57$, $p < 0.001$. No difference was found between 0- and 1-back, $t(132) = 1.05$, $p > 0.20$.

Analysing P300 mean amplitude did not change the pattern of results obtained using peak amplitude measures. The Stimulus Type \times Group interaction remained significant, $F(1, 32) = 7.14$, $p < 0.05$, as did the main effect of Electrode, $F(1, 32) = 25.56$, $p < 0.001$ and N -back Load,

$F(3, 96) = 14.39$, $p < 0.001$. As with P300 peak amplitude results, Group did not interact with any other factor using mean P300 amplitude measures.

P300 peak latency

A significant main effect of Electrode was found, $F(1, 32) = 10.91$, $p < 0.01$, such that the CPz electrode had longer latencies compared to the Pz electrode (see Table IV). There were no main effects of any other factors and no significant interactions with group.

Correlation analyses

Results showed that, compared to the 0-back condition, participants in both the 2- and 3-back conditions had smaller P300 amplitudes and longer response times, regardless of group membership. This led one to question if P300 amplitude, previously suggested as a neural signature of available processing resources for target identification, was related to response processes.

Pearson correlations were conducted between P300 peak amplitude and match response times separately for each group, as the concussion group had a significantly lower mean P300 peak amplitude compared to controls that was limited to match responses. These correlations were conducted at each N -back Load. This study also examined the correlation between P300 amplitude and accuracy rate. After applying Bonferroni corrections (significance level adjusted to $p < 0.01$), negative correlations were found for the control group between P300 peak amplitude and match response times in the 2-back condition, $r = -0.70$, $p < 0.01$, and the 3-back condition, $r = -0.65$, $p < 0.01$, but not the 0-back condition, $r = -0.27$, $p > 0.30$ or the 1-back condition, $r = -0.55$, $p > 0.01$, (see Figure 7). The pattern of results was similar for the concussion group: significant negative correlations were identified between P300 amplitudes and match response times for the 2-back condition, $r = -0.62$, $p < 0.01$ and approached significance for the 3-back condition, $r = -0.55$, $p = 0.02$. Correlations were not significant for the 0-back, $r = -0.23$, $p > 0.30$ or 1-back condition, $r = 0.27$, $p > 0.30$. Results imply P300 amplitude accounted for 38–49% of variance in participants' match response times during 2-back loads ($r^2 = 0.38$ for concussion group; $r^2 = 0.49$ for controls) and 30–42% during 3-back loads ($r^2 = 0.30$ for concussion group; $r^2 = 0.42$ for controls). The correlations between accuracy and P300 were not significant for either group at any of the n -back loads.

Due to the significant difference between groups on age and years of education, these variables were correlated with the main dependent variable that dissociated the groups: P300 peak amplitude for match trials. Pearson correlations showed that neither age, $r = -0.31$, $p > 0.05$, nor education, $r = -0.22$, $p > 0.05$ correlated significantly with average P300 amplitude on match trials.

Discussion

This study showed that, long after a concussion, sensitive electrophysiological measures can reveal subtle changes in brain activity during cognitive processing. Compared to

Table IV. Mean P300 peak amplitude and latency measures for each group in match and non-match conditions, recorded from CPz and Pz electrodes.

<i>n</i> -back	Control				Concussion			
	Match		Non-match		Match		Non-match	
	CPz	Pz	CPz	Pz	CPz	Pz	CPz	Pz
P300 peak amplitude								
0	9.64 (3.1)	10.31 (2.8)	4.63 (1.8)	4.87 (1.7)	7.75 (3.5)	8.91 (3.0)	3.39 (2.6)	4.06 (2.4)
1	9.15 (2.6)	10.10 (2.4)	3.98 (2.0)	4.87 (1.4)	6.53 (3.0)	7.89 (2.3)	2.41 (2.0)	3.89 (1.6)
2	7.91 (3.7)	8.29 (3.1)	3.82 (2.3)	4.89 (1.9)	5.71 (3.4)	6.56 (2.8)	2.96 (2.4)	4.63 (2.5)
3	6.88 (2.9)	7.78 (2.7)	2.96 (1.9)	4.10 (1.7)	4.56 (2.5)	5.93 (2.3)	1.96 (1.7)	3.18 (1.5)
P300 peak latency								
0	366.7 (29.8)	352.4 (31.2)	366.4 (28.6)	354.3 (25.8)	363.9 (30.7)	359.0 (33.7)	374.1 (33.0)	350.6 (36.6)
1	351.5 (27.6)	344.6 (21.1)	362.8 (32.6)	354.4 (31.1)	352.6 (33.3)	345.2 (26.3)	362.5 (44.2)	348.8 (41.1)
2	343.0 (34.3)	341.8 (32.5)	365.4 (25.7)	352.6 (25.3)	358.9 (29.3)	357.3 (26.7)	351.7 (35.1)	348.0 (39.5)
3	348.4 (27.2)	348.1 (25.2)	366.3 (31.3)	348.7 (32.2)	352.3 (29.1)	355.4 (27.7)	359.3 (39.7)	344.6 (35.8)

Mean P300 peak amplitudes (μV) and mean P300 peak latencies (ms). Standard deviations in parentheses.

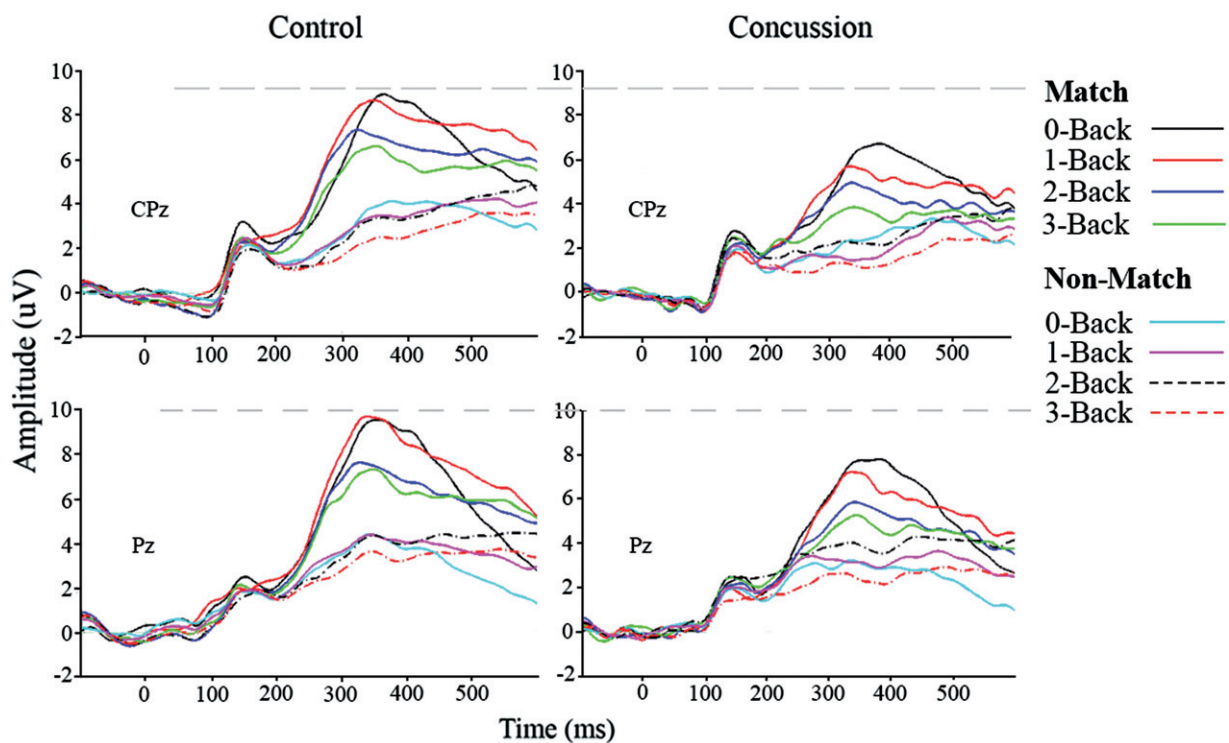


Figure 5. Mean group P300 components for each *n*-back load (0- to 3-back) across trial type conditions (match and non-match) recorded at CPz (top graphs) and Pz electrodes (bottom graphs).

controls, these changes were apparent with no observable performance deficits on an *n*-back task, neuropsychological tests and self-report measures. To the authors' knowledge, this is the first report of altered ERP recordings during a working memory task, with no performance differences in high functioning university students with a history of concussion in their remote past. Specifically, young adults who sustained their concussion at least 1 year earlier showed an average decrease in P300 amplitude during accurate target detection on an *n*-back working memory task compared to young adult controls with no history of TBI.

As expected, attenuated P300 amplitudes were recorded in both groups at higher working memory loads compared to the lowest load, yet concussion participants did not show the predicted larger reduction in amplitude at these high loads

compared to controls. Instead, the attenuated P300 amplitude recorded in concussion participants was independent of working memory load. In other words, the concussion group had an average P300 component that was consistently smaller in amplitude compared to controls for accurate target detections at all *n*-back loads. Since longer response times were also evident in both groups when working memory loads were high compared to when they were lowest, it was questioned if there was a relation between P300 amplitude and response times. To the authors' knowledge, this is the first study to find significant relationships between P300 amplitude and response time in each group that were limited to relatively difficult working memory loads. In particular, response times increased as P300 amplitude decreased, only at moderate (2-back) and high (3-back) loads.

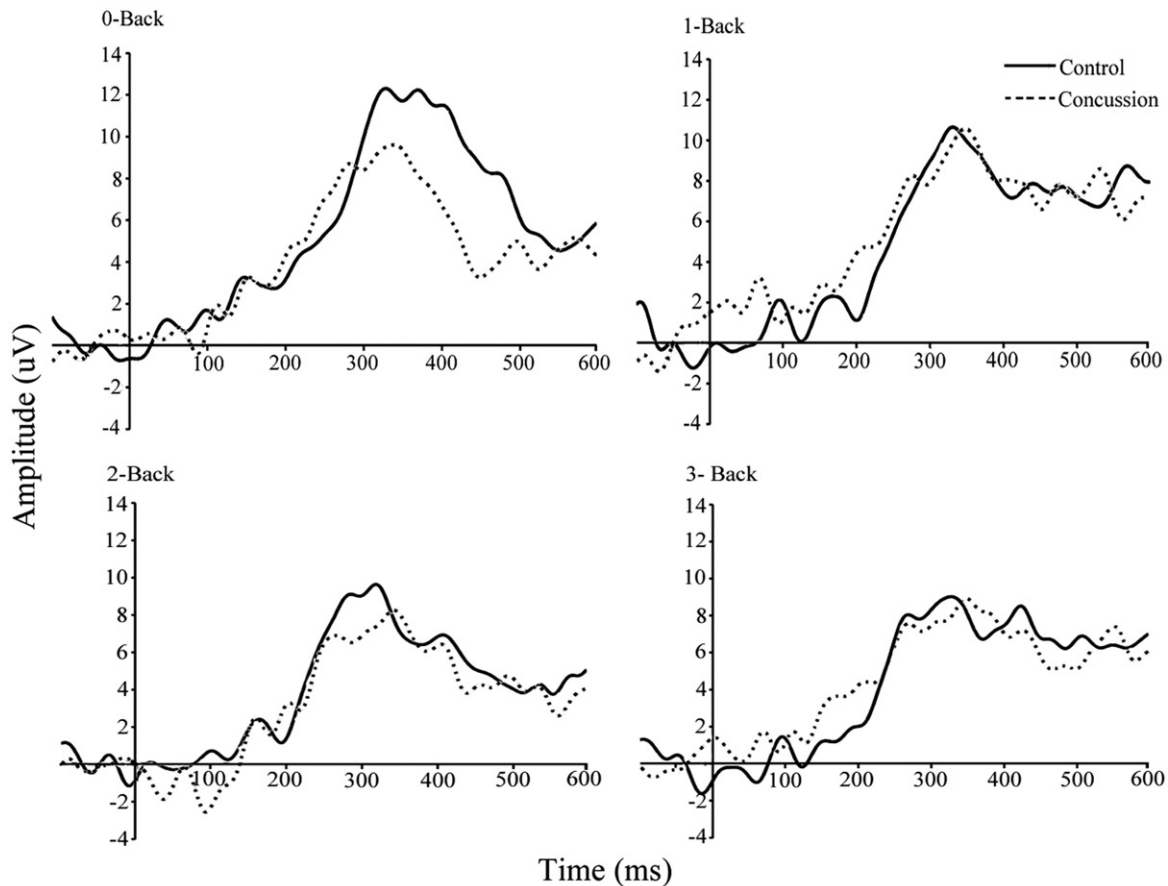


Figure 6. Representative P300 from one control participant and one concussion participant at each n -back level. P300 recorded at the midline parietal electrode (Pz) in both participants at each n -back level.

Effect of concussion on the P300

The main finding of P300 amplitude reduction in concussion participants is in line with previous reports of smaller P300 amplitudes observed at least 6 months following a single concussion [9, 13, 14, 16] and after multiple concussions [20–22] compared to non-head-injured controls during standard oddball tasks. The current study not only replicated these oddball findings (i.e. smaller P300 in concussion group on 0-back condition), but added to the extant literature by also showing a consistent attenuation of P300 amplitude size at least 1 year after concussion on a working memory task that varied in the amount of information that had to be processed. As mentioned, the P300 component is thought to be a neural signature of target classification and evaluation and its amplitude has been conceptualized as the efficiency by which cognitive resources are allocated [41].

P300 latency differences were not found between concussion and control groups in the current study, further specifying the precise changes that occur in the early stages of information processing at least 1 year after concussion. Only a couple of studies have reported delayed P300 latencies at least 6 months after one [15] and after multiple concussions [20], which has been conceptualized as delayed target classification [30]. Thus, the current study's findings suggest long-term inefficiencies in resource allocation or fewer processing resources (P300 amplitude) available for target classification long after concussion [23] during selective attention and

working memory tasks, but do not provide evidence for delayed target classification (P300 latency).

Effect of N -back load on the P300

Regardless of group, significantly smaller P300 amplitudes were observed for infrequent targets compared to frequent stimuli (main effect of stimulus type) and for higher compared to lower working memory loads (main effect of n -back load). The effects are in line with previous reports of P300 recording during visual n -back task performance [24, 25]. Particularly, as working memory load increases from 0- to 3-back loads, P300 amplitude decreases along with typical decreases in accuracy and increases in response time. It has been posited that this inverse relationship between P300 amplitude and working memory load is a result of dual-task demands, with attentional resources being reallocated from the demands of matching sub-task (i.e. oddball selection) to the increasing demands of the working memory sub-task (i.e. storage, encoding, manipulating and searching [24, 25]). Similar results from dual-task paradigms also show that P300 amplitude is dependent on the amount of attentional resources engaged, evident by amplitude decreases during target detection on oddball tasks when cognitive demands increase on a concurrent task [42–44]. The main effect of n -back load in the current study replicates these results in both controls and concussion participants, further supporting that attentional resources are

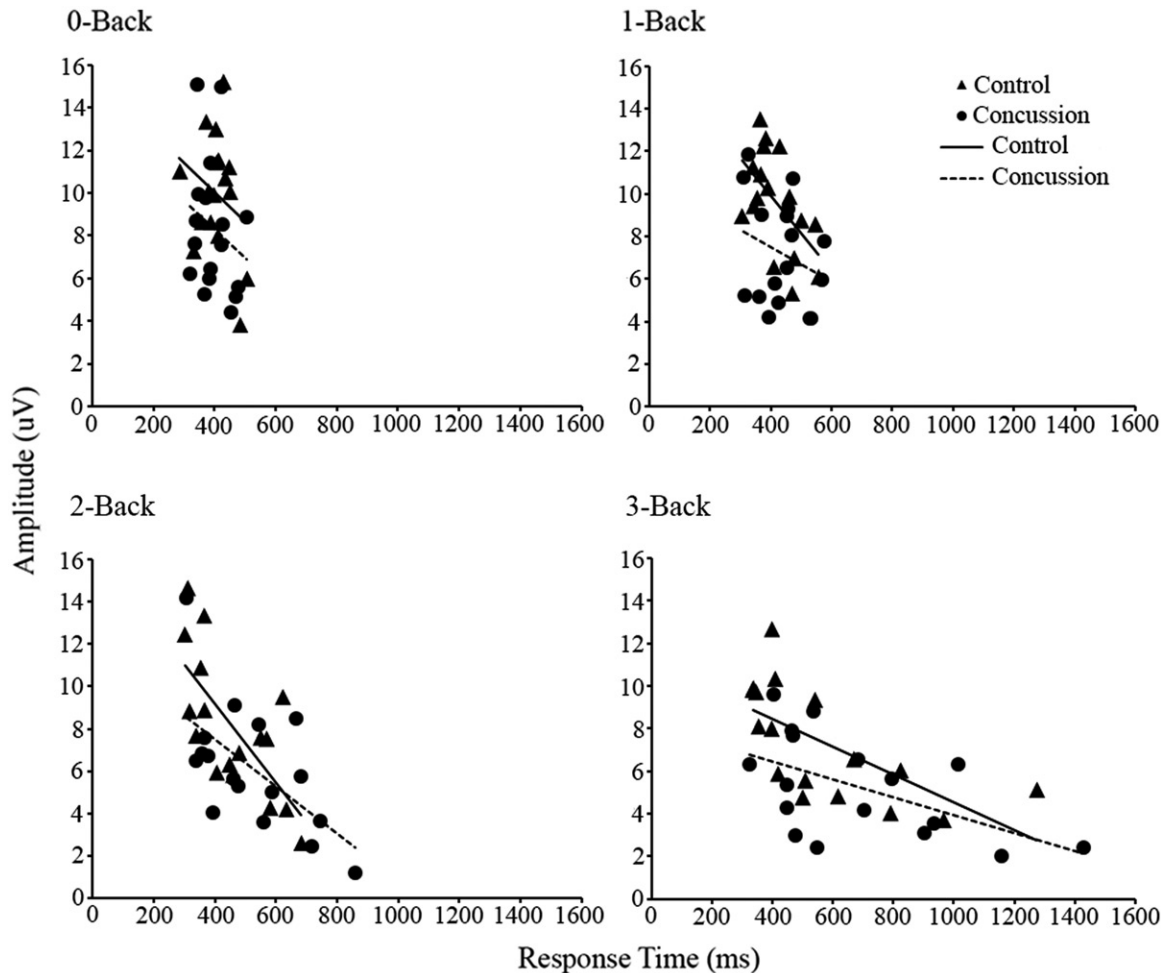


Figure 7. Relation between P300 amplitude and response time for participants at each n -back load on match trials.

being re-allocated from the primary oddball sub-task to the secondary working memory sub-task.

Effect of concussion and N -back load on P300

As mentioned, the significantly reduced P300 amplitude observed in concussion participants compared to controls in the current study was independent of working memory load. Compared to controls, it was predicted that the concussion group may show even larger decreases in P300 amplitude at high working memory loads where additional processing resources are required. Such predictions were based on past reports of inefficient processing resource allocation after concussion, as indexed by P300 amplitude, during simple oddball detection. Instead, the findings suggest that concussion participants are not any less efficient at reallocating processing resources away from target identification to working memory processing demands when loads are high compared to controls.

It seems as though a concussion results in inefficient allocation of processing resources during target detection, even on oddball tasks with very minimal working memory requirements (i.e. 0-back load) and that these resources, as measured by P300 amplitude, are similarly reallocated to increasing working memory demands (i.e. 1-, 2- and 3-back loads) compared to controls. It is proposed that, although

limited or inefficient, the available pool of processing resources long after concussion is sufficient to accurately detect target stimuli in a timely manner during a simple oddball task, as well as during a complex working memory n -back task.

Relation between P300 and response processes

To the authors' knowledge, this is the first study to find relations between P300 amplitude and response times in each group that were limited to relatively difficult working memory loads. In particular, as P300 amplitude decreased, response times increased on moderate (2-back) and high (3-back) loads. Thus, the current findings suggest that response times may increase when there are fewer or less efficient allocation of processing resources (indexed by reduced P300 amplitude) available for target identification, especially evident during moderate-to-high working memory loads. Due to the significantly attenuated P300 amplitude in concussion participants across n -back loads, it is suggested that less efficient allocation of processing resources in this group may be related to the slowing pattern observed in response times as n -back load increases (see Figure 4). While not significant in the current study, this pattern of greater slowing with increasing n -back load in concussion participants compared to controls should not be overlooked

considering that cognitive slowing is the most consistent finding long after concussion [7], especially during complex working memory tasks [10–12]. Thus, the current findings suggest that, as response times increase, the less efficient allocation of processing resources are for target identification, especially evident during moderate-to-high working memory loads.

Single vs dual-task paradigms after concussion

In line with past reports [6–8], the standard neuropsychological tests of attention, working memory, processing speed and short-term memory used in the present study did not distinguish the concussion and control groups, nor did self-report measures of cognitive and affective functioning. Previous experimental studies have also reported no cognitive impairments when concussion participants performed a single oddball task, but response slowing [10, 12] and accuracy decrements [12] when simultaneously performing a working memory task. Past reports also document P300 amplitude decreases in the absence of performance decrements on simple tone discrimination oddball task at least 1 year post-concussion, but when participants were required to concurrently perform a working memory task (e.g. a digit-span task), behavioural deficits were also detected [9, 16].

Even though the *n*-back task has been considered a dual-task paradigm (i.e. oddball and working memory sub-tasks), a possible explanation is suggested for the discrepancy between the lack of performance differences between groups on the *n*-back task and the cognitive impairments reported in concussion participants in studies using dual-task paradigms. In the aforementioned studies, the two tasks completed simultaneously are entirely unrelated, whereas, in the current study, working memory demand is incrementally added to the oddball task and is relevant for successful oddball detection. It may be that the inefficient processing resources after concussion are not sufficient to meet large cognitive demands of simultaneously dividing attention between two disparate tasks, but are sufficient to meet the high working memory *n*-back demands embedded in an oddball task. Given the non-significant differences on basic neuropsychological and cognitive paradigms in the current study, ERP better elucidated the relationship between cognitive processing capacity after concussion and the effect of incrementally increasing working memory demand.

Neural imaging after concussion

That increasing working memory demand in the *n*-back task did not distinguish concussion from control performance is not unique to the current study. Even within the acute stages after concussion (<3 months post-injury), McAllister et al. [26, 27] reported no differences in accuracy between groups; response time data was not reported. Similar to the present study, they did show neural processing group differences despite a lack of behavioural group differences. Specifically, using functional magnetic resonance imaging (fMRI), they reported a greater extent of activation in bilateral frontal and parietal brain regions in concussion participants at moderate processing load (2-back) compared to controls. It was concluded that concussion participants may recruit additional

processing resources to compensate for processing deficiencies. Recent research has also shown additional brain activation without performance decrements in concussion participants 1 month post-injury, not observed in controls, during a spatial navigation working memory task [45]. In the current study, the fact that groups did not show performance differences, even though concussion participants had smaller average P300 amplitudes, could also be due to the ability to recruit extra resources in order to compensate for the inefficient processing during target detection.

This is the first study, to the authors' knowledge, to provide evidence for inefficient information processing capacity during a working memory task in healthy young adults at least 1 year post-injury, as well as to show a relationship between available resources during early cognitive processes and later stage response processes in the post-acute phase after concussion. Strong negative correlations were found between P300 amplitude and response times during moderate and high working memory demands, in both control and concussion participants. In lieu of the fact that the P300 amplitudes corresponding to correct target identification were also smaller in the concussion group, it is suggested that concussion-related deficits in cognitive resource allocation may result in response slowing when processing demands are high. In the current study's sample of high-functioning university students, however, it seems as though these demands did not exceed the processing capacity of the limited or inefficient resource pool in concussion participants as their performance was not statistically different from controls. Future research may benefit from continuing to investigate the residual effects of concussion on cognitive and neural functioning through the implementation of novel experimental tasks. Such studies may also further elucidate the relationship between the neural and cognitive effects of a remote concussion and could ultimately inform future studies/programmes designed to provide strategies to individuals who are experiencing lingering cognitive difficulties after concussion.

Acknowledgements

We acknowledge Dr Dan Nemrodov for his generous contribution during the planning stages of EEG recording and assistance with ERP analysis.

Declaration of interest

The authors report no conflicts of interest. This work was supported by an NSERC Discovery grant to MAF, an NSERC post-graduate scholarship to LJO and funds from the ORF, CFI and the CRC program to RJJ.

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