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Electrophysiology reveals cognitive-linguistic alterations after concussion

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ABSTRACT

Language deficits and alterations to the N400 ERP are commonly reported in aphasia and moderate-to-severe traumatic brain injury (TBI), but have seldomly been investigated after mild TBI, such as concussion. In the present study, the N400 was recorded from young adults within 1-month after concussion and matched controls during a sentence processing task. The N400 recorded to semantically incongruent sentence-final words was significantly more negative and with a more anterior distribution in the concussion group than control group. Among the concussion group, a weaker N400 was associated with more concussion symptoms, slower response time, and poorer executive functioning. Multiple regression results showed that concussion occurrence and male gender were independently associated with a more negative N400-effect, whereas symptoms were associated with a weaker N400. These findings provide novel evidence that alterations to lexical-semantic networks may occur after concussion and vary based on individual differences in post-concussion symptoms and cognitive function.

1. Introduction

Approximately 55.9 million mild traumatic brain injuries (mTBI), including concussion, occur globally each year (Dewan et al., 2019). Concussions result from biomechanical forces applied to the head, neck, or body that induce a cascade of diffuse pathophysiological processes and typically result in a sequalae of symptoms (e.g., headaches, dizziness) and neuropsychological disruptions which often occur in the domains of memory, information processing, impulsivity, attention, and executive functioning (for reviews see Knollman Porter et al., 2014; McCrory et al., 2013). Post-concussion symptoms and cognitive dysfunction typically occur within the days and weeks after injury but may continue for up to 3 months (Belanger & Vanderploeg, 2005; Carroll et al., 2004; McCrea et al., 2009; Rabinowitz et al., 2015). Relatively unexplored, however, are the impacts of concussion on cognitive-linguistic function and its electrophysiological correlates. Therefore, the present study was designed to investigate the impacts of concussion on the N400 event-related potential (ERP), a marker of lexical-semantic retrieval, and traditional assessments of cognition and language.

Typical language tests, such as those examined on aphasia batteries, often do not identify cognitive-linguistic changes after concussion. However, some research has identified acute (Barrow et al., 2006; King et al., 2006; Salvatore et al., 2017) and long-term (Galetto et al., 2013) cognitive-linguistic deficits following mild TBI, including confrontation-naming (Barrow et al., 2006; King et al., 2006) and auditory comprehension (Białuńska & Salvatore, 2017; Salvatore et al., 2017). Mild TBI does not seem to impact micro-level language abilities (e.g., words generated, speech rate), but these individuals' discourse production tends to be disorganized and tangential, such as during story retell tasks (i.e., reduced *global coherence*) (Galetto et al., 2013). The diffuse pathophysiology of traumatic brain injury among highly interconnected fronto-temporal networks may make high-level cognitive-linguistic processing during discourse vulnerable to impairment, particularly lexical-semantics during sentence processing (Hinchcliffe et al., 1998).

ERPs are portions of the ongoing electroencephalogram (EEG) that are time-locked to visual/auditory stimuli and sensitive to changes in sensory, cognitive, and psycholinguistic domains. A prior sports-related concussion is associated with changes to the N200 and P300 ERP components. For example, Ledwidge and Molfese (2016) reported larger N200/P300 amplitudes and delayed P300 latencies in contact-sport athletes with a history of concussion compared to matched controls during an auditory oddball task. Others have reported altered P300

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amplitudes in contact-sport soccer athletes with a history of concussion compared to non-contact athletes (Moore et al., 2017). These findings would suggest that neuroelectrical markers of cognitive control/novelty detection (N2; Folstein & Van Petten, 2008) and elements of attentional processing (P3; Polich, 2007) may be impacted by concussion. However, post-concussion participants in these studies and others (e.g., Hudac et al., 2018) are years post-concussion and thus findings fail to establish neurocognitive changes in acute post-concussion stages. Furthermore, cognitive-linguistic function is seldomly examined after concussion (although see Stockbridge & Newman, 2019). It has recently been suggested that ERPs may identify concussion-induced alterations to the cognitive-linguistic system through examination of psycholinguistic ERPs, such as the N400 component of the ERP (Ledwidge, 2018).

The N400 is a negative deflection in the EEG beginning 200 ms after the presentation of a semantic-item, peaks at approximately 400 ms at centroparietal scalp electrodes (Kutas & Hillyard, 1980), and reflects a lexical-semantic access/retrieval process (Kutas & Federmeier, 2011). A large body of research has demonstrated N400 reductions in populations with language dysfunction, including post-stroke aphasia (Hagoort et al., 1996), primary progressive aphasia (Hurley et al., 2009), and Alzheimer's disease (Revonsuo et al., 1998). Few have investigated alterations to the N400 after TBI. But Münte and Heinze (1994) recorded weaker N400 effects in severe TBI patients, and similar results are reported in adults with prior childhood TBI (Knuepffer et al., 2012). To the authors' knowledge, only one study has examined the N400 after concussion: Young ice hockey athletes had a greater N400 amplitude within 24 h of concussion during a two-word semantic priming task compared to their baseline (Fickling et al., 2019).

In the present study the morphology of the N400 was compared between young adults with a recent concussion and matched controls and elicited similar to prior work (Kutas & Hillyard, 1980). In this sentence processing task, the N400-effect is isolated by comparing its amplitude elicited to semantically incongruent sentence-final words to semantically congruous counterparts. Although the N400 is typically reduced in populations with language dysfunction (e.g., Hagoort et al., 1996) and severe TBI (Münte and Heinze, 1994), others report a larger N400 after concussion (Fickling et al., 2019). Larger P300 amplitudes have also been identified in athletes with a history of concussion (Ledwidge & Molfese, 2016). Therefore, we hypothesize that the N400 will discriminate between those with and without a concussion, but we were agnostic to hypothesizing the direction of the group difference. Because the N400 amplitude is sensitive to individual differences in language recovery in other populations, such as aphasia (Chang et al., 2016; Kojima & Kaga, 2003), we also hypothesized that N400 amplitudes would vary with individual differences in post-concussion symptoms and cognitive-linguistic functioning.

2. Method

2.1. Participants

A sample of 32 young adults, 16 with a recent concussion and 16 age-, gender-, and sport- (if athlete) matched controls, participated in study procedures. All concussions were diagnosed by a sports-medicine physician or general practitioner and referred to a licensed and certified speech-language pathologist (C.J.). During this referral session, concussion participants were informed of the study and provided their contact information to be scheduled for research testing. Concussion participants recruited their own matched control who were also recruited through word of mouth. All participants were 18 years or older at the time of testing and consented to all study procedures as approved by the host institutional review board. All participants were native English speaking, had normal/corrected-normal vision of 20/25 or better, reported five or more hours of sleep the night before their research session, and refrained from using alcohol or illicit drugs within 24 hrs before testing. Neurological history among participants was unremarkable and no participant reported a history of learning disability, reading disability, developmental disorders, ADHD, nor major psychiatric disorder. Participants self-reported any additional concussion history beyond the present concussion. Three participants were left-handed.

2.2. Procedure

All research procedures were carried out between January 2019-October 2021 and aligned with ethical guidelines set forth in the Declaration of Helsinki. Testing procedures lasted approximately 90–120 min and included a symptom report, medical and concussion case history interview, two EEG tasks, and the Cognitive-Linguistic Quick Test (CLQT; Helm-Estabrooks, 2001). Control participants completed all testing on the same day[1] and the CLQT always followed the EEG tasks. Post-concussion participants were administered the CLQT an average of 11.9 days ($SD = 7.23$) before research testing as part of clinical evaluation by a licensed and certified speech-language pathologist (C.J.). This evaluation occurred an average of 6.31 days post-concussion ($SD = 3.72$). The order of the EEG tasks was counterbalanced. Only findings from the sentence processing EEG task are reported here. Participants were compensated $20–30 for their participation.

2.2.1. Symptoms and cognitive-linguistic function

Participants rated their current experience of 22 concussion-like symptoms on a 7-point Likert scale from 0 (*No symptom*) to 6 (*Severe*) (Lovell & Collins, 1998). Item responses demonstrated a high-level of internal consistency (Cronbach's alpha = 0.922). Scores on each item were summed to derive an overall symptom score for each participant. Symptom scores were missing for one control participant. The CLQT is a criterion-referenced test designed to assess cognitive-linguistic function following acquired neurological disruption in adults. A licensed and certified speech-language pathologist or Ph.D. level psychologist administered the CLQT to participants. On average, the test takes about 15–30 min to administer and consists of 10 subtests which are used to derive five domain scores (attention, memory, executive function, language, visuospatial skills; Helm-Estabrooks, 2001). A severity score from 1 (*severe*) to 4 (*within normal limits*) is given to each domain score. These scores are averaged to derive an overall severity score.

2.2.2. Stimulus materials

EEG was recorded while participants read individual sentences and determined whether each "made sense." Sentence-final words were semantically congruent or incongruent (i.e., *semantic anomalies*) completions to the sentences. Semantically incongruent words elicit the canonical N400 ERP, a negative component deflection with a centroparietal maximum, beginning approximately 200 ms and peaking 400 ms after word onset (Kutas & Federmeier, 2011; Kutas & Hillyard, 1980). Stimuli in the present study consisted of 132 sentences previously normed using the cloze judgment task (Block & Baldwin, 2010; Bloom & Fischler, 1980) in which participants finished an incomplete sentence with the word that "fits best" (Taylor, 1953). The *expectancy* of a given sentence-final word is calculated as the percentage of participants who finished the sentence with that particular word, known as the word's

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[1] Five controls participated in study procedures between March 2020-October 2021 when there was a heightened risk of COVID-19 spread. To reduce contact time between participants and researchers, the informed consent, medical and concussion case history interview were administered over videoconference up to 7 days prior to completing the in-person research. The research procedures for the EEG tasks and the administration procedures for the CLQT were unchanged except for additional safety precautions (e.g., donning personal protective equipment, social distancing when possible). One concussion participant was administered the CLQT over videoconference.

cloze probability. To update previous norms (Block & Baldwin, 2010; Bloom & Fischler, 1980), 79 English-speaking undergraduates participated in the online cloze judgement task for course credit. Participants were presented with each individual mutilated sentence frame and instructed to type in the sentence-final word that fit best. Participants were instructed that responses must be single word English nouns and not include proper nouns or hyphenated words.

Responses were first screened individually to identify morphological errors and misspellings. Singular and plural versions of the same words were treated as identical (e.g., "cars" and "car"). Compound words that contained a portion of a unique cloze unit (e.g., "paintbrush" and "brush") were treated as identical. Synonyms were treated as unique cloze units. Cloze entries were treated as inappropriate if responses were not a noun, more than one word, or incomprehensible (Block & Baldwin, 2010). Participants were removed if >5% of responses were inappropriate; otherwise, all responses were retained. Of the original 79 participants, 23 were flagged and excluded from data analysis based on the following criteria: (a) participation time greater than 70 min ($n = 3$); (b) <18 years of age ($n = 1$); (c) non-native English speaking ($n = 5$); (d) fluent multi-lingual speaker ($n = 6$); (e) did not complete all study procedures ($n = 8$). All data screening was based on consensus from two authors (P.L., B.B.). Responses were analyzed from the remaining 56 participants (M age = 20.11, $SD = 5.42$). All cloze probabilities reported here were from these 56 participants.

The sentence-final words from the original norming studies were retained (Block & Baldwin, 2010; Bloom & Fischler, 1980). All words were nouns and monosyllabic. The cloze probabilities (i.e., expectancy) of the sentence-final words were classified as *low constraint* (≤66%, 66 sentences) or *high constraint* (≥75%, 66 sentences) (Block & Baldwin, 2010). By definition, in low-constraint sentences, the words that participants select to logically finish the sentence are more variable and thus the sentence-final word that is ultimately presented during EEG recording is less expected than in high constraint sentences. Sentence stimuli that varied in constraint were used in the present study to explore if the association between concussion and the N400 varied based on contextual ambiguity. This was motivated by findings that post-mTBI individuals tend to produce discourse that is more ambiguous and tangential (Galetto et al., 2013).

A semantically incongruent word was associated with each sentence stem to create a total of 264 sentences from the 132 sentence stems—a congruent and incongruent ending for each sentence—for a total of 66 sentence stems per combination of constraint and congruence (e.g., Low constraint: *They rested under a tree in the* ***shade/horn***; e.g., High constraint: *It was windy enough to fly a* ***kite/treat***). Then two sets of 132 sentence stimuli were created, such that the 33 of each trial type were reflected across the task but no sentence frame was repeated per participant. All sentence-final words in the high constraint condition were best completions. Approximately two-thirds of the sentence-final words in the low constraint condition were best completions.

An ANOVA with constraint and congruence as repeated measures factors and set as a between-subjects factor demonstrated the expected interaction between constraint and congruence ($F(1, 64) = 693.63$, $p < .001$, $\eta_p^2 = 0.916$). Cloze probabilities were lower to incongruent than congruent sentence-final words in both low constraint sentences ($F(1, 64) = 159.01$, $p < .001$, $\eta_p^2 = 0.713$) and high constraint sentences ($F(1, 64) = 12752.16$, $p < .001$, $\eta_p^2 = 0.995$). Specifically, congruent words were more expected in high constraint sentences ($M = 0.91$, $SD = 0.07$) than in low constraint sentences ($M = 0.30$, $SD = 0.19$) ($F(1, 64) = 693.63$, $p < .001$, $\eta_p^2 = 0.92$), whereas expectancy was 0% for all incongruent words. There was no main effect or interactions involving set (p's > 0.05). Word length, frequency (SUBTLEX US; Brysbaert & New, 2009), and concreteness (Brysbaert et al., 2014) were equivalent between conditions and sets (p's > 0.05).

2.3. EEG recording

Participants performed the sentence processing task in a dimly lit, sound attenuated room. Unfiltered EEG was recorded using 257 Ag/AgCl electrodes and 1000 Hz sampling rate with NetStation 5.4 software and a NetAmps 300 amplifier (Magstim EGI, Eugene, OR). Electrode impedances were kept below 50 kΩ at the start of the task and adjusted between two equal blocks of 66 sentences. Stimuli were presented using E-prime 2.0 (Psychology Software Tools, Inc., Sharpsburg, PA). Participants were seated 150 cm from a 21.5″ LCD monitor and instructed to read each sentence silently to themselves. Participants read 33 sentences randomly presented from each of the four conditions based on sentence constraint and semantic congruence of the sentence-final word: low constraint-congruent, low constraint-incongruent, high constraint-congruent, and high constraint-incongruent. Sentence stems and sentence-final words were presented in white, bold, and 18-point Times New Roman Font on a black background. The experimental block followed a practice block of four trials, one of each condition. Each trial began with a fixation cross (1000 ms) then the sentence stem (without final word) appeared in the center of the screen for 3000 ms. Next, a time-varying fixation cross (400–700 ms), to eliminate the anticipatory contingent negative variation (CNV), was followed by a blank screen (400–700 ms). The sentence-final word was then presented in the center of the screen (1000 ms). Lastly, participants used a 2-button press (Chronos, Psychology Software Tools; Sharpsburg, PA) to identify if the sentence "made sense" (congruent) or not (incongruent). Participants used the same button-press to advance to the next trial.

2.4. EEG/ERP processing

Preprocessing was performed in EEGLAB v2021.1 (Delorme & Makeig, 2004) and ERPLAB v8.10 (Lopez-Calderon & Luck, 2014). The EEG processing pipeline was adapted from Makoto's pipeline (Makoto, n.d.). The EEG was first downsampled to 250 Hz then bandpass filtered using a 4th order (24 db/octave) infinite impulse response (IIR) Butterworth filter from 0.1 to 30 Hz. Computer timing offsets were corrected and the EEG segmented from −500 to 1000 ms around the onset of the sentence-final words in each of the four conditions. The segmented ERPs were baseline corrected using the entire pre-stimulus period. Semi-automated methods were used to identify bad channels and was performed blind to condition and group membership. First, bad channels with kurtosis greater than six were identified and removed after visual inspection ($M = 17$ electrodes, $SD = 7.07$). Groups did not differ in number of electrodes excluded ($t(30) = 0.25$, $p = .807$). Data were re-referenced to the average of all channels. Bad epochs were detected using semi-automated methods. Because ICA was used to parse out motor, ocular, and cardiac artifacts, automatic artifact detection parameters were selected to retain those artifacts (e.g., eye blinks) but mark otherwise erroneous segments. Trials were detected with abnormal values (< −500, > 500 μV) and improbable data with single channel limit of six or greater standard deviations (All channel limit = 2 SD). Artifact detection results were visually inspected blind to condition and group and rejected. Following, dimensionality was reduced to 128 PCA factors and then independent components derived using ICA (AMICA). Components with scalp topographies correlating with template maps of ocular, cardiac, and muscle artifacts (ICLabel > 0.70) were eliminated from the data ($M = 1.94$ artifacts, $SD = 1.32$). After component removal, any ocular artifacts not eliminated were detected using a moving window (200 ms) peak-to-peak threshold of 50 μV at eye channels and rejected. Trials with a > 200 μV moving window peak-to-peak threshold (200 ms, 100 ms window step) or a simple voltage threshold less than −200 μV or greater than 200 μV at any channel were also rejected.

Trials were averaged within each of the four combinations of constraint and congruence. An average of 85% ($SD = 8.54\%$) of trials were retained across participants. Groups did not differ in number of trials retained for each of the four conditions (t's$(30) < 1.33, p$'s > 0.05). ERPs were averaged across midline electrodes to form clusters (4–6 electrodes each) surrounding Fz, FCz, Cz, CPz, Pz, and Oz, and their left and right lateralized counterparts (See Supplemental Fig. 1). Group differences on P100 mean amplitudes (50–150 ms) were first examined at posterior electrode clusters (Pz, Oz) given prior reports of this finding in concussion samples (Moore et al., 2014), followed by the N400 component, which was measured as the mean amplitude between 200 and 500 ms. Group comparisons were examined using the mean amplitude of the N400 difference wave (incongruent minus congruent) at each cluster. Statistical analyses were carried out using IBM SPSS Statistics version 26.0. Alpha level was set at 0.05 for statistical significance. Multiple comparisons were Bonferroni corrected and Greenhouse-Geisser corrected for violations of sphericity.

3. Results

Sample characteristics for each group are reported in Table 1. Concussion participants completed research procedures within 8–33 days post-injury ($M = 17.50$, $SD = 7.81$). Symptoms were significantly higher in the concussion group ($t(16.58) = -2.99, p = .008$), and 75% of this group was symptomatic at time of research testing. Twelve participants were athletes and experienced sports-related concussions. Most of the sample was white, female, and not Hispanic/Latino. Concussion and control groups did not significantly differ in age, number of prior concussions, years of formal education, or gender identity (p's > 0.05).

3.1. CLQT

Two concussion participants were administered an alternative assessment battery, because of recent exposure to the CLQT, and thus are not included in the CLQT analyses. Shapiro-Wilks tests demonstrated that CLQT domain scores violated the assumption of normality. Thus, group comparisons were performed using Mann-Whitney U tests. Across all six domains, only 11% of scores in the concussion group were classified as a "mild impairment," and only one participant from the concussion group was classified as having an overall mild impairment (mild range = 3.4–2.5; Helm-Estabrooks, 2001). Outliers were identified as any domain score beyond 1.5 × IQR and excluded for that domain analysis only. As shown in Fig. 1, the concussion group had lower memory ($U = 58.0$, $p = .025$), language ($U = 50.0$, $p = .016$), and executive function ($U = 55.0$, $p = .029$) domain scores than the control group. When outliers were included, the group-differences on the memory and language domains remained statistically significant (p's < 0.05) and the executive function domain was marginally significant ($p = .07$). The attention, visuospatial, and overall severity domains did not vary between groups (p's > 0.05).

3.2. N400 task: Accuracy and response time

A repeated measures ANOVA with constraint and congruence as repeated measures variables and group as a between-subjects variable showed that the effect of word congruence on response time varied by sentence constraint ($F(1, 30) = 7.04$, $p = .013$, $\eta_p^2 = 0.190$). In the low constraint condition, participants were slower to respond to congruent than incongruent words ($F(1, 30) = 4.24, p = .048, \eta_p^2 = 0.124$), whereas this was not shown in the high constraint condition ($p > .05$). Response times did not vary between groups ($p > .05$). Response accuracies violated the assumption of normality, thus condition effects were first examined using Friedman's K tests, followed by Mann-Whitney U tests for examining between-groups differences. Although overall accuracy was high ($Mdn = 1.0$), performance significantly varied between sentence ending types ($X^2(3) = 36.39$, $p < .001$): Accuracy in the low constraint-congruent condition ($Mdn = 0.94$, $IQR = 0.06$) was significantly worse than the other three sentence ending types (Z's < -3.43, p's < 0.001). Concussion and control groups did not differ in accuracy for either of the four conditions (p's > 0.05).

Table 1
Group demographic characteristics.

	Control (n = 16)	*Concussion (n = 16)*
N Female	10	10
N white	15	13
N Hispanic/Latino	1	0
Age	20.32 ± 1.52	20.33 ± 1.81
Number of prior concussions	0.56 ± 0.73	0.94 ± 1.70
Symptom total	2.27 ± 3.13	13.06 ± 14.06**
Years of education	14.63 ± 1.26	14.25 ± 1.24
Days since concussion	N/A	17.50 ± 7.81

Note. N = number of participants. Means and standard deviations reported unless otherwise noted.
**Significant between-groups difference (p <.01).

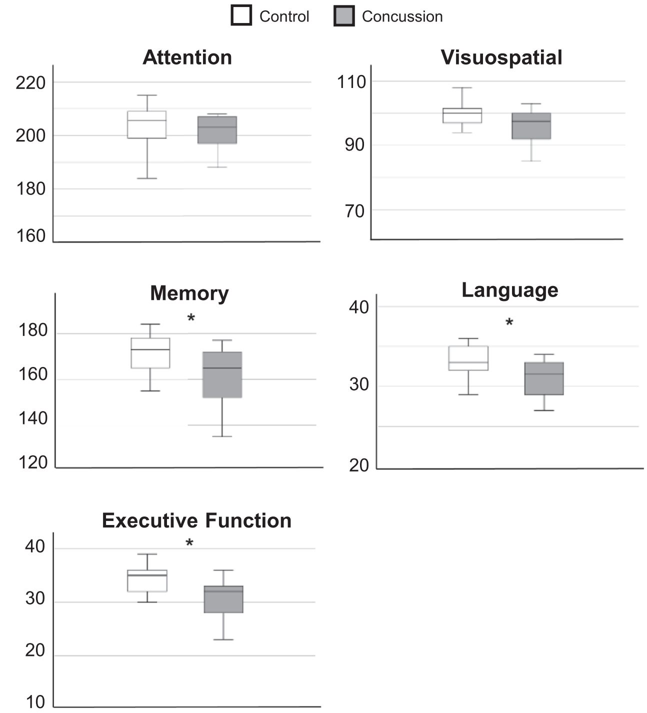

Fig. 1. Group-differences on CLQT domain scores. *Scores significantly lower for concussion group compared to control group (p <.05). Y-axis represents domain scores, derived from performances on relevant subtests (see Section 2.2.1).

3.3. P100

An ANOVA with word congruence, sentence constraint, cluster, and laterality as repeated measures factors and group as a between subjects factor revealed that the P100 was largest at occipital clusters, $F(1, 30) = 18.39$, $p < .001$, $\eta_p^2 = 0.380$. The P100 did not significantly differ between groups or levels of congruence, constraint, or laterality (p's > 0.05).

3.4. N400

The N400 component is inconspicuously seen in both groups as a large negative deflection peaking approximately 400 ms after the presentation of incongruent words in both low and high constraint sentences (Fig. 2). The negative N400 peak appears maximal at central/centroparietal clusters, and with a larger and more anterior distribution in the concussion group. To verify the presence of the N400-effect for

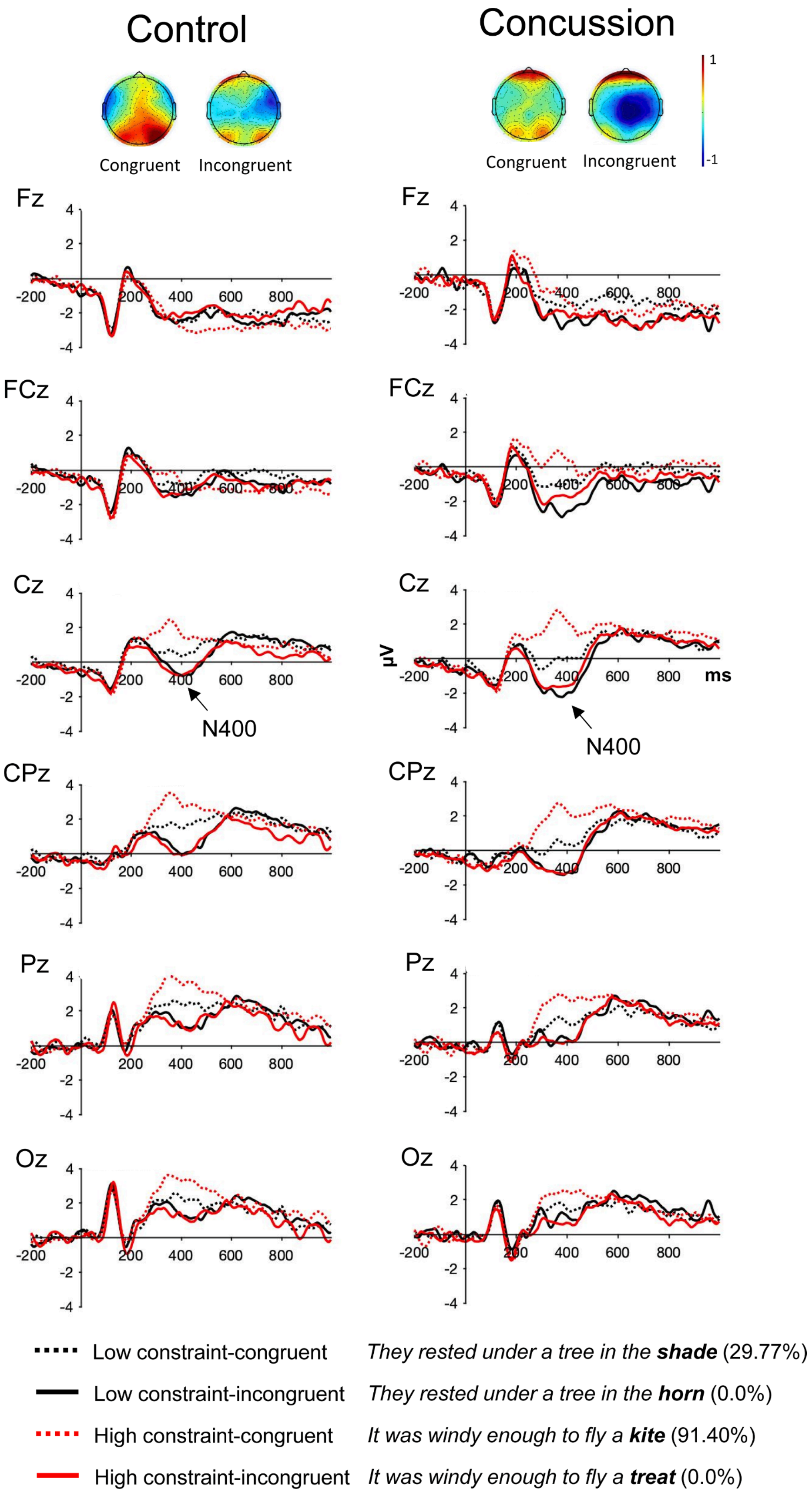

Fig. 2. ERP plots by level of constraint and congruence for each group at midline electrode clusters. The key illustrates examples of each of the four combinations of sentence constraint and word congruence, with the conditions' average cloze probabilities in parentheses. The N400 is identified at central midline channels for both groups. The distribution of the N400-effect and the topo plots (200–500 ms, average of low and high constraint conditions) illustrate a larger and more anterior N400 for the concussion group.

each individual group, N400 mean amplitudes (200–500 ms) were submitted to individual ANOVAs with repeated measures of word congruence (congruent, incongruent), sentence constraint (low, high), cluster (Fz, FCz, Cz, CPz, Pz, Oz), and laterality (left, midline, right; See supplemental Fig. 1). ANOVAs with constraint, cluster, and laterality as repeated measures and concussion status as a between groups variable examined group differences in the amplitude of the N400 difference wave (incongruent minus congruent) within the entire segment (200–500 ms). Follow-up ANOVAs examined group-differences in the N400 difference wave at midline electrode clusters within consecutive 100 ms bins (200–300 ms, 300–400 ms, 400–500 ms) with constraint, cluster, and group as independent variables.

N400 amplitudes were more negative to incongruent than congruent words for the control group ($F(1, 15) = 22.20, p < .001, \eta_p^2 = 0.597$) and the concussion group ($F(1, 15) = 37.85, p < .001, \eta_p^2 = 0.716$). This N400-effect (larger amplitude for incongruent than congruent words) was significantly larger to high constraint than low constraint sentence endings for both groups (p's ≤ 0.006), which was driven by the larger amplitude to congruent words in high constraint sentences than low constraint sentences (Fig. 2; p's < 0.001). The N400-effect significantly varied between clusters for the control group ($F(1.51, 22.65) = 8.49, p = .003, \eta_p^2 = 0.362$) and marginally varied between clusters for the concussion group ($F(1.57, 23.58) = 2.79, p = .092$): The control group's more negative N400 to incongruent words than congruent words was largest centroparietally ($F(1, 15) = 30.46, p < .001, \eta_p^2 = 0.670$) but also significant centrally, parietally, and occipitally (p's ≤ 0.001; Fig. 2). For the concussion group, the N400-effect was present at frontal ($p = .024$), frontocentral, ($p < .001$), central ($p < .001$), centroparietal ($p < .001$), and parietal ($p = .006$) clusters. For both groups, significant congruence by laterality interactions (Control: $F(1.53, 22.98) = 4.93, p = .023, \eta_p^2 = 0.247$; Concussion: $F(1.41, 21.10) = 7.50, p = .007, \eta_p^2 = 0.33$) revealed the N400-effect was largest at midline (p's < 0.001) but also present over right clusters for both groups (p's ≤ 0.001) and also left clusters for the concussion group ($p = .025$).

When comparing group differences on the amplitude of the N400 difference wave, the interaction between group and cluster on the N400-effect approached significance ($F(1.57, 47.07) = 3.011, p = .070, \eta_p^2 = 0.091$). Planned comparisons indicated that the concussion group had a more negative N400-effect than the control group frontally ($F(1, 30) = 5.40, p = .027, \eta_p^2 = 0.153$) and frontocentrally ($F(1, 30) = 4.27, p = .048, \eta_p^2 = 0.124$), but not centrally or centroparietally (Fig. 2). The cluster by laterality interaction ($F(4.64, 139.05) = 2.43, p = .042, \eta_p^2 = 0.075$) showed that the N400-effect was largest at centroparietal and central midline across groups. A three-way interaction with the added variable of constraint ($F(4.20, 125.84) = 2.52, p = .042, \eta_p^2 = 0.078$) showed that N400 amplitudes to high constraint sentence endings were more negative at midline than right lateral sites for central and centroparietal clusters (p's ≤ 0.003), whereas there was no difference between midline and right frontal and frontocentral clusters (p's > 0.05). The high-constraint N400-effect was larger at midline than all left clusters except Fz (p's < 0.001). In the low-constraint condition, there were no laterality differences at any cluster, except the centroparietal N400 was largest at midline than left cluster ($p = .042$). The laterality distribution of the N400-effect did not vary between groups ($F(1.46, 43.92) = 1.67, p > .05$). When left-handed participants were excluded ($n = 3$, all in concussion group), the cluster by group interaction ($p = .039$) and significant pairwise group differences at frontal ($p = .019$) and frontocentral clusters ($p = .029$) remained. Because these group differences remained irrespective of left-handedness, these participants were retained for the following analyses. Furthermore, because the N400-effect was significantly larger at midline clusters and its laterality did not significantly vary between groups, remaining analyses were carried out on midline clusters only.

3.4.1. *Early N400-effect (200–300 ms)*

Fig. 3 illustrates group-differences through the time course of the N400-effect. The amplitude of the N400 difference wave between 200 and 300 ms was significantly more negative for the concussion than control group ($F(1, 30) = 5.25, p = .029, \eta_p^2 = 0.149$). There was no significant interaction between group and cluster. Group differences were significant at frontal ($F(1, 30) = 4.55, p = .041, \eta_p^2 = 0.132$), frontocentral ($F(1, 30) = 5.34, p = .028, \eta_p^2 = 0.151$), and central clusters ($F(1, 30) = 5.55, p = .025, \eta_p^2 = 0.156$; Fig. 3). The N400-effect was larger in high constraint than low constraint sentences ($F(1, 30) = 24.87, p < .001, \eta_p^2 = 0.453$), which did not vary between groups.

3.4.2. *Middle N400-effect (300–400 ms)*

An examination of group-differences during the peak of the N400 (Fig. 3) showed a larger N400-effect for the concussion group ($F(1, 30) = 4.18, p = .050, \eta_p^2 = 0.122$), which significantly varied between clusters ($F(2.08, 62.32) = 3.20, p = .046, \eta_p^2 = 0.096$): The concussion group had a more negative N400-effect than the control group frontally ($F(1, 30) = 5.69, p = .024, \eta_p^2 = 0.159$), frontocentrally ($F(1, 30) = 5.69, p = .024, \eta_p^2 = 0.160$), and centrally ($F(1, 30) = 5.80, p = .022, \eta_p^2 = 0.162$). The N400-effect was larger to high constraint than low constraint sentence endings ($F(1, 30) = 49.22, p < .001, \eta_p^2 = 0.621$). An interaction between constraint and cluster ($F(1.46, 43.77) = 3.84, p = .041, \eta_p^2 = 0.113$), revealed that high constraint sentence endings elicited a larger N400-effect than low constraint sentence endings at central, centroparietal, parietal, and occipital clusters (p's ≤ 0.002). The effect of constraint did not vary between groups ($p > .05$).

3.4.3. *Late N400-effect (400–500 ms)*

A marginal interaction between cluster and group, ($F(1.37, 41.07) = 3.43, p = .059, \eta_p^2 = 0.103$) revealed that the N400-effect was larger for the concussion group than control group frontally ($F(1, 30) = 6.02, p = .020, \eta_p^2 = 0.167$) and frontocentrally ($F(1, 30) = 4.70, p = .038, \eta_p^2 = 0.135$). A significant interaction between constraint and cluster ($F(1.30, 39.02) = 6.23, p = .011, \eta_p^2 = 0.172$) revealed that the N400-effect was larger in high constraint than low constraint sentences at all central and posterior clusters (p's ≤ 0.008). The effect of constraint did not vary between groups ($p > .05$).

3.5. *Correlations*

With the aim of explaining between-subjects variability in the N400-effect, we examined correlations between N400 amplitudes, clinical outcomes, response time in the N400 task, and CLQT domain scores. N400-effects were considered at midline frontocentral, central, and centroparietal clusters (incongruent minus congruent, averaged across levels of constraint). The amplitude of the N400-effect was not associated with duration PTA, loss of consciousness, or disorientation (p's > 0.05). However, the centroparietal N400-effect was positively correlated with post-concussion symptoms ($r(14) = 0.607, p = .013$): Concussion participants with fewer symptoms tended to generate a larger N400-effect whereas the N400-effect was smaller for those reporting more symptoms (Fig. 4A).

Response times across the four sentence ending types were highly correlated with each other (r's$(14) > 0.865$, p's < 0.001) and thus were averaged together for each participant. Response time was significantly correlated with the N400-effect centrally ($r(14) = 0.723, p = .002$) and centroparietally ($r(14) = 0.542, p = .030$) (Fig. 4B): Concussion participants with faster response times tended to generate a larger N400-effect. Higher executive function domain scores were also significantly associated with a more negative central N400-effect ($r(12) = -0.591, p = .026$) (Fig. 4). There were no other significant correlations between the size of the N400-effect and memory or language domain scores (p's $>$

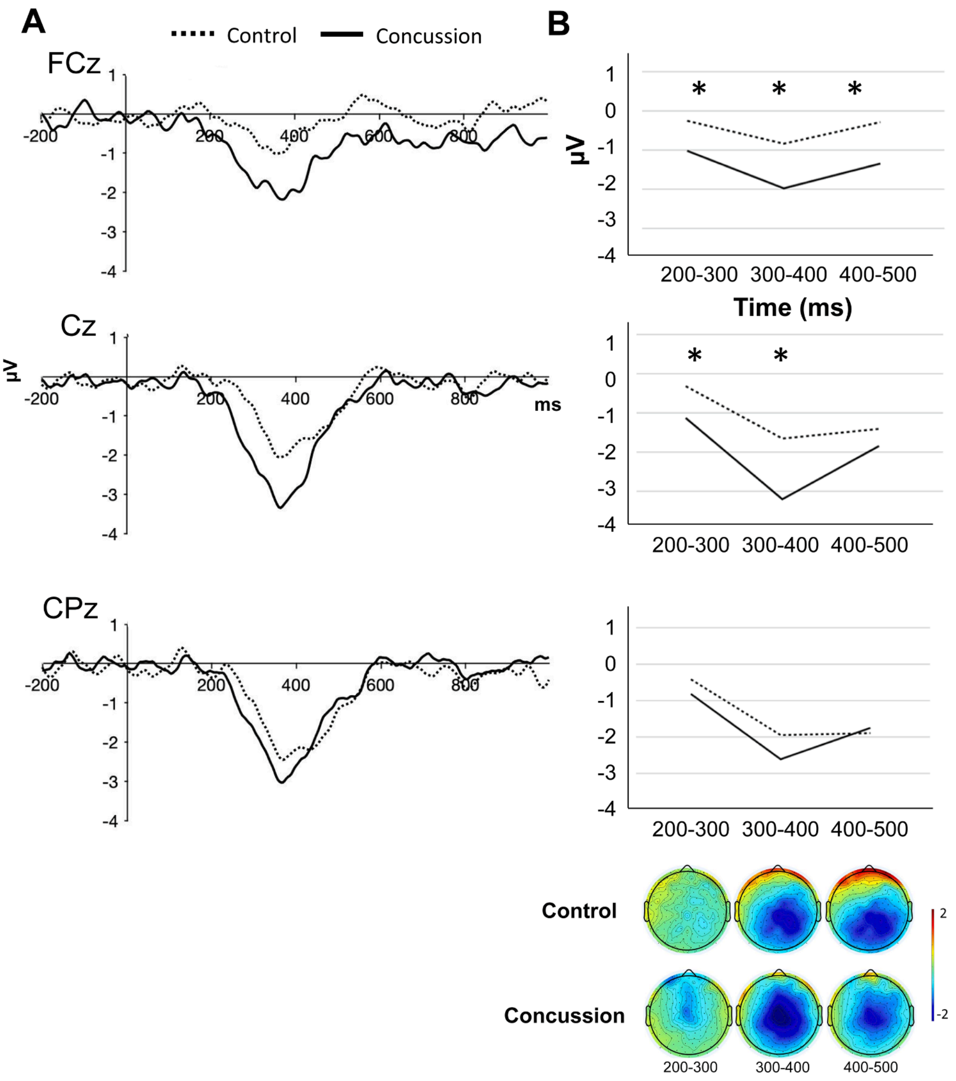

Fig. 3. Group differences in the N400-effect by electrode cluster. ERR plots (3A), line graphs (3B), and topo plots (3B) illustrate group differences in the N400-effect (incongruent minus congruent difference wave) from 200 to 500 ms after final word presentation. *Amplitudes significantly more negative for concussion than control group ($p < .05$).

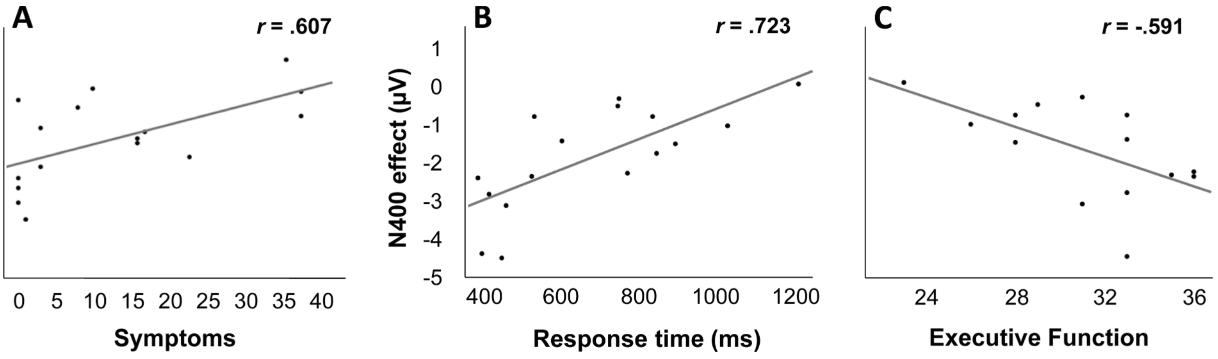

Fig. 4. Amplitude of N400-effect associated with better performance and fewer symptoms. Scatterplots represent significant correlations between the amplitude of the N400-effect and concussion-like symptoms (4A), response time during N400 task (4B), and CLQT executive function scores (4C) for the concussion group.

0.05).

A follow-up multiple regression showed that a significant portion of the variance of the centroparietal N400-effect ($R^2 = 0.27$, $SE = 0.99$, $p = .012$) was explained by concussion status (0 = control, 1 = concussion; $\beta = -0.37$, $t(28) = -2.036$, $p = .051$) and symptoms ($\beta = 0.58$, $t(28) = 3.18$, $p = .004$). Adding gender (0 = female, 1 = male) significantly increased model fit (R^2 change = 0.233, $p <.001$) and explained 51% of the variance in the amplitude of the N400-effect (Fig. 5). Concussion status ($\beta = -0.27$, $t(27) = -1.75$, $p = .091$) and male gender ($\beta = -0.53$, $t(27) = -3.57$, $p < .001$) were independently associated with a more

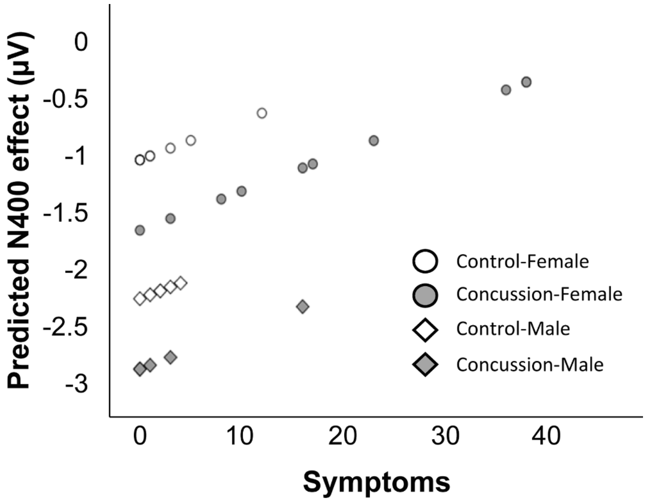

Fig. 5. Gender, Symptoms, and Concussion status uniquely predict N400-effect. Plot illustrates the results from the three-predictor multiple regression model: $y = -1.078 + -0.602X_1$ (concussion status) + $.033X_2$ (symptoms) – $1.188X_3$ (gender). Predicted associations between unstandardized N400 amplitudes (incongruent minus congruent) by concussion-like symptoms are plotted for each combination of concussion occurrence and gender. Points on the plot with darker borders indicate multiple participants with the same predicted N400 value.

negative N400-effect. The model predicted opposite associations between concussion occurrence and symptoms ($\beta = 0.35$, $t(27) = 2.06$, $p = .049$): Concussions were associated with a more negative N400-effect whereas the size of the N400-effect became weaker as post-concussion symptoms increased (Fig. 5).

4. Discussion

The present study investigated alterations of the N400 ERP component within 1-month after concussion and its association with individual differences in symptom recovery. In support of our hypothesis, we recorded an enhanced N400-effect in the concussion group, which also had a more anterior distribution across the scalp, whereas the distribution for the control group was predominantly localized to central/centroparietal electrode clusters. These group differences were identified as early as 200–300 ms post-word onset.

Few have investigated how mTBI may influence neuroelectrical correlates of lexical-semantic processing. Most ERP investigations of concussion, typically experienced during sport, concern the P300 and N200 ERP components. These studies typically report reduced P300 amplitudes (Broglio et al., 2009; Dupuis et al., 2000; Lavoie et al., 2004) and delayed latencies associated with concussion history (Ledwidge & Molfese, 2016). Some report enhanced P300 amplitudes (Fickling et al., 2019; Hudac et al., 2018; Ledwidge & Molfese, 2016) and no latency differences (Dupuis et al., 2000; Lavoie et al., 2004). Others have identified greater N200 amplitudes associated with a history of concussion in both pediatric samples (Moore et al., 2015) and adults (Olson et al., 2018; Rugg et al., 1988). Findings from fMRI similarly indicate that concussions are associated with both increases (Dettwiler et al., 2014; Jantzen, Anderson, Steinberg, & Kelso, 2004; McAllister et al., 2001) and decreases (Chen et al., 2004; Hammeke et al., 2013) in BOLD signal amplitude in brain regions of interest specialized for carrying out working memory and attention, predominantly the dorsolateral prefrontal cortex (dlPFC) and frontoparietal networks. The lexical-semantic process investigated in the present study, the N400, was recorded maximally at its centroparietal peak (Kutas & Federmeier, 2011). However, we failed to find post-concussion changes in the N400 at this expected electrode site. Rather, our results indicate that concussion is associated with a greater N400-effect at central/frontocentral electrodes, outside the N400′s maximum, which is consistent with others who report the recruitment of additional, compensatory brain sources after concussion (Chen et al., 2004; Chen, Johnston, Collie, McCrory, & Ptito, 2007; Dettwiler et al., 2014).

The lack of effect of concussion on the amplitude of the centroparietal N400 may be explained by individual differences in post-concussion symptoms. In a multiple regression, concussion occurrence and symptoms had opposite associations with the centroparietal N400 (Fig. 5): Concussion occurrence was marginally associated with a more negative N400 ($p = .051$), whereas the experience of concussion-like symptoms significantly weakens the effect. Said otherwise, when concussion status and symptoms are both considered, both an enhanced N400 (due to concussion) or one that is degraded (related to symptoms) may be possible variations from the norm, which may also vary between genders. For example, an asymptomatic male post-concussion is predicted to have a larger centroparietal N400-effect than an asymptomatic male without concussion (lower left portion of Fig. 5), whereas the N400 would be much weaker in a symptomatic female after concussion (upper right portion of Fig. 5). Others have reported reduced P300 amplitudes in symptomatic but not asymptomatic concussion patients (Dupuis et al., 2000; Lavoie et al., 2004). Therefore, it is possible that the individual differences in gender and symptom recovery may explain inconsistent associations between concussion and greater/weaker cognitive brain activity patterns reported in the literature.

Even within a single sample, greater post-concussion symptoms are associated with heightened and weakened brain activity patterns across different brain regions (Gosselin et al., 2011; Pardini et al., 2010). The inconsistencies between studies notwithstanding, some report that greater post-concussion symptoms are associated with reduced BOLD signal amplitude in task-based regions of interest (Chen et al., 2004, 2007; Hammeke et al., 2013) similar to the smaller centroparietal N400 for symptomatic concussed participants in the present study (but see Smits et al., 2009). Although the N400 reflects broad activity of the left perisylvian language network (Maess et al., 2006; Simos et al., 1997), its neural generator is in the medial anterior temporal lobe (McCarthy et al., 1995). Findings from magnetoencephalography (MEG) demonstrate that the brain activity underlying the N400 spreads anteroventrally to include the dlPFC by the temporal peak of the N400 (Halgren et al., 2002). Symptomatic athletes with a concussion history generated less dorsolateral prefrontal cortex (dlPFC) activity during working memory tasks than controls (Chen et al., 2004), which increased as symptoms alleviated (Chen et al, 2007; Hammeke et al., 2013). We identified the same pattern in the present study: Fewer symptoms were associated with a more negative centroparietal N400-effect. Taken together with ERP findings in concussion (Dupuis et al., 2000; Lavoie et al., 2004), it may be that an individual's pattern of lexical-semantic brain activity after concussion may depend on different trajectories of symptoms and/or cognitive recovery.

Post-concussion differences in the N400 may also be related to variability in cognitive-linguistic recovery. Those with faster response times and better executive functioning were more likely to generate an enhanced centroparietal N400-effect, whereas this effect was weaker in those with slower response times and poorer executive functioning. We interpret these findings to suggest that in the absence of symptoms, concussions may be associated with a larger, adaptive brain response during word retrieval to meet task demands. However, experiencing post-concussion symptoms may limit the lexical-semantic system's ability to generate a larger N400 response. Although neurophysiological changes in the language network are seldomly examined after concussion, fMRI findings suggest that hyperactive brain activity is similarly adaptive in supporting language function after more severe TBI and in cases of aphasia. For example, recovery of language function 6-months after severe TBI is associated with increases in left superior temporal gyrus activity (Coffey et al., 2021). In addition, a dynamic bilateral shift in brain activation to non-language sources is also associated with improved language function in aphasia (Fernandez et al., 2004; Fridriksson et al., 2009; Heiss et al., 1999; Richter et al., 2008). The N400-effect is similarly weaker/absent in aphasia patients with more severe comprehension deficits but greater in those with milder deficits (Chang et al., 2016; Hagoort et al.,1996; Kawohl et al., 2010; Kojima & Kaga, 2003).

Although concussion and control groups did not differ in response time or accuracy, concussion participants with faster response times tended to generate larger centroparietal N400-effects. Typically, when others have reported greater brain activity after concussion in absence of task performance differences, its functional significance has been interpreted as a *compensatory* response to increase cognitive resources to rise to the demands of the task (McAllister et al., 2001; Turner et al. 2011). However, this explanation is at odds with others who suggest that increased brain activity after TBI is due to a *latent support mechanism*, likely mediated by the anterior cingulate, which enhances cognitive control processing similar to when demands increase in non-neurological samples (Hillary, 2008; Hillary et al., 2010; see Dettwiler et al., 2014 for more discussion). Even though accuracy was high, it was significantly lower to low constraint congruent words, suggesting this condition was more challenging. However, accuracy did not vary between groups and, although the N400-effect was smaller for low constraint than high constraint sentences, this effect did not vary between groups. It is possible that a greater N400 response after concussion may facilitate lexical-semantic retrieval in non-speeded, relatively low demanding tasks such as in the present study, whereas a greater brain response in more cognitively demanding tasks may reflect greater cognitive control mechanisms (Hillary, 2008; Hillary et al., 2010). To examine the functional significance of a greater N400 after concussion, future research should consider employing more demanding comprehension tasks, such as in ambiguous discourses and inferencing.

In addition to the N400-effects reported in the present study, the concussion group performed worse than controls on more traditional assessments of memory, language, and executive function. This finding is expected given that participants were tested within 1-month of their concussion and 75% were still symptomatic. However, it is noteworthy that 90% of concussion participants' scores in the memory, language, and executive function domains were within normal ranges. Therefore, it is possible that some individuals may perform normatively on cognitive-linguistic tests after concussion, but still experience functional brain changes which may interfere with day-to-day language functioning. Alternatively, it is possible that other neuropsychological batteries may be more sensitive to identifying clinically significant cognitive and language deficits after mild TBI.

The present study is not without limitations. Participants were tested within 8–33 days post-concussion, and the present findings may not reflect dynamics brain changes in a more acute period. Therefore, it is possible that the present findings relate to differences in the concussion management and recovery process rather than the concussion in and of itself. Although our sample size is comparable to similar reports (Fickling et al., 2019; Knuepffer et al., 2012), future work should seek to replicate these findings in a larger sample. We also did not examine neuropsychological alterations immediately after concussion as would be assessed on a computerized battery such as the ImPACT test. Although athletes completed baseline and post-concussion ImPACT testing, we did not limit our sample to sports-related concussion. It is also important to recognize that our use of a traditional control group, rather than an orthopedically injured control group, cannot rule out that the present results may be due to injuries more generally rather than specific to concussion. Because the present study was a cross-sectional examination of naturally occurring groups, it is also possible that group-differences may be due to pre-existing individual differences unaccounted for in the present study (e.g., personality). This study does not address the time course of N400 alterations throughout concussion recovery and in more post-acute concussion phases.

Lastly, future research may consider the use of prospective, longitudinal designs in order to establish how acute N400 changes post-concussion may predict different trajectories of cognitive, communication, and psychosocial recovery after concussion. Mild TBI's are associated with cognitive-linguistic and communication deficits (Galetto et al., 2013; Lê et al., 2022; Stockbridge & Newman, 2019). As reviewed in Ledwidge (2022), cognitive and functional communication deficits after TBI are associated with poorer psychological health (Draper et al., 2007; Pagulayan et al., 2008; Uiterwijk et al., 2021) and greater difficulty in developing and maintaining social relationships (Dahlberg et al., 2006). The extent to which neuroelectrical markers of cognitive-linguistic processing (e.g., N400) after concussion may predict individual differences in communication competence and psychosocial function provides an exciting opportunity for further investigation.

5. Conclusion

Up until the present study, the extent to which concussions are associated with psycholinguistic alterations has seldomly been considered. We report that participants within 1-month after concussion performed worse on tests of memory, language, and executive function. The primary finding was that N400 amplitudes during visual sentence processing were larger and more frontally distributed after concussion, which may reflect increased neural resources necessary to engage in lexical-semantic retrieval. We also report that male gender and increased post-concussion symptoms are associated with greater and weaker N400-effects, respectively. Fewer symptoms, faster response time, and better executive functioning were all associated with a larger N400-effect in the concussion group. These findings suggest that alterations to the semantic language network are associated with concussion occurrence but also vary based on individual differences in concussion recovery.

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CRediT authorship contribution statement

Patrick S. Ledwidge: Conceptualization, Methodology, Software, Validation, Investigation, Data curation, Visualization, Supervision, Project administration, Formal analysis, Funding acquisition, Resources, Writing - original draft, Writing - review & editing. **Christa M. Jones:** Conceptualization, Methodology, Investigation, Funding acquisition, Writing - original draft, Writing - review & editing. **Chloe Huston:** Investigation, Formal analysis, Writing - original draft, Writing - review & editing. **Madison Trenkamp:** Methodology, Investigation, Writing - review & editing. **Bryan Bator:** Methodology, Writing - original draft, Writing - review & editing. **Jennie Laeng:** Investigation, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bandl.2022.105166.

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