



Neural activity and emotional processing following military deployment: Effects of mild traumatic brain injury and posttraumatic stress disorder

Daniel V. Zuj^{a,*}, Kim L. Felmingham^b, Matthew A. Palmer^a, Ellie Lawrence-Wood^c,
Miranda Van Hooff^c, Andrew J. Lawrence^c, Richard A. Bryant^d, Alexander C. McFarlane^c

^a Division of Psychology, School of Medicine, University of Tasmania, Australia

^b School of Psychological Science, University of Melbourne, Melbourne, Australia

^c Centre for Traumatic Stress Studies, School of Medicine, University of Adelaide, Adelaide, Australia

^d School of Psychology, University of New South Wales, Sydney, Australia

ARTICLE INFO

Keywords:

Traumatic brain injury
PTSD
ERP
Attention bias
Emotion

ABSTRACT

Posttraumatic Stress Disorder (PTSD) and mild traumatic brain injury (mTBI) are common comorbidities during military deployment that affect emotional brain processing, yet few studies have examined the independent effects of mTBI and PTSD. The purpose of this study was to examine distinct differences in neural responses to emotional faces in mTBI and PTSD. Twenty-one soldiers reporting high PTSD symptoms were compared to 21 soldiers with low symptoms, and 16 soldiers who reported mTBI-consistent injury and symptoms were compared with 16 soldiers who did not sustain an mTBI. Participants viewed emotional face expressions while their neural activity was recorded (via event-related potentials) prior to and following deployment. The high-PTSD group displayed increased P1 and P2 amplitudes to threatening faces at post-deployment compared to the low-PTSD group. In contrast, the mTBI group displayed reduced face-specific processing (N170 amplitude) to all facial expressions compared to the no-mTBI group. Here, we identified distinctive neural patterns of emotional face processing, with attentional biases towards threatening faces in PTSD, and reduced emotional face processing in mTBI.

1. Introduction

Posttraumatic Stress Disorder (PTSD) is a common consequence of war exposure, affecting approximately 12–16% deployed United States military veterans (Hoge & Castro, 2006). PTSD is characterised by intrusive memories and distress to trauma reminders, and sleep and concentration problems. Up to 25% of combat veterans report sustaining a mild traumatic brain injury (mTBI) during deployment (Vasterling, Verfaellie, & Sullivan, 2009). PTSD in combat veterans often occurs following blast exposures, with a co-occurring risk of mTBI (Hoge et al., 2008). The overlapping etiology and symptoms of mTBI and PTSD causes complications in identifying their separate effects (Carlson et al., 2011). Despite this, longitudinal studies reveal that sustaining an mTBI during deployment significantly increases PTSD-risk (Bryant, 2011; Yurgil et al., 2014).

PTSD patients show attentional biases towards threat in eye tracking and dot probe studies (Felmingham, Rennie, Manor, & Bryant, 2011; Kimble, Fleming, Bandy, & Zambetti, 2010; Olatunji, Armstrong, McHugo, & Zald, 2013). Consistent with heightened threat processing,

neurobiological evidence suggests PTSD is associated with hyper-activity of amygdala, insula and dorsal anterior cingulate cortex in response to threatening stimuli, and hypo-activity of frontal regulatory networks (Pitman et al., 2012; Williams et al., 2006). mTBI also shows deficits in ventromedial prefrontal activation (Vasterling et al., 2009) and impairments in white matter tract integrity (MacDonald et al., 2011; Sponheim et al., 2011; Stevens et al., 2012). This suggests impaired prefrontal functioning associated with mTBI may exacerbate hypofrontality in PTSD, leading to greater emotion dysregulation and exaggerated neurobiological deficits in comorbid mTBI and PTSD (Bryant, 2008; Williamson, Heilman, Porges, Lamb, & Porges, 2013).

To date, few neuroimaging studies have examined the independent or overlapping effects of PTSD and mTBI. A meta-analysis of fMRI studies conducted in mTBI and PTSD suggested that the middle-frontal gyrus is implicated in both disorders (Simmons & Matthews, 2012). A recent study reported reduced amygdala volume in a comorbid PTSD and mTBI group, but this group was compared to a combined non-PTSD and non-mTBI control group (Depue et al., 2014). Imaging studies are limited by low temporal resolution (Simmons & Matthews, 2012).

* Corresponding author at: Division of Psychology, University of Tasmania, Locked Bag 1342, Launceston, TAS 7250, Australia.
E-mail address: Daniel.Zuj@utas.edu.au (D.V. Zuj).

Event-related Potentials (ERPs) are high-resolution indices of electrical brain activity providing an index of cortical function and processing speed. Early components of the ERP (P100, N100) are thought to reflect automatic attentional processing (Naataanen, 1990), whereas later components (Vertex positive potential (VPP), N200, P300) are thought to reflect conscious processing (Jeffreys & Tukmachi, 1992; Polich & Kok, 1995). Earlier ERP studies of attention tasks revealed reduced P300 amplitudes (reflecting impaired attention allocation) in PTSD and mTBI samples (Elting et al., 2008; Felmingham, Rennie, Gordon, & Bryant, 2012). Emotional ERP studies in PTSD typically revealed an increase in P300 amplitude to threat or trauma-relevant stimuli (Karl et al., 2006), whereas ERP studies in mTBI typically reveal reduced amplitudes and slower ERP components to emotional faces (Duncan, Summers, Perla, Coburn, & Mirsky, 2011).

Two recent ERP studies have examined cortical function in PTSD comorbid with mTBI relative to single disorder conditions. The first compared a comorbid mTBI-PTSD veterans group with mTBI (without PTSD) veterans using an inhibitory motor processing task (Shu, Onton, O'Connell, Simmons, & Matthews, 2014). They found greater N2 amplitudes, reflecting greater inhibitory processing, in the comorbid mTBI-PTSD group compared to the mTBI group only, and greater N200 negativity correlated with greater PTSD severity. The second ERP study employing a facial empathy task found larger emotional face processing ERPs in the comorbid mTBI-PTSD veteran group when compared to the mTBI alone group, and greater N300 amplitudes correlated with increased PTSD symptoms (Shu, Onton, Prabhakar, et al., 2014).

These studies, although highlighting the effect of PTSD over and above mTBI, do not identify the independent effects of these disorders. Furthermore, no ERP studies have examined the effects of mTBI and PTSD on neural activity when processing differing facial expressions (including angry, fearful, happy and neutral expressions). This is important as mTBI has not been associated with attentional biases towards threat, rather, individuals with mTBI have shown difficulty recognizing and discriminating emotional expressions (Bornhofen & McDonald, 2008). Finally, previous ERP studies were cross-sectional and subject to selection bias.

The current study examined the independent effects of mTBI and PTSD on neural processing (using ERPs) of different emotional facial expressions (angry, fearful, happy and neutral) in a military sample pre and post-deployment, controlling for pre-deployment mTBI exposure. To examine the effects of mTBI, a post-deployment mTBI group was compared to a no-mTBI group whilst matching PTSD symptom level, and to examine the effects of PTSD, a separate non-mTBI sample was studied comparing those with high and low post-deployment PTSD symptoms. It was hypothesized that the high-PTSD group would demonstrate a post-deployment attentional bias (reflected in larger ERP amplitudes) towards threatening faces (angry, fearful), which would not exist in the mTBI group.

2. Materials and methods

2.1. Participants

Seventy-four participants of Australian Defence Force personnel deployed to the Middle East Area of Operations (MEAO) (70 males, 4 females, aged 19–49 years ($M = 29$, $SD = 6.9$)) were selected from personnel who completed pre and post-deployment (within four months of return) electrophysiological recordings in the MEAO prospective health study.

PTSD symptoms were assessed using the PTSD Checklist (PCL-M; Weathers, Litz, Huska, & Keane, 1994), and mTBI was assessed by the incidence of head injury that resulted in loss of consciousness greater than five minutes, or altered mental states during deployment as per previously published criteria for screening for mTBI in OEF/OIF veterans (King, King, & Vogt, 2008; U.S.G.A. Office., 2008). Specific criteria included experiencing: blast, rocket propelled grenade attack,

motor vehicle accident, fragment/bullet wound, or fall which resulted in loss of consciousness or altered mental states (confusion, attention difficulties) during deployment (U.S.G.A. Office, 2008). The no-mTBI group were chosen on the basis of no reported injury or blow to the head during deployment. It should be noted that this classification of mTBI was made on the basis of self-reported symptoms and experience of events in line with screening criteria used for OEF/OIF veterans, but objective clinical assessments from the deployment were unavailable. Sixteen participants were identified as having experienced an mTBI during current deployment, and were matched to a no-mTBI group (with PTSD symptom severity matched according to total PCL-M score). To analyse the effect of PTSD symptoms, in the remaining no-mTBI sample, 21 participants were classified as having high PTSD symptoms (with a total PCL-M score of 30 or above) and were compared to a group with low PTSD symptoms ($n = 21$). On the basis of these criteria participants were allocated to one of four groups: high PTSD symptoms with no-mTBI ($n = 21$), low PTSD symptoms with no-mTBI ($n = 21$), mTBI ($n = 16$) and no-mTBI ($n = 16$). Two separate analyses were conducted, one examining the effects of mTBI vs no-mTBI, and a second analysis examined the effects of high PTSD symptoms (compared to low) in a sample with no-mTBI during deployment. Participants in both analyses were matched on age, war exposure and total months deployed at post-deployment, with the mTBI compared to no-mTBI groups also being matched on their total PCL-M scores.

In an effort to reduce the influence of pre-existing factors, selected participants were closely matched on key pre-deployment variables including history of prior mTBI (U.S.G.A. Office, 2008), pre-deployment PTSD symptomatology (PCL-M) and psychological distress rating (K10; Kessler et al., 2002), number of prior military deployments and number of months previously spent on deployment, total number of prior combat experiences and total number of prior life-time trauma exposures. Participants reporting pre-deployment mTBI of greater than moderate severity were excluded from analyses in the current study.

This study received approval from the Australian Defence Human Research Ethics Committee (ADHREC) and the University of Adelaide Human Research Ethics Committee (UA HREC). Written informed consent was obtained prior to participation.

2.2. Self-report measures of PTSD symptoms, psychological distress, and war exposure

PTSD symptom severity was assessed using the PCL-M, which provides an ordinal range of symptom severity with a recommended cutoff of 30–34 when screening post-combat military personnel (Bliese et al., 2008). Psychological distress was assessed using the K10 at pre and post-deployment (Kessler et al., 2002). War exposure was assessed using the Deployment Risk and Resilience Inventory (King et al., 2008).

2.3. Facial emotion processing task

Participants completed an emotional face passive viewing task whilst cortical electrical activity was recorded using ERPs as part of the standardized paradigms from the Brain Resources LabNeuro platform. Emotional face stimuli were selected from a standardized set of facial emotion stimuli (Gur et al., 2002) including fearful, angry, happy and neutral facial expressions. Each stimulus was a greyscale image matched for size and luminance that was presented to participants on a computer screen. Data were recorded under two conditions: conscious and preconscious.

During the conscious condition, blocks of eight stimuli per emotion (fear, angry, happy and neutral) were presented for 500 ms in pseudo-randomized order. There were four repeat blocks for each expression, making a total of 32 stimuli per expression. The inter-stimulus interval was 700 ms, making a total stimulus asynchrony of 1200 ms. This design was used to elicit neural activation representative of conscious emotional processing.

In the preconscious condition, a backward masking protocol was used for stimulus presentation. Target stimuli (fear, angry, happy and neutral facial expressions) were presented for 10 ms followed immediately by a neutral facemask presented for 150 ms. These durations were based on parameters established in a previous psychophysiological experiment (Williams et al., 2004), and have been shown to prevent conscious detection of the stimulus. The masking stimulus was superimposed over the target stimulus, but spatially offset by 1° to one of the randomly allocated diagonals. The ISI in the preconscious condition was set to 1040 ms to create a total stimulus onset asynchrony of 1200 ms, thereby ensuring that stimulus presentation was equivalent between conscious and preconscious conditions.

Participants were instructed to pay attention to the faces in preparation for post-test questions to enhance attention towards the stimuli.

2.4. EEG data collection and analysis

Data were acquired using a Quikcap and 32 channel Nuamps system according to the International 10/20 electrode system in a sound and light attenuated room. Data were recorded continuously at 500 Hz with skin resistance < 5 Kohms in relation to the virtual ground and referenced offline to linked mastoids. Data were also collected from four EOG channels to allow for detection of any eye movement artefacts. Eye movement correction was undertaken offline using procedures from Gratton, Coles, and Donchin (1983). Data were analysed at specific sites of interest which have been previously implicated in face emotion processing (Eimer & Holmes, 2002; Felmingham, Bryant, & Gordon, 2003). Data from the following electrode sites were used in the analysis: Fz and Pz (for midline analyses), T5 and T6 (for temporal analyses).

Average ERPs were calculated for each emotional facial expression in each condition (conscious, preconscious). Individual single-trial ERP epochs were filtered with a low-pass Tukey (cosine) filter (−0.01 to 25 Hz) that attenuated frequencies above 25 Hz. Single trials were then averaged and peak components were identified within defined latency windows according to previous ERP emotional face studies (Klimova, Bryant, Williams, & Felmingham, 2013; Williams et al., 2004) and validated by visual inspection across individual participants for each emotional stimuli, within each condition, at each site. At midline sites (Fz and Pz), the following components were examined: P100 (maximum positive peak amplitude from 50 to 150 ms post-stimulus), N100 (maximum negative peak from 80 to 150 ms post-stimulus), VPP (maximum positive peak from 120 to 220 ms post-stimulus), N200 (maximum negative peak from 180 to 220 ms post-stimulus), and P300 (maximum positive peak from 230 to 450 ms). To assess cortical processing over face-specific processing regions, the N170 component (maximum negative peak from 150 to 220 ms) was assessed over temporal (T5, T6) and occipital (O1, O2) sites. ERP components were scored using baseline to peak method.

2.5. Statistical analysis

All statistical analyses were conducted in SPSS version 20. Clinical and demographic data were analysed using one-way analyses of variance (ANOVAs). Repeated measures ANOVAs were used to analyse the amplitude of each ERP component, with group (high-PTSD vs low-PTSD, or mTBI vs no-mTBI) as the between factor, and time (pre-deployment vs post-deployment), condition (conscious vs pre-conscious) and valence (fear vs neutral, or happy vs neutral) as within factors. Separate 2 (group) × 2 (time) × 2 (condition) × 2 (valence) ANOVAs were conducted for each component at specific sites (Fz for negative midline components, Pz for positive midline components, and T5/T6 for N170 face-specific processing). Alpha levels were set at $\alpha = 0.05$, and sidak pair-wise post hoc analyses were conducted. Given that the hypotheses of this study centred on group differences (high vs low PTSD, mTBI vs no-mTBI), only significant group main effects and

Table 1

Mean demographic and clinical data for the High PTSD/Low PTSD analysis and for the mTBI vs no mTBI analysis.

	High PTSD	Low PTSD	Test statistic	Sig
Age (years)	30.1 (7.8)	30.1 (7.9)	F = 0.89	$p > 0.05$
Sex	19 M, 2 F	19 M, 2 F	–	–
Pre-deployment mTBI	6	7	–	–
PCL-M total	33.7 (8.2)	17 (2.5)	F = 11.2	$p < 0.05$
Total months deployed	11.7 (10.9)	11.8 (5.9)	F = 1.2	$p > 0.05$
War exposure	36.8 (17.3)	37.2 (17.1)	F = 1.1	$p > 0.05$
	mTBI	No mTBI	Test statistic	Sig
Age (years)	27.6 (5.1)	28.9 (5.5)	F = 1.3	$p > 0.05$
Sex	16 M	16 M	–	–
Pre-deployment mTBI	6	6	–	–
PCL-M total	27.4 (13.2)	27.4 (13.4)	F = 0.7	$p > 0.05$
Total months deployed	11.5 (8.3)	16.9 (9.8)	F = 3.2	$p > 0.05$
War exposure	53.8 (12)	50.4 (12)	F = 2.2	$p > 0.05$

Note: PCL-M = PTSD Checklist-Military version; PTSD = Posttraumatic Stress Disorder; mTBI = mild Traumatic Brain Injury.

interactions involving group will be reported.

3. Results

3.1. Clinical and demographic data

Clinical and demographic data for each group are summarized in Table 1. As expected, participants in the high-PTSD group had significantly higher PCL-M total and K10 scores at post-deployment compared to the low-PTSD group. Participants in the high-PTSD group did not differ significantly from those in the low-PTSD group in terms of age, gender distribution, total war exposure or total months deployed. Participants in the no-mTBI group did not differ significantly on age, PTSD symptom severity (PCL-M total score), K10 total score, gender distribution, total war exposure or total months deployed. Both groups reported similar levels of pre-deployment mTBI, defined as the incidence of a head injury that resulted in loss of consciousness greater than five minutes, or altered mental states.

3.2. ERP data

3.2.1. P100 amplitude

For the high versus low PTSD analysis comparing angry and neutral face, there was a significant group × time × valence interaction, $F(1, 40) = 5.88$, $p = 0.020$, $\eta_p^2 = 0.128$. Test of simple interaction effects revealed a significant group × time interaction to angry faces, $F(1, 40) = 4.58$, $p = 0.038$, $\eta_p^2 = 0.103$, but not neutral faces ($p > 0.05$). As seen in Fig. 1, means showed an increase in P100 amplitude to angry faces from pre to post-deployment in the high-PTSD group, but not the low-PTSD group. No further PTSD group main effects or interactions were found for the angry-neutral, fear-neutral, or happy neutral analyses.

In contrast, for the mTBI/no-mTBI analysis, there were no significant main effects of group or any significant interactions with group for the angry-neutral contrast – therefore, this effect appeared specific to the high-PTSD group. Further, there were no significant group main effects or interactions for the mTBI/no-mTBI happy-neutral, or fear-neutral analyses.

3.2.2. N100 amplitude

For the high-low PTSD analysis, there were no significant group main effects or interactions for N1 amplitude for angry-neutral, fear-neutral, or happy-neutral contrasts.

However for the mTBI/no-mTBI analysis, there was a significant group × valence interaction, $F(1, 30) = 10.99$, $p = 0.002$,

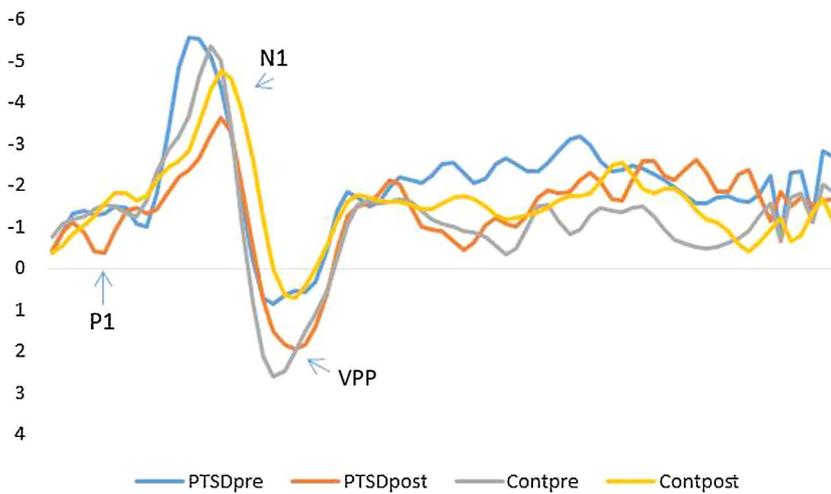


Fig. 1. Averaged ERP amplitude in Control and PTSD groups to angry conscious faces at midline sites at pre and post-deployment. The PTSD group reveals greater P1 amplitude at post than pre-deployment, where there is minimal difference in controls. The PTSD group also reveals greater VPP amplitude at post than pre, and a significantly delayed P200 compared to controls.

$\eta_p^2 = 0.268$. Sidak pairwise comparisons revealed reduced N1 amplitude to angry compared to neutral faces in the no-mTBI group, but there were no significant differences for the mTBI group.

3.2.3. VPP amplitude

For the high-low PTSD analysis, a significant group \times time \times valence interaction for VPP amplitude was observed, $F(1, 40) = 12.74, p = 0.001, \eta_p^2 = 0.128$. Post-hoc analyses of simple interaction effects revealed a significant group \times time interaction to angry faces, $F(1, 40) = 9.74, p = 0.003, \eta_p^2 = 0.196$, but not to neutral faces ($p > 0.05$). As depicted in Fig. 2, means showed increased VPP amplitude in the high-PTSD group from pre to post-deployment which was not observed in the low-PTSD group. No significant group main effect or interactions were observed for the angry-neutral analysis. A significant group \times time \times valence interaction, $F(1, 40) = 7.79, p = 0.008, \eta_p^2 = 0.163$, was also evident in the high-low PTSD fear-neutral analysis, as seen in Fig. 3. Post-hoc analyses of simple effects revealed a significant group \times time interaction for fearful faces, $F(1, 40) = 5.79, p = 0.021, \eta_p^2 = 0.126$, but not to neutral faces ($p > 0.05$). Similar to that of angry faces, means revealed an increase in VPP amplitude in the high-PTSD group from pre-deployment to post-deployment to fearful faces, whereas the low-PTSD group showed reduced VPP amplitude to fear faces from pre to post-deployment. There were no further significant effects in the fear-neutral analysis, and no significant group main effects or interactions in the happy-fear analysis.

In contrast, there were no significant main effects of group or any significant interactions with group for the mTBI/no-mTBI analysis for

angry-neutral, fear-neutral or happy-neutral contrasts.

3.2.4. N200 amplitude

No significant group main effects or interactions were observed for the high-low PTSD comparison, or the mTBI/no-mTBI comparison for any valence contrast.

3.2.5. P300 amplitude

No significant group main effects or interactions were observed for the high-low PTSD comparison, or the mTBI/no-mTBI comparison for any valence contrast.

3.2.6. N170 amplitude at temporal sites (T5 and T6)

There were no significant group main effects or interactions between group and other variables for N170 amplitude for the high-low PTSD analysis at T5 or T6 sites.

In contrast, significant group main effects were observed at T5, $F(1, 30) = 6.65, p = 0.015, \eta_p^2 = 0.18$, and T6, $F(1, 30) = 6.96, p = 0.013, \eta_p^2 = 0.188$, for the angry-neutral contrast at T5, $F(1, 30) = 5.60, p = 0.025, \eta_p^2 = 0.166$ and T6, $F(1, 30) = 12.3, p = 0.002, \eta_p^2 = 0.305$ for the fear-neutral contrast, and at T5, $F(1, 30) = 4.3, p = 0.049, \eta_p^2 = 0.146$, and T6, $F(1, 30) = 8.1, p = 0.009, \eta_p^2 = 0.25$ for the happy-neutral contrast. These group main effects consistently revealed that the mTBI group had reduced N170 amplitudes across facial expressions compared to the non-mTBI group (see Fig. 4).

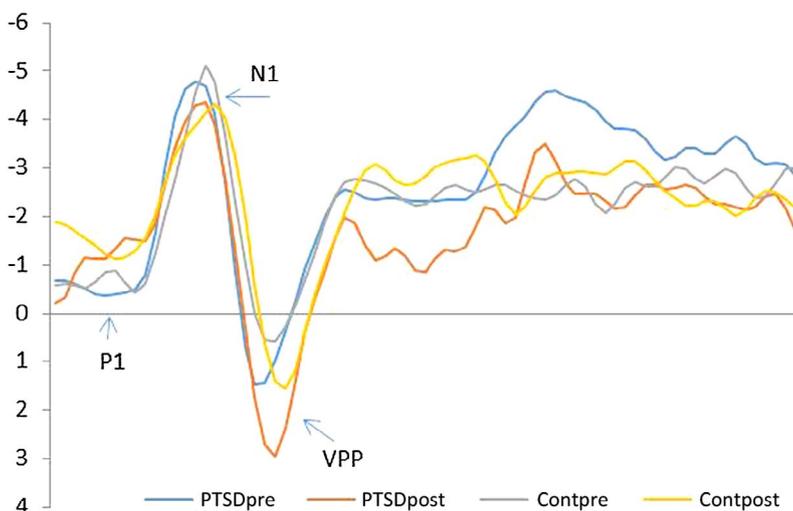


Fig. 2. Averaged ERP waveforms to fear conscious faces at pre and post-deployment in PTSD and Controls – VPP amplitude significantly increases from pre to post deployment in PTSD to fear faces, but not to controls.

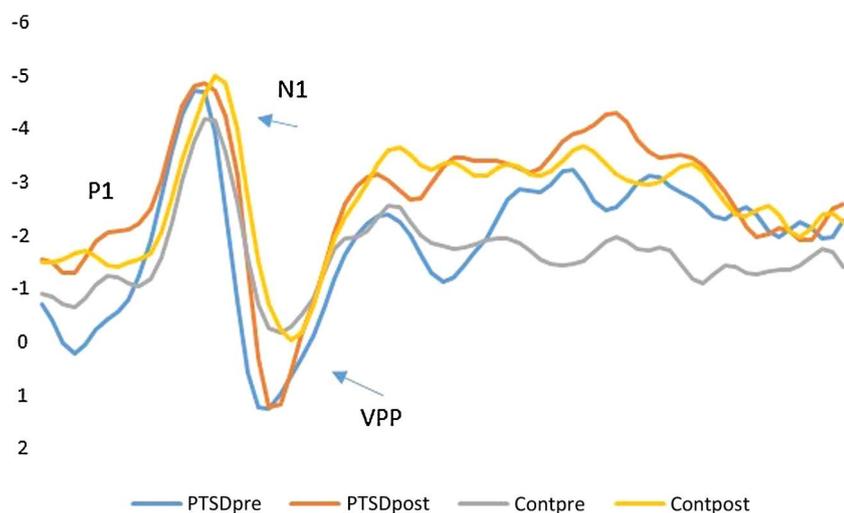


Fig. 3. Averaged ERP waveforms to happy conscious faces at midline sites at pre and post-deployment. There were no significant differences between the PTSD group and controls, or significant interactions.

4. Discussion

This study examined the relative effects of deployment-related mTBI and PTSD on the processing of emotional facial expressions. Key findings revealed an attentional bias towards threatening facial expressions (indexed by increased P1 and P2 amplitudes to angry and fearful faces) developed during deployment in those with high post-deployment PTSD symptoms compared to low PTSD symptoms. This effect was found in a non-mTBI sample but not in veterans who sustained an mTBI, suggesting a PTSD-specific attentional bias to threat. In contrast, the mTBI group showed a significant reduction in N170 amplitude at temporal sites to all facial expressions compared to the non-mTBI group, suggesting an mTBI-specific generalized reduction in cortical processing of emotional expressions.

Early ERP components (such as P1) are thought to reflect pre-attentive processing, which is modulated by arousal (Naataanen, 1990) and P1 amplitude has been related to amygdala functioning (Rotshtein et al., 2010). ERP studies examining responses to emotional faces reveal ERP components between 100 and 200 ms reflect rapid emotional processing (Eimer & Holmes, 2002). The finding that P1 amplitude increased in the high-PTSD group from pre to post-deployment to angry faces, but not in the low-PTSD group, suggests that an attentional bias towards threat develops during deployment only in those with high PTSD symptoms post-deployment. This finding is consistent with previous studies revealing an attentional bias towards threat in PTSD (Felmingham et al., 2011; Kimble et al., 2010; Olatunji et al., 2013).

Consistent with this early attentional bias, VPP amplitude was increased to both angry and fearful faces following deployment in the high-PTSD group, but not the low-PTSD group. VPP amplitude is a midline frontal analogue of the face-specific N170 waveform and reflects conscious processing of emotional stimuli (Jeffreys & Tukmachi, 1992). ADF members with high PTSD symptoms post-deployment revealed a significant increase in VPP amplitude to angry and fearful faces compared to neutral faces. Increased ERP amplitudes to fearful expressions have been indicative of a greater attentional bias to threatening stimuli (Olatunji et al., 2013). Therefore, this finding reflects increased emotional processing of fear and angry faces in the high-PTSD group, consistent with an increased attention bias towards threat following deployment.

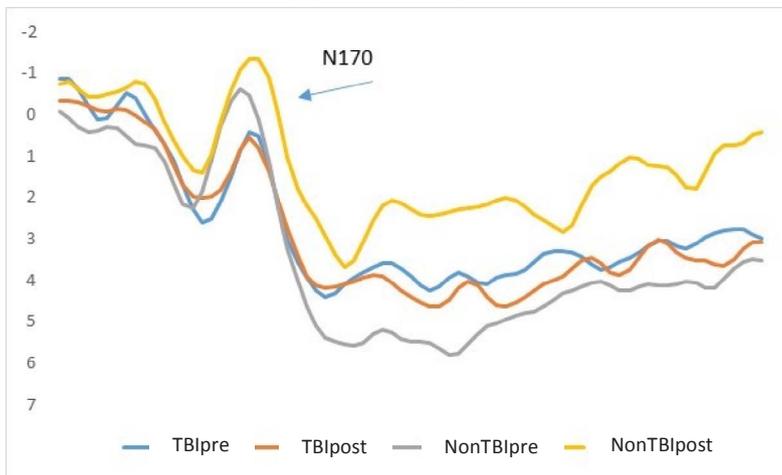
This pattern of findings is in line with previous ERP studies showing increased conscious cortical processing (P300) to trauma-stimuli (Attias, Bleich, Furman, & Zinger, 1996; Kimble et al., 2010), but extends these findings to demonstrate that this attentional bias develops with exposure to war trauma concurrently with increasing PTSD symptoms in a longitudinal design. A recent ERP model of the temporal processing of facial emotions suggested an early detection system

operates around 100 ms post-stimulus. Activation of this early detection system leads to enhanced processing resources being directed to salient stimuli, resulting in more detailed conscious processing of facial stimuli between 150 and 200 ms post-stimulus (Utama, Takemoto, Koike, & Nakamura, 2009). In this light, the current findings in the high-PTSD group suggest that with military deployment, those who develop high PTSD symptoms have a more reactive early detection system to threat, which leads to enhanced later conscious processing of threatening faces.

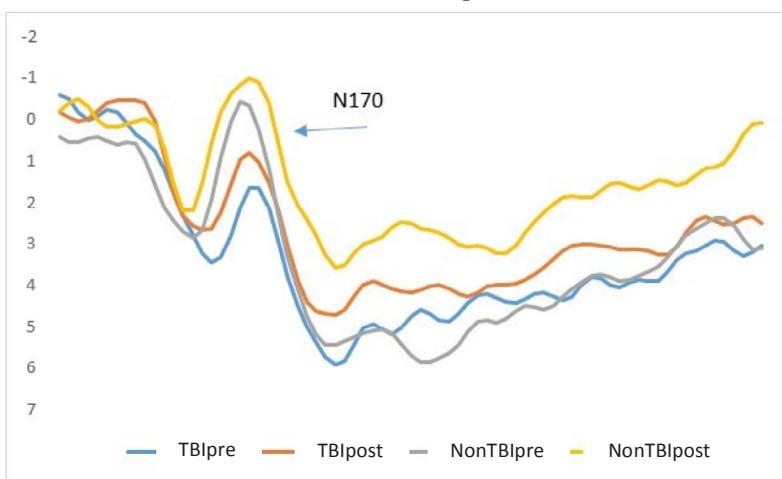
In contrast, the mTBI-no mTBI analysis revealed no evidence of attentional biases or enhanced processing of threatening facial expressions. In contrast, this analysis revealed a generalized reduction in N170 amplitude across a range of facial expressions, including angry, fearful and happy faces. The N170 component of the ERP is centred over temporo-occipital face-processing regions of the brain, and N170 amplitude has been found to be modulated specifically by the detection and processing of facial expressions (Eimer, 2011). This face-selective waveform thus reflects the extent of cortical processing of facial expressions. The findings that N170 amplitude is reduced in the mTBI compared to the no-mTBI group across all facial expressions is consistent with previous behavioural evidence of reduced capacity to discriminate emotional facial expressions in mTBI (Bornhofen & McDonald, 2008), and with generally reduced cortical emotional processing associated with mTBI (Elting et al., 2008). Interestingly, these mTBI findings are not in line with the enhanced N200 amplitudes found in the inhibitory motor task (Shu, Onton, Prabhakar, et al., 2014), or the enhanced emotional ERP amplitudes found in the Reading the Mind empathy task in a comorbid PTSD-mTBI group compared to single disorder groups (Shu, Onton, O'Connell, et al., 2014), however these studies compared an mTBI group with a comorbid PTSD-mTBI group, thus it is difficult to disentangle the independent effects of mTBI and PTSD in these studies.

Whilst the effects of high levels of PTSD symptoms developed during deployment were assessed in ADF members who did not sustain an mTBI during deployment, approximately one quarter of participants in the PTSD analysis reported a lifetime history of mTBI. However, whilst mTBI is common in wartime exposure, and is a known precursor of PTSD symptoms (Yurgil et al., 2014), these distinctive patterns of emotional ERPs remained in the high-PTSD group compared to the mTBI group when controlling for premorbid mTBI. A further limitation in the study was in the mTBI-no mTBI analysis: although the effect of PTSD symptoms was controlled by carefully matching level of PTSD symptoms in those who had sustained an mTBI during deployment compared to those who had not, the level of PTSD symptoms on the PCL-M was mild to moderate rather than minimal for both groups. Importantly, however, the average PCL-M total score for the mTBI and

A. Angry Faces – Temporal Sites



B. Fearful Faces – Temporal Sites



C. Happy Faces – Temporal Sites

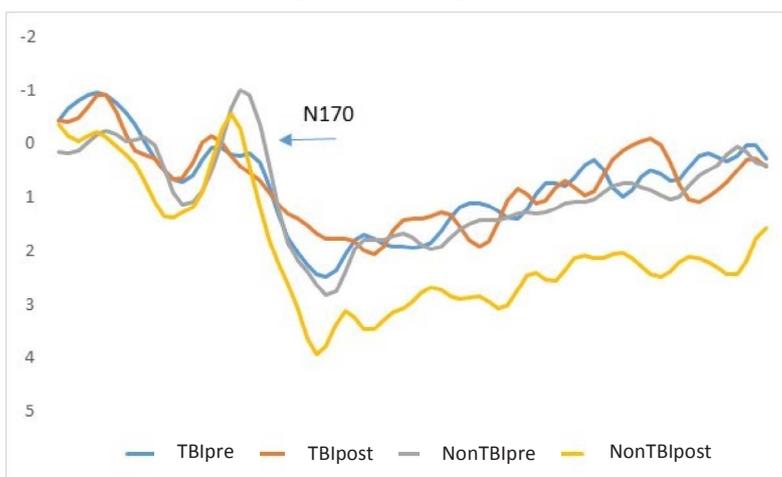


Fig. 4. Averaged ERP waveforms at temporal sites for the mTBI vs no-mTBI group. The mTBI group displayed significantly reduced N170 amplitudes compared to the no-mTBI group for angry, fearful and happy facial expressions.

no mTBI groups was below the recommended cutoff of 30 for PTSD screening in post-combat soldiers (Bliese et al., 2008). Future research should aim to compare the impact of mTBI and high PTSD symptoms in a 2 × 2 design. However, this was beyond the scope of this study given sample size restrictions. Finally, the mTBI group was classified according to screening procedures based on self-reported experience of events during deployment that can cause an mTBI coupled with

consequent symptoms (King et al., 2008). The use of the current mTBI screening tool is not optimal, and future research would benefit from the combination of optimal screening indices and objective neurological assessments.

Although this study was limited by small sample sizes and requires replication, the particular strengths of the study included the longitudinal case-control design, the careful matching of prior and current

war exposure, time-of-deployment, age, gender, and the use of high temporal resolution measures of cortical functioning to assess both automatic and conscious processing. Data on education or premorbid IQ was absent from the current sample, and as this might be expected to correlate with neural integrity, this data would ideally be included in future research. The large number of analyses conducted in the current study increases the risk of Type I error, however significant findings report effect sizes of medium to large magnitudes, suggesting that these are not trivial effects or the result of artefact. Nevertheless, these findings require replication in order to make robust conclusions. Finally, this study examined a predominantly male combat sample; many of whom had been exposed to particularly high levels of trauma and findings may not generalize to other populations.

5. Conclusions

These limitations notwithstanding, this study found evidence of distinct patterns of cortical processing of facial emotions following military deployment in those who sustained an mTBI during deployment, and those who developed PTSD symptoms. Individuals who developed PTSD symptoms developed an attentional bias towards threatening faces, whereas those who sustained an mTBI displayed a generalized reduction in conscious cortical processing of all facial expressions. Both of these phenomenon suggest potential, but divergent risk pathways for PTSD and mTBI during deployment, as attentional biases towards threat may facilitate further development of anxiety and stress reactions, whereas reduced capacity to discriminate facial emotions may place an individual at further risk of trauma exposure.

Funding

This project was funded by the Department of Defence through the Middle East Area of Operations Study, the Defence Health Foundation, and an NHMRC Program Grant APP1073041.

Conflict of interest

Prof McFarlane and Dr Van Hooff are supported by research funding from the Department of Defence and the Department of Veterans Affairs. Prof McFarlane is a Specialist Advisor in Psychiatry to the Department of Veterans Affairs and is a Group Captain in the RAAF SR.

References

- Attias, J., Bleich, A., Furman, V., & Zinger, Y. (1996). Event-related potentials in post-traumatic stress disorder of combat origin. *Biological Psychiatry*, *40*(5), 373–381.
- Bliese, P. D., Wright, K. M., Adler, A. B., Cabrera, O., Castro, C. A., & Hoge, C. W. (2008). Validating the primary care posttraumatic stress disorder screen and the posttraumatic stress disorder checklist with soldiers returning from combat. *Journal of Consulting and Clinical Psychology*, *76*(2), 272–281.
- Bornhofen, C., & McDonald, S. (2008). Emotion perception deficits following traumatic brain injury: A review of the evidence and rationale for intervention. *Journal of the International Neuropsychological Society*, *14*(4), 511–525.
- Bryant, R. A. (2008). Disentangling mild traumatic brain injury and stress reactions. *New England Journal of Medicine*, *358*(5), 525–527.
- Bryant, R. A. (2011). Post-traumatic stress disorder vs traumatic brain injury. *Dialogues in Clinical Neuroscience*, *13*(3), 251–262.
- Carlson, K. F., Kehle, S. M., Meis, L. A., Greer, N., Macdonald, R., Rutks, I., ... Wilt, T. J. (2011). Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: A systematic review of the evidence. *The Journal of Head Trauma Rehabilitation*, *26*(2), 103–115.
- Depue, B. E., Olson-Madden, J. H., Smolker, H. R., Rajamani, M., Brenner, L. A., & Banich, M. T. (2014). Reduced amygdala volume is associated with deficits in inhibitory control: A voxel- and surface-based morphometric analysis of comorbid PTSD/mild TBI. *BioMed Research International*, *2014*, 691505.
- Duncan, C. C., Summers, A. C., Perla, E. J., Coburn, K. L., & Mirsky, A. F. (2011). Evaluation of traumatic brain injury: Brain potentials in diagnosis, function, and prognosis. *International Journal of Psychophysiology*, *82*(1), 24–40.
- Eimer, M. (2011). The face-sensitivity of the n170 component. *Frontiers in Human Neuroscience*, *5*, 119.
- Eimer, M., & Holmes, A. (2002). An ERP study on the time course of emotional face processing. *NeuroReport*, *13*(4), 427–431.
- Elting, J. W., Maurits, N., van Weerden, T., Spikman, J., De Keyser, J., & van der Naalt, J. (2008). P300 analysis techniques in cognitive impairment after brain injury: Comparison with neuropsychological and imaging data. *Brain Injury*, *22*(11), 870–881.
- Felmingham, K. L., Bryant, R. A., & Gordon, E. (2003). Processing angry and neutral faces in post-traumatic stress disorder: An event-related potentials study. *NeuroReport*, *14*(5), 777–780.
- Felmingham, K. L., Rennie, C., Gordon, E., & Bryant, R. A. (2012). Autonomic and cortical reactivity in acute and chronic posttraumatic stress. *Biological Psychology*, *90*(3), 224–227.
- Felmingham, K. L., Rennie, C., Manor, B., & Bryant, R. A. (2011). Eye tracking and physiological reactivity to threatening stimuli in posttraumatic stress disorder. *Journal of Anxiety Disorders*, *25*(5), 668–673.
- Gratton, G., Coles, M. G., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology*, *55*(4), 468–484.
- Gur, R. C., Sara, R., Hagendoorn, M., Marom, O., Hughett, P., Macy, L., ... Gur, R. E. (2002). A method for obtaining 3-dimensional facial expressions and its standardization for use in neurocognitive studies. *Journal of Neuroscience Methods*, *115*(2), 137–143.
- Hoge, C. W., & Castro, C. A. (2006). Post-traumatic stress disorder in UK and US forces deployed to Iraq. *Lancet*, *368*(9538), 837–837.
- Hoge, C. W., McGurk, D., Thomas, J. L., Cox, A. L., Engel, C. C., & Castro, C. A. (2008). Mild traumatic brain injury in U.S. Soldiers returning from Iraq. *New England Journal of Medicine*, *358*(5), 453–463.
- Jeffreys, D. A., & Tukmachi, E. S. (1992). The vertex-positive scalp potential evoked by faces and by objects. *Experimental Brain Research*, *91*(2), 340–350.
- Karl, A., Schaefer, M., Malta, L. S., Dörfel, D., Rohleder, N., & Werner, A. (2006). A meta-analysis of structural brain abnormalities in PTSD. *Neuroscience & Biobehavioral Reviews*, *30*(7), 1004–1031.
- Kessler, R. C., Andrews, G., Colpe, L. J., Hiripi, E., Mroczek, D. K., Normand, S. L., ... Zaslavsky, A. M. (2002). Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological Medicine*, *32*(6), 959–976.
- Kimble, M. O., Fleming, K., Bandy, C., & Zambetti, A. (2010). Attention to novel and target stimuli in trauma survivors. *Psychiatry Research*, *178*(3), 501–506.
- King, D. W., King, L. A., & Vogt, D. S. (2008). *Manual for the deployment risk and resilience inventory (DRRI): A collection of measures for studying deployment-related experiences in military veterans*. Boston, MA: National Center for PTSD.
- Klimova, A., Bryant, R. A., Williams, L. M., & Felmingham, K. L. (2013). Dysregulation in cortical reactivity to emotional faces in PTSD patients with high dissociation symptoms. *European Journal of Psychotraumatology*, *4*.
- MacDonald, C. L., Johnson, A. M., Cooper, D., Nelson, E. C., Werner, N. J., Shimony, J. S., ... Brody, D. L. (2011). Detection of blast-related traumatic brain injury in U.S. military personnel. *New England Journal of Medicine*, *364*(22), 2091–2100.
- Naataanen, R. (1990). The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. *Behavioural Brain Research*, *13*, 201–288.
- Olatunji, B. O., Armstrong, T., McHugo, M., & Zald, D. H. (2013). Heightened attentional capture by threat in veterans with PTSD. *Journal of Abnormal Psychology*, *122*(2), 397–405.
- Pitman, R. K., Rasmusson, A. M., Koenen, K. C., Shin, L. M., Orr, S. P., Gilbertson, M. W., ... Liberzon, I. (2012). Biological studies of post-traumatic stress disorder. *Nature*, *13*, 769–787.
- Polich, J., & Kok, A. (1995). Cognitive and biological determinants of P300: An integrative review. *Biological Psychology*, *41*(2), 103–146.
- Rotshtein, P., Richardson, M. P., Winston, J. S., Kiebel, S. J., Vuilleumier, P., Eimer, M., ... Dolan, R. J. (2010). Amygdala damage affects event-related potentials for fearful faces at specific time windows. *Human Brain Mapping*, *31*(7), 1089–1105.
- Shu, I. W., Onton, J. A., O'Connell, R. M., Simmons, A. N., & Matthews, S. C. (2014). Combat veterans with comorbid PTSD and mild TBI exhibit a greater inhibitory processing ERP from the dorsal anterior cingulate cortex. *Psychiatry Research*, *224*(1), 58–66.
- Shu, I. W., Onton, J. A., Prabhakar, N., O'Connell, R. M., Simmons, A. N., & Matthews, S. C. (2014). Combat veterans with PTSD after mild TBI exhibit greater ERPs from posterior-medial cortical areas while appraising facial features. *Journal of Affective Disorders*, *155*, 234–240.
- Simmons, A. N., & Matthews, S. C. (2012). Neural circuitry of PTSD with or without mild traumatic brain injury: A meta-analysis. *Neuropharmacology*, *62*(2), 598–606.
- Sponheim, S. R., McGuire, K. A., Kang, S. S., Davenport, N. D., Aviyente, S., Bernat, E. M., & Lim, K. O. (2011). Evidence of disrupted functional connectivity in the brain after combat-related blast injury. *NeuroImage*, *54*(Suppl 1), S21–29.
- Stevens, M. C., Lovejoy, D., Kim, J., Oakes, H., Kureshi, I., & Witt, S. T. (2012). Multiple resting state network functional connectivity abnormalities in mild traumatic brain injury. *Brain Imaging Behavior*, *6*(2), 293–318.
- U.S.G.A. Office. (2008). VA health care: Mild traumatic brain injury screening and evaluation implemented for OEF/OIF veterans, but challenges remain. In U. S. G. A. Office (Ed.) (pp. 42–44). Washington DC.
- Utama, N. P., Takemoto, A., Koike, Y., & Nakamura, K. (2009). Phased processing of facial emotion: An ERP study. *Neuroscience Research*, *64*(1), 30–40.
- Vasterling, J. J., Verfaellie, M., & Sullivan, K. D. (2009). Mild traumatic brain injury and posttraumatic stress disorder in returning veterans: Perspectives from cognitive neuroscience. *Clinical Psychology Review*, *29*, 674–684.
- Weathers, F. W., Litz, B. T., Huska, J. A., & Keane, T. M. (1994). *The PTSD checklist-civilian version (PCL-C) for DSM-IV*. Boston: National Center for PTSD, Behavioral Sciences Division.
- Williams, L. M., Kemp, A. H., Felmingham, K., Barton, M., Olivieri, G., Peduto, A., ...

- Bryant, R. A. (2006). Trauma modulates amygdala and medial prefrontal responses to consciously attended fear. *Neuroimage*, 29(2), 347–357.
- Williams, L. M., Liddell, B. J., Rathjen, J., Brown, K. J., Gray, J., Phillips, M., ... Gordon, E. (2004). Mapping the time course of nonconscious and conscious perception of fear: An integration of central and peripheral measures. *Human Brain Mapping*, 21(2), 64–74.
- Williamson, J. B., Heilman, K. M., Porges, E. C., Lamb, D. G., & Porges, S. W. (2013). A possible mechanism for PTSD symptoms in patients with traumatic brain injury: Central autonomic network disruption. *Frontiers in Neuroengineering*, 6, 13.
- Yurgil, K. A., Barkauskas, D. A., Vasterling, J. J., Nievergelt, C. M., Larson, G. E., Schork, N. J., ... Baker, D. G. (2014). Association between traumatic brain injury and risk of posttraumatic stress disorder in active-duty Marines. *JAMA Psychiatry*, 71(2), 149–157.