Reduced electrophysiological habituation to novelty after trauma reflects heightened salience network detection

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ABSTRACT

Background: Event-Related Potential (ERP) studies of PTSD have reported enhanced P3 amplitudes in response to trauma-related stimuli that are less likely to habituate over time.

Methods: In the present study, we compared ERPs to the first and last half of an auditory novelty oddball task using neutral (trauma-unrelated) stimuli. Participants were 59 young students who were: trauma-exposed with “Probable PTSD”, trauma-exposed without PTSD, or non-traumatized controls.

Results: Reduced P3 amplitudes were observed for the last half of the trials for the entire sample, but this habituation was less profound for both trauma-exposed groups, demonstrating reduced habituation over time. Arousal symptom severity and trauma history negatively correlated with P3 amplitude habituation across the entire sample. Reduced N1 amplitudes for the last half of the trials were found in both trauma-exposed groups, but not among controls.

Conclusions: Our findings suggest that trauma-exposed individuals exhibit information processing alterations in response to neutral environmental stimuli that may be related to a general pattern of heightened activity of the Salience Network. Implications for the neurobiological model of PTSD and PTSD psychotherapy are discussed.

1. Introduction

Post-Traumatic Stress Disorder (PTSD) prevalence rates are estimated between 3 and 12% among the U.S. adult population (Kessler et al., 1995; Pietrzak et al., 2011). Moreover, those suffering from post-traumatic stress (PTS) symptoms that do not meet the diagnostic threshold for PTSD compound these rates significantly (Fink et al., 1995; Pietrzak et al., 2011). Moreover, those suffering from post-traumatic stress (PTS) symptoms that do not meet the diagnostic threshold for PTSD compound these rates significantly (Fink et al., 1995; Pietrzak et al., 2011). Moreover, those suffering from post-traumatic stress (PTS) symptoms that do not meet the diagnostic threshold for PTSD compound these rates significantly (Fink et al., 1995; Pietrzak et al., 2011).

Information processing in PTSD has been studied using Event-Related Potentials (ERPs) in the context of an oddball task in which participants are asked to respond to low frequency “target” stimuli presented amongst high frequency, repetitive “standard” stimuli and low frequency salient “distractors.” During the task, P3, a centro-parietal positive ERP component occurring around 300 ms after stimulus onset, is elicited (Karl et al., 2006a,b). This cerebral response to targets (referred to as P3b) or distractors (referred to as P3a) is affected by stimuli probability, with lower probability leading to higher amplitudes (Duncan-Johnson and Donchin, 1977). In a novelty oddball task, a variation of the classic, distractors are novel stimuli characterized by low probability, task irrelevance, and contextual salience. The P3 component elicited by such novelty (Novelty P3) is considered the most likely correlate of the orienting reflex (Barry et al., 2016; Johnson et al., 2013; Karl et al., 2006a,b), notwithstanding some controversy in the

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literature whether Novelty P3 is a discrete entity from P3a. Nevertheless, in healthy adults, when novel stimuli are repeated, rapid habituation of the Novelty P3 component is observed, expressed in decreased amplitudes during later presentations of novel stimuli within an oddball task (Cycowicz and Friedman, 1997; Cycowicz et al., 1996; Friedman and Simpson, 1994; Richardson et al., 2011). This pattern of amplitude reduction was postulated to reflect familiarization with previously novel stimuli (Courchese, 1978).

ERP studies have indicated that, when presented with a novelty oddball task involving trauma-related distractors, individuals with PTSD show enhanced P3 amplitudes in response to targets (P3b) as well as distractors (P3a); in the context of neutral (trauma-unrelated) distractors, response to both targets (P3b) and distractors (P3a) is reduced (Johnson et al., 2013; Karl et al., 2006a,b; see Javanbakht et al., 2011, for review). Such alterations have also been found among trauma-exposed participants without PTSD (Covey et al., 2013; Gjini et al., 2013; Karl et al., 2006a,b; Kimble et al., 2010; Thomas et al., 2013). Novelty oddball task studies utilizing neutral (trauma-unrelated) novel distractors have produced conflicting findings regarding the possible effects of trauma on P3 indices (Kimble et al., 2010; Kimble et al., 2000; Neylan et al., 2005). Indeed, two meta-analyses concluded that trauma exposure does not affect responsivity to targets (P3b) or distractors (Novelty P3) in a novelty paradigm (Johnson et al., 2013; Karl et al., 2006a,b). Nevertheless, PTSD ERP studies have reported trauma-related alterations in earlier ERP components such as N1 (Ehlers et al., 2006; Klimova et al., 2013), a short latency (80–120 ms) exogenous ERP component associated with perceptual processing (Rosburg et al., 2008).

Although the ERP literature tends to indicate no significant PTSD-related alterations in Novelty P3 (Johnson et al., 2013), the effects of trauma exposure on this component may be subtle and may be expressed by less habituation (failure to habituate), as has been reported in other populations (Richardson et al., 2011; Tsuchiya et al., 2000; West et al., 2010). Thus, trauma may manifest in reduced habituation of the Novelty P3 in response to repeated presentations of novel stimuli, rather than in global amplitude differences across an entire novelty task. Indeed, a previous study of war veterans with PTSD found reduced habituation to repeated traumatic distractors (combat pictures), while habituation to target stimuli remained intact (Bleich et al., 1996). However, to our knowledge, the effect of traumatic event exposure on habituation to novel, trauma-unrelated distractors (e.g., everyday novel, neutral stimuli) has not been studied before (Javanbakht et al., 2011; Johnson et al., 2013; Karl et al., 2006a,b).

This study examined the extent of cerebral habituation of the Novelty P3 component elicited by repeated novel, neutral auditory distractor stimuli among individuals with high levels of PTS and “probable PTSD” (PPTSD), trauma-exposed individuals without PTSD (Non-PTSD), and trauma-unexposed controls. We hypothesized that participants in both trauma-exposed groups (PPTSD, Non-PTSD) would exhibit reduced habituation of the Novelty P3 response, compared to controls. In addition, since hyperactivity of the Salience Network in PTSD has been associated with hypervigilance (Hayes et al., 2012), we hypothesized that reduced habituation of the Novelty P3 component would be significantly linked to higher PTSD arousal symptoms. Lastly, we hypothesized that trauma exposure would also negatively affect earlier ERP components such as N1.

2. Material and methods

2.1. Participants

Participants were recruited via postings on local university advertisement boards, at medical centers, and at a student counseling center. Forty-two participants (28 females) reported experiencing at least one traumatic event meeting DSM 5 PTSD “Criterion A” (APA, 2013) and were divided into a “Probable PTSD” - PPTSD group (21 participants, 16 females, $M_{age} = 25.60 \ SD = 4.58$) whose Posttraumatic Diagnostic Scale (PDS) scores were $\geq 15$ (Foa et al., 1997), and a “Non-PTSD” group (21 participants, 12 females, $M_{age} = 24.47, \ SD = 2.41$) whose PDS scores were $\leq 14$. A PDS cutoff point $\geq 15$ is considered to indicate significant post-traumatic symptom (PTS) severity corresponding to a clinical diagnosis of PTSD (Daie-Gabai et al., 2011; Foa et al., 1999). Although a clinical psychologist evaluation verified that trauma-exposed participants met DSM criteria A, and a PDS score $\geq 15$ served as an inclusion criteria, we use the term “Probable PTSD” (PPTSD) with this group, since the reported level of PTS was based on self-reported questionnaires. In addition, a control group of 17 university students (11 females, $M_{age} = 23.85, \ SD = 1.77$) with no previous traumatic history was also recruited. No significant group differences in age were observed ($p = .310$). Normal hearing was verified by audiometric screening (i.e., pure tone thresholds of 20 dB HL at 500–4000 Hz in both ears). No participant reported medical problems (including traumatic brain injury), being in psychological or psychiatric treatment, or medication use. The study was approved by the University Institutional Review Board, written informed consent was obtained prior to participation, and participants were compensated for their time.

2.2. Measures and procedure

2.2.1. Clinical interview

A licensed clinical psychologist (trained to evaluate PTSD symptoms) conducted a clinical interview to assess whether trauma-exposed participants met DSM 5 PTSD “Criterion A” (APA, 2013).

2.2.2. Questionnaires

2.2.2.1. Posttraumatic Diagnostic Scale (PDS). The PDS is a 49-item self-rating scale assessing PTSD diagnosis according to DSM-IV criteria (Foa, 1995). Its three subscales measure re-experiencing, avoidance, and arousal symptoms (Foa et al., 1997); the summed responses on 17 PTSD symptoms comprise the symptom severity score. High internal consistency and test-retest reliability, as well as satisfactory agreement with PTSD-related diagnostic interviews (e.g., Structural Clinical Interview for DSM Disorders – SCID; Foa et al., 1997), were previously reported.

2.2.2.2. Trauma History Questionnaire (THQ). The THQ, widely used to measure previous traumatic history, is a 24-item self-report questionnaire measuring exposure to potentially traumatic events from DSM-IV’s “Criterion A” for PTSD (Hooper et al., 2011). Moderate to high test-retest reliability and validity were previously reported (Hooper et al., 2011). The score reflects the total number of different types of traumatic events reported, from 0 to 24. THQ data were available for only 58 participants.

2.2.3. Traumatic exposure type and symptom severity

On the Posttraumatic Diagnostic Scale – PDS (Foa, 1995), the majority of participants in trauma-exposed groups reported motor vehicle accidents (20, 47.61%) as their major traumatic experience. Table 1 presents the distribution of “major events.” No significant statistical differences were found in the distribution of major trauma event type between the trauma-exposed groups, $\chi^2 (5, N = 59) = 3.49, p = .634$.

### Table 1

<table>
<thead>
<tr>
<th>Trauma Type</th>
<th>Major Traumatic Event</th>
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</thead>
<tbody>
<tr>
<td>Motor vehicle accidents</td>
<td>20 (47.60%)</td>
</tr>
<tr>
<td>War- or combat-related experience</td>
<td>7 (16.70%)</td>
</tr>
<tr>
<td>Sexual assault</td>
<td>4 (9.50%)</td>
</tr>
<tr>
<td>Non-sexual assault</td>
<td>2 (4.80%)</td>
</tr>
<tr>
<td>Disease</td>
<td>2 (4.80%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (16.70%)</td>
</tr>
</tbody>
</table>

2
Table 2 presents demographic and trauma-related variables. No significant gender differences were found between groups, \( \chi^2 (2, N = 59) = 1.72, p = .432 \), despite female predominance. As expected, a significant effect of Group on the PDS score was observed, \( F (2, 55) = 83.71, p < .001, \eta^2_p = .75 \). Participants in the PPTSD and Non-PTSD groups reported “moderate to severe” and “mild” PTS levels, respectively, according to PDS norms (McCarthy, 2008). Significantly higher levels of PTS among the PPTSD group, compared to the Non-PTSD (\( p < .001 \)) group, were observed (Bonferroni post-hoc testing), as well as among the trauma-exposed groups (PPTSD, Non-PTSD) compared to the asymptomatic Control group (\( p < .001 \)). Lastly, a significant effect of Group on the level of previous traumatic exposure in the Trauma History Questionnaire – THQ (Hooper et al., 2011) indicated significantly higher reported rates of previous traumatic exposure among the trauma-exposed groups (Bonferroni post-hoc testing).

2.2.4. Auditory novelty oddball task

EEG brain activity was recorded while participants performed an auditory novelty oddball task based on the random sequence of three types of stimuli consisting of Target (2000 Hz, 180 ms, pure tone, 60 db SPL, 1 ms rise/fall time, \( p = .2, n = 50 \)), Novel (\( p = .20, n = 51 \)), and Standard (1000 Hz, 180 ms, pure tone, 60 db SPL, 1 ms rise/fall time, \( p = .6, n = 150 \)) sounds. We used 17 different novel sounds, each randomly repeated 3 times, including computer-generated whistles, buzzes, and unidentifiable sounds (clunks, pings, buzzes, etc.) with varying duration times (355–1100 ms) and 60 db SPL intensity. All 251 stimuli were presented binaurally through earphones (Sony, MDR-V700). Inter-stimulus intervals were 2201 ms.

Participants were seated in a comfortable armchair, told they would hear different kinds of sounds, and asked to press a joystick button upon identifying the Target sound. Fig. 1 illustrates the experimental paradigm.

2.2.5. Electrophysiological testing and measures

Continuous EEGs were recorded in a room free of noise and electromagnetic fields, using the Micromed SD 64 channel system, and a Neuroscan 64 channel elastic cap with electrode locations based on the international 10/10 system. All electrodes referenced to an electrode at the tip of the nose. A ground electrode was placed on the right mastoid. A vertical electrooculogram (EOG) was recorded using two electrodes, located above and below the right eye. The impedance measure for each electrode was kept below 5 kΩ. Raw data were continuously recorded with 16 bit A/D, a band pass filter of 0.15–463 Hz, and a sampling rate of 1024 Hz. All data were analyzed using BPM software. EEG recordings were segmented into intervals time-locked to stimuli, and extended from 200 ms pre-stimulus to 2000 ms post-stimulus. An eye-movement correction procedure was performed offline using an eye-movement correction algorithm (Henkin et al., 2002). The algorithm detects an epoch with ocular artifacts by comparing the signals recorded from above and below the eye. Assuming that the signal above the eye contained both EEG and electrooculogram (EOG) activity and the signal below the eye contained just EOG activity, a cross-correlation between these two signals was evaluated. A cross-correlation value higher than −0.3 defined EOG artifact. Corrections were performed by a linear regression between each electrode signal within the detected epoch and the recorded signal in the electrode below the eye. EEG signals were also visually scored on a high resolution computer monitor, and portions of data containing eye movement not corrected by algorithm, muscle movements, or other sources of artifact, were removed. Baseline correction for each trial was performed using the 200 ms prior to stimuli onset for each channel separately. Amplitude rejection was applied to the data prior to averaging. Records with amplitude higher than 250 μV (even in a single channel) were excluded. For each participant, all trials were averaged per stimulus Trial Type (Target, Novel, and Standard).

Global Field Power (GFP) was calculated by the root mean square (RMS) of the grand averaged waveform (Murry et al., 2008) across 12 electrodes (see the statistical analysis section for specification) and Groups (PPTSD, Non-PTSD, Control) for each Trial Type (Target, Novel, Standard). GFP provides a reference-independent measure of response strength and produces positive values for either positive or negative components (Murry et al., 2008). For clearer illustration, Fig. 2 presents the GFP components in either negative or positive format: (1) A negative component between 30 and 120 ms identified as N1; and (2) A positive component between 250 and 450 ms identified as P3. For both components, ERPs were quantified in terms of peak amplitudes (microvolts) and latency (milliseconds).

To explore habituation (Time factor), the novelty oddball task’s 251 auditory stimuli were divided into stimuli #1–125 and #126–251 (first and last half, respectively). All trials were averaged per stimulus Trial Type (Target, Novel and Standard) for each participant. A \( 2 \times 3 \) repeated-measures analysis of variance (ANOVA) indicated that the number of stimuli presented in each half of the task for each stimulus Trial Type (Target, Novel, Standard) was not affected by Group affiliation (no main effect of Group, Group × Time, or Group × Time × Trial Type interactions were observed; all \( Fs < 1 \)). The mean number of trials for the first and last halves of the trials was 17 and 22 for Target; 20 and 21 for Novel, and 63 and 55 for Standard stimuli, respectively. These trial rates for each stimulus Trial Type indicate an adequate signal to noise ratio, and were reported in a previous study of P3 habituation (Richardson et al., 2011). No significant statistical differences were found in the distribution of stimulus Trial Type (Target, Novel, Standard) between the first and last halves, \( \chi^2 (18, N = 251) = 20.94, p = .282 \). Additionally, topographical maps for each of the difference waves (first minus last trials) for each Trial Type and Group affiliation were generated. Topographical distribution was calculated for 350 ms post-stimulus.

2.3. Statistical analyses

Analyses were conducted with SPSS version 25 (Armonk, NY; IBM Corp., 2013). For comparison of demographics (age), and group differences in trauma-related variables (PDS, THQ), an ANOVA with Group (PPTSD, Non-PTSD, Control) as an independent variable was used. All comparisons were conducted with gender as a covariate. A non-parametric chi-square test compared gender differences among the three groups.

ERP component amplitude and latency comparisons between groups were analyzed with a five-way repeated-measures ANOVA with Group (PPTSD, Non-PTSD, Control) as a between-participants factor, and Time (First half; Last half), Trial Type (Target, Novel, Standard), Electrode Midline Site (Prefrontal, Frontal, Central, Parietal), and Electrode Side
3. Results

3.1. ERP component analysis

3.1.1. N1 amplitude. A significant effect of Electrode Midline Site was observed, $F(1,76) = 9.45$, $p < .001$, $\eta^2_p = .14$. Bonferroni post-hoc testing indicated significant ($p < .001$) N1 amplitude differences between the Frontal Midline Sites ($M = -4.57$, $SE = .33$) and both the Prefrontal ($M = -3.68$, $SE = .34$, $p < .001$) and Parietal ($M = -3.28$, $SE = .30$) Midline Sites. A significant amplitude difference also was found between Central ($M = -4.29$, $SE = .30$) and Parietal Midline Site electrodes. Moreover, a significant effect of Electrode Side Site was observed, $F(1,76) = 9.41$, $p = .002$, $\eta^2_p = .12$, with no significant N1 amplitude differences between either of the Electrode in the Side Sites factor (Bonferroni). No other significant main effects were obtained.

Importantly, a significant Group $\times$ Time interaction was observed, $F(2,55) = 4.66$, $p = .013$, $\eta^2_p = .14$. Fig. 4 presents this interaction across trial types. Planned comparisons revealed a significant decrease in N1 amplitudes in the last half, compared to the first half, of the ERP task trials in both trauma-exposed groups, $F(1,55) = 7.65$, $p < .007$, $\eta^2_p = .12$. These first versus last differences did not vary between the two trauma-exposed groups ($F < 1$). Among the control group, an inverse pattern was observed, indicating higher N1 amplitudes in the last half, compared to the first half, of trials. However, this pattern was not statistically significant, $F(1,55) = 2.98$, $p = .089$. When examining only the first half of trials, contrasting the trauma-exposed groups (PTSD, Non-PTSD) with the Controls revealed a marginal effect of Group ($p = .055$) on N1 amplitude in response to Standard stimuli; PTSD ($M = -4.33$, $SD = 2.49$) and Non-PTSD ($M = -4.81$, $SD = 3.01$) groups reported larger N1 amplitudes compared to the Control group ($M = -2.90$, $SD = 3.77$). No other significant interactions involving Group and Time factors were obtained.

3.1.1.2. P3 amplitude. A significant main effect of Time, $F(1,55) = 5.76$, $p = .021$, $\eta^2_p = .10$, indicated a larger P3 amplitude in the first half ($M = 9.63$, $SE = .62$) than in the last half ($M = 6.98$, $SE = .60$).
of the novelty oddball task trials. A significant effect of Trial Type, $F(2, 54) = 10.20, p < .001, \eta^2_p = .27$, was observed. Bonferroni post-hoc testing indicated significant amplitude differences ($p < .001$) between all Trial Types: Target ($M = 7.81, SE = 0.68$), Novel ($M = 11.0, SE = 0.81$), and Standard ($M = 5.19, SE = 0.60$). Additionally, a significant effect of Electrode Midline Site was observed, $F(1.60, 87.63) = 34.51, p < .001, \eta^2_p = .63$, indicating a significant P3 amplitude differences at $p < .001$ level for all Midline Sites (Prefrontal $M = 5.78, SE = 0.54$; Frontal $M = 7.70, SE = 0.57$; Central $M = 9.23, SE = 0.64$, and Parietal $M = 10.47, SE = 0.63$; Bonferroni). No other significant main effects were obtained.

Importantly, a significant Group $\times$ Time interaction was found, $F(2, 55) = 3.21, p = .047, \eta^2_p = .11$. Fig. 5 presents this interaction across Trial Types. Planned comparisons indicated that despite a significant decrease in P3 amplitudes in the last half (compared to the first) of the ERP task in both of the trauma-exposed groups, $F(1, 55) = 10.54, p = .002, \eta^2_p = .16$, and the Control group, $F(1, 55) = 25.46, p < .001, \eta^2_p = .32$, this decrease was significantly smaller (i.e., reduced habituation) in the trauma-exposed groups, $F(1, 55) = 6.32, p = .015, \eta^2_p = .10$. The degree of habituation (first vs. last half differences) did not differ between the two trauma-exposed groups ($F < 1$). No significant group effects were observed on P3 amplitude for the first half of the Novelty ERP task ($p = .776$). No other significant interactions involving Group and Time factors were obtained.

Fig. 6 presents the topographic distribution for the first minus last half of the trials (difference wave) of the Novelty oddball task at 350 ms post stimulus onset for the three Trial Types (Target, Novel, Standard) among the PPTSD, Non-PTSD, and Control groups.

3.1.1.2. ERP component latency

3.1.1.2.1. N1 latency. A significant effect of Trial Type was observed, $F(1.78, 97.89) = 6.87, p = .002, \eta^2_p = .11$, indicating significantly shorter latencies in response to Target stimuli ($M = 100.97, SE = 1.92$) compared to Novel stimuli ($M = 107.98, SE = 2.06, p = .01$; Bonferroni). A significant effect of Midline Site, $F(1.96, 107.81) = 3.84, p = .025, \eta^2_p = .06$, was observed. Frontal Site latency was longer.
Fig. 5. P3 amplitude in first and last halves of trials in the novelty oddball task among the three study groups (PPTSD, Non-PTSD, Control). Vertical bars denote standard error.

Fig. 6. Topographic distributions (top view) of the first minus last half of trials in the Novelty oddball task at 350 ms post-stimulus onset for each of the trial types among the three study groups.

(M = 105.42, SE = 1.57) than among Prefrontal (M = 104.52, SE = 1.94), Central (M = 104.80, SE = 1.62), and Parietal (M = 104.01, SE = 1.67) Sites. However, no statistically significant difference between the various Midline Sites was observed (Bonferroni). Additionally, a significant interaction of Time × Midline Sites × Group interaction was found, F (3.68, 101.42) = 2.69, p = .039, η²_p = .09. Probing the interaction revealed a significant interaction of Time × Group only for Parietal Midline Sites, F (2, 55) = 3.28, p = .04, η²_p = .11, indicating that among the PPTSD and Non-PTSD groups a reduction in latency between the first half (M = 103.67, SE = 3.58; M = 106.95, SE = 3.57) and the last half of the ERP task trials (M = 102.17, SE = 2.70; M = 100.02, SE = 2.69, respectively), along with an inverse pattern denoting shorter latencies among the first (M = 103.56, SE = 3.94) compared to the last half (M = 107.70, SE = 2.92) of trials among Controls. No other significant interactions involving Group and Time factors were obtained.

3.1.1.2.2. P3 latency. A significant effect of Trial Type was observed, F (2, 54) = 8.87, p < .001, η²_p = .25. indicating significantly longer latencies in response to Target (M = 359.28, SE = 4.26) compared to Novel (M = 340.92, SE = 3.80, p = .01) and Standard (M = 342.26, SE = 4.12, p = .02) stimuli (Bonferroni). A significant effect of Midline Site was observed F (1.99, 109.68) = 5.79, p = .004, η²_p = .10, with significantly shorter latencies at Prefrontal (M = 342.26, SE = 4.12), compared to Frontal (M = 344.94, SE = 2.91, p < .001), Central (M = 344.24, SE = 2.91, p < .001), and Parietal (M = 345.87, SE = 3.23, p = .004) Sites (Bonferroni). No other significant interactions involving Group and Time factors were obtained.

3.1.1.2.3. Correlational analysis. A significant correlation was observed between PDS Arousal subscale scores and P3 amplitude habituation levels for the Central electrodes (Mean C3,Cz, C4 in the first half of trials minus Mean C3,Cz, C4 in the last half of trials) in response to Standard stimuli, r (59) = −0.333, p = .005. Furthermore, a significant correlation was found between THQ trauma history score and P3 amplitude habituation level for the Central electrodes, r (58) = −0.357, p = .003 (see Fig. 7). No other significant correlations between PDS subscale scores or trauma history and P3 amplitude habituation were observed.

4. Discussion

In the current study, P3 amplitude habituation in the presence of novel, neutral auditory stimuli was evident among all the participants, although the level of habituation was reduced among the trauma-exposed groups (PPTSD, Non-PTSD). Habituation of the N1 component was observed only for the trauma-exposed participants. P3 habituation levels were negatively correlated with arousal and trauma exposure levels in response to Standard (non-target) stimuli. Generally, the findings are indicative of information processing alterations at both early and late ERP components after trauma exposure, while the P3 component findings suggest heightened arousal occurring even in response to neutral novel sounds.

In accordance with previous findings (Cycowicz and Friedman, 1997; Richardson et al., 2011; Romero and Polich, 1996), and consistent with our hypothesis, P3 amplitudes decreased in the second half of the novelty oddball task trials (compared with the first half) across the entire study sample. However, this reduction was significantly less profound among the trauma-exposed. Previous studies among healthy young adults (Cycowicz and Friedman, 1997; Cycowicz et al., 1996) have reported their specific habituation to novel stimuli (Novelty P3)
but not target stimuli (P3b), possibly reflecting familiarization with previously unusual incoming stimuli (Bleich et al., 1996; Richardson et al., 2011). However, in this study, the modulation of habituation by Group affiliation (i.e., reduced habituation among trauma-exposed participants) was not affected by stimulus Trial Type. The absence of response specificity (to novel stimuli only) may reflect a more general pattern of altered information processing.

Moreover, a reduction in N1 amplitude in the last half of trials, compared to the first half, was evident only among the trauma-exposed groups. Significantly (though marginal) larger N1 amplitudes in response to standard stimuli were observed among trauma-exposed groups in the first half of trials. N1 is primarily considered to reflect initial sensory response (Gregg and Snyder, 2012). However, it has been also shown to be modulated by attention; elevated attention is associated with larger N1 amplitudes (Hillyard et al., 1973; Hillyard et al., 1995). These findings suggest that, after trauma, early stages of information processing (N1) might be characterized by elevated attention followed by swift habituation, while later stages (P3) are marked by reduced habituation in response even to trauma-unrelated novel stimuli. However, this characterization is tentative, since the current study only examined SN activity variably using trauma-unrelated (neutral) stimuli; future research would be enhanced by comparing responses to novel trauma-related auditory stimuli.

The lack of significant P3, as well as N1, amplitude differences between the trauma-exposed groups (PPTSD, Non-PTSD) suggests that these findings may be more linked to trauma exposure than to the probable presence of PTSD. This is consistent with our hypothesis, and previous data, that trauma itself, even without the development of PTSD, can significantly affect cerebral functioning (Karl et al., 2006a,b; Thomas et al., 2013). Accordingly, it is possible that, among traumatized individuals, exposure to novel stimuli facilitates threat detection mechanisms that, in turn, affect processing all types of incoming stimuli.

The neurobiological model of PTSD proposes dysfunction in one of three intrinsic connectivity large scale networks: the default mode network (DMN), linked to intrusive symptoms; the central executive network (CEN), associated with memory and emotional control deficits; and the salient network (SN), associated with symptoms of hypervigilance and exaggerated threat detection (Akiki et al., 2017; Aupperle et al., 2012; Bryant et al., 2008; Dunkley et al., 2015; Hayes et al., 2012; Liberzon and Abelson, 2016; Menon, 2011; Sripada et al., 2012). Heightened SN activity is suggested to result from difficulty identifying the contextual meanings of stimuli (possibly due to altered hippocampal activity essential for contextual learning; Holland and Bouton, 1999). Thus, impaired ability to discriminate threat from safety leads to elevated detection mechanism activity (Dunkley et al., 2014; Liberzon and Abelson, 2016; Sripada et al., 2013). In this study, arousal symptom levels (not re-experiencing or avoidance) negatively correlated with P3 habituation to Standard stimuli; this may reflect impaired ability to habituate to benign stimuli, stemming from SN hyperarousal. Indeed, previous studies report significant associations between SN activity and PTSD symptom severity (Dunkley et al., 2015; Shin and Liberzon, 2010). However, this is the first study to report such an association using ERP methodology. The observed alterations in N1 and P3 may reflect the varying effect of heightened Salience Network activity at two distinct stages of information processing: one associated with early sensory processing and another related to late decision processes. However, it is important to note that since the current study used neutral (trauma-unrelated) stimuli, the interpretation of altered SN activity after trauma should be carefully examined in future research.

Notwithstanding the innovative findings of the study, it has limitations. Similar to related studies (e.g., Felmingham et al., 2002; Lobo et al., 2014), our sample was characterized by higher representation of females (39 of 59 participants). While no statistically significant differences in male to female ratios were found between groups (females constituted 16 of 21 PPTSD, 12 of 21 Non-PTSD, and 11 of 17 Control group participants) and all analyses were conducted with gender as a covariate, future research should attempt a more balanced ratio between groups. Moreover, the relative homogeneity of our sample (young, healthy students with minimal comorbidity; only moderate to severe PTSD symptomatology) may reduce generalizability; notwithstanding, the youth and varied traumatic experiences of our sample simultaneously add diversity to the body of PTSD research primarily conducted among aging war veterans. In addition, as previously mentioned, while the use of neutral, trauma-unrelated stimuli enabled the uncovering of a general pattern of cerebral hypervigilance after trauma, caution is necessary to associate this pattern with SN activity in the absence of comparison to novel trauma-related stimuli. Another methodological limitation may be the current study’s sample size, which may be considered slightly under-powered in the context of a five-way repeated measure ANOVA. Finally, while the use of instruments such as the Posttraumatic Diagnostic Scale is quite practical and well-supported by the literature, future work would be enhanced by including full formal diagnostic evaluation.

Our findings have important potential implications for PTSD intervention and psychotherapy. Though our findings relate to cerebral function in response to neutral stimuli, the uncovered correlation between reduced habituation to neutral stimuli and higher arousal symptoms suggests that exposure to trauma may be followed by a general pattern of hyper-activation of the Salience Network, affecting various stages of information processing. This is corroborated by previous findings linking PTSD to decreased fear response inhibition even in safe environments, possibly associated with impaired contextual learning.
A common form of psychotherapy for PTSD is cognitive behavioral therapy (CBT). A primary CBT principle involves the extinction of learned fear through exposure to traumatic memories (Foa, 2011), and teaching fear reduction in safe environments through contextual learning (Shipherd and Salters-Pedneault, 2008; Smith et al., 2017). However, trauma-exposed individuals often exhibit impaired inhibition and reduced contextual learning (Garfinkel et al., 2014; Jovanovic et al., 2012) associated with SN hyper-activation (Strapada et al., 2012). Thus, fear extinction may not be efficiently targeted by psychological interventions focusing on exposure to trauma-associated memories or semantic-based cognition (van Rooij et al., 2015). Enhancing inhibition learning through targeted behavioral therapies or techniques that alter neural structure function, such as transcranial Direct Current Stimula

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