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An Analysis of Inhibitory Functioning in Individuals with Chronic Posttraumatic Stress Disorder

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Abstract

Cognitive abnormalities in posttraumatic stress disorder (PTSD) may be a function of underlying inhibitory deficits. Prepulse inhibition (PPI) and attentional blink (AB) are paradigms thought to assess inhibition. Using a sample of 28 individuals with PTSD compared to 20 trauma-exposed and 19 healthy individuals, PPI was examined using white noise that was preceded by a tone, and AB was examined using a presentation of letters in a stream of numbers. Relative to the control group, the PTSD and trauma-exposed groups did not follow the u-shaped pattern in AB, suggesting trauma-exposure and subsequent PTSD are associated with similar impairment in attention. Individuals with PTSD showed reduced PPI compared to trauma-exposed and healthy individuals, suggesting individuals with PTSD exhibit faulty automatic processing. For individuals with PTSD, PTSD severity was associated with a decline in PPI. These findings suggest a general faulty inhibitory mechanism associated with trauma exposure and PTSD.

Keywords

inhibition; attentional blink; prepulse inhibition; posttraumatic stress disorder

1.1 An Analysis of Inhibitory Functioning in Individuals with Chronic Posttraumatic Stress Disorder

Following exposure to a traumatic event, many individuals will experience stress-related reactions with the vast majority experiencing a marked drop in these reactions over time (Resnick, Kilpatrick, Dansky, Saunders, & Best, 1993). However, a substantial minority will continue to experience these stress reactions well past the traumatic event, resulting in the development of PTSD and other trauma-related psychopathology (e.g., Kessler, Sonnega,

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Bromet, Hughes, & Nelson, 1995). Specifically, many researchers and theorists (e.g., Rothbaum & Davis, 2003) conceptualize PTSD as an overgeneralization of this stress response to non-fearful stimuli. Importantly, although pre-existing inhibitory deficits may increase the likelihood of this overgeneralization, over time this overgeneralization may further lead to a breakdown of inhibitory processes associated with executive functioning (Bremner et al., 1993; Sutker, Vasterling, Brailey, & Allain, 1995). Specifically, there is accumulating evidence from neuroimaging studies that the medial prefrontal cortex (mPFC) assumes an inhibitory role in cognition (Bush 1998; 2000; MacDonald et al., 2000). Consistent with this, neuroimaging studies in PTSD often show reduced activity in the mPFC and greater activity in the amygdala (Gilboa et al., 2004), reflecting a potential failure of the mPFC to inhibit an overactivated amygdala (e.g., Morgan & LeDoux, 1995; Bremner, 1999). The functional decline in the mPFC and amygdala is presumed to have a negative impact on information processing (Bremner et al., 1990).

Prepulse inhibition (PPI) and attentional blink (AB) are two cognitive paradigms that examine how inhibition affects the processing of sensory stimuli. More specifically, PPI is a psychophysiological index of inhibition used to examine gating of sensory and attentional information, and AB is a cognitive measure used to assess temporal attention. Interestingly, AB may reflect inhibitory processes similar to those seen in PPI (Echiverri, Cornwell, & Grillon, 2006). Given that inhibition may be a critical factor in PTSD, deficits in PPI and AB may reflect dysfunction in the mPFC and amygdala neural circuitry and may further clarify an inhibitory role of the mPFC in PTSD.

One way to measure diminished inhibition is a form of startle modulation called PPI, which occurs when a non-startling prepulse precedes the startling pulse by a short interval (120 ms), resulting in inhibition of the startle reflex (Blumenthal, 1999). PPI is thought to occur through a sensorimotor gating system that functions as an attentional filter to protect limited capacity systems from being overloaded with incoming sensory information (Graham, 1979). PPI is proposed to index early stages of low-level, automatic processing and voluntary, controlled, attentional processing. PPI has been shown to follow different time courses, such that automatic processing occurs before 120 ms (Wynn, Schell, & Dawson, 1996) while controlled processing occurs at or after 120 ms (Blumenthal, 1999). Increased PPI is presumed to be associated with more effective information processing (e.g., Giakowmake, Bitsios, Frangou, 2006), whereas reduced PPI is thought to reflect reduced efficiency in inhibiting information (Light & Braff, 2001). Thus, impaired PPI may reflect a reduced ability to inhibit sensory information and potentially a failure of sensorimotor gating.

To date, three studies show reduced PPI in individuals with PTSD compared to controls (Grillon, Morgan, Davis, & Southwick, 1998a; Grillon, Morgan, Southwick, Davis, & Charney, 1996; Ornitz & Pynoos, 1989). Lower PPI is also associated with higher overall PTSD severity, reexperiencing, and hyperarousal symptoms (e.g., Grillon, Morgan, Southwick, Davis, & Charney, 1996). A growing number of studies report no differences in PPI across PTSD and control groups (Butler, Braff, Rausch, Jenkins, Sprock, & Geyer, 1990; Grillon, Morgan, Davis, & Southwick, 2005; Holstein, Vollenweider, Jancke, Schopper & Csomor, 2010; Morgan, Grillon, Lubin, & Southwick, 1997; Lipschitz, Mayes,

Rasmusson, Anyan, Billingslea, Gueorguieva et al., 2005; Vrana, Calhoun, McClernon, Dennis & Lee, 2013). However, a number of these studies have potential sampling and experimental confounds that may have affected the results (i.e., self selection, noise bursts). Given these issues, a recent review concluded that, to date, it is not clear whether individuals with PTSD show impaired PPI responding or not (Kohl, Heekeren, Klosterkotter, & Kuhn, 2013).

AB is a cognitive paradigm that is thought to be linked to inhibitory processes by directing attentional resources to one target thereby affecting the processing of the subsequent target (Raymond et al., 1992). The AB effect refers to a deficit in the ability to identify the second target of a pair of stimuli presented closely in time. Participants are instructed to identify the targets that are separated by intervening distractors also referred to as a lag (L). Participants show high rates of identification of both targets with no intervening distractors between targets; however, the identification of the second target is reduced when one or two distractors are presented between targets. With more than two intervening distractors, participants are again able to identify both targets quickly. This is thought to happen because the presentation of two or more distractors allows the participant to recover from the impairment in attention. Hence, termed an “attentional blink.” Accordingly, when plotting accuracy of identification of the second target (T2), a u-shaped pattern emerges as a function of length of lag.

Cognitive models of AB that explain this U-shaped pattern of cognitive performance fall into two categories: early (Attentional Gating Model; Weighselgartner & Sperling, 1987; Inhibition Model, Raymond et al., 1992) or late selection (Two-Stage Processing Model; Chun & Potter, 1995, Interference Model; Shapiro, Raymond, & Arnell, 1994) in which both highlight the limitations in processing two targets close in time within a stream of stimuli. Early selection refers to the recruitment of attentional resources in the early stage of visual processing initiated by the processing resources involved in the identification of the first target that leads to poor identification of the second target, whereas with late selection, attentional resources are recruited by an item in the distractor position immediately following the first target leading to limited resources in processing the second target. Electro- and magneto-encephalography (EEG, MEG) studies have largely been more consistent with late selection (Vogel & Luck, 2002) than early selection theories (e.g., Giesbrecht, Bischof, & Kingstone, 2004), while others adopt a connectionist interpretation (Kessler et al., 2005), suggesting that inhibitory mechanisms may operate at multiple levels of perception. Consistent with this, Dux and Harris (2007) propose AB results from a general failure to inhibit distractors. Overall, AB measures the ability to direct attention to multiple stimuli and assess temporal processing, providing a solid cognitive index of inhibitory processing. Although AB has not been examined in PTSD, other inhibition-related disorders show deficits in AB. These include: schizophrenia (Wynn et al., 2006); attention deficit hyperactivity disorder (Li et al., 2004), and dysmorphic mood (Rokke, Arnell, Koch, & Andrews, 2002).

Interestingly, AB may reflect inhibitory processes similar to those seen in PPI. Specifically, Cornwell et al. (2006) examined the shared inhibitory properties of both AB and PPI tasks in a non-clinical sample. They found that the AB deficit occurred in Lag 2, and a correlation

with PPI occurred during this interval. As the magnitude of PPI with both target and distractor lead stimuli increased across participants, deficits in identifying the second target during the AB increased, suggesting similar inhibitory mechanisms underlying these tasks. Thus, the inhibitory processes in both paradigms may be functionally related such that PPI may reflect the strength of inhibitory processes required to protect the processing of a stimulus, and AB may indicate the rate of change in inhibitory processes over the temporal course of attention. The present study sought to replicate the functional association between PPI and AB and extend this association to a sample of individuals with chronic PTSD to further concretize both as similar, yet distinct, measures of inhibition.

In summary, there is a growing but mixed evidence that a deficit in inhibition may underlie impairment seen across executive functioning tasks in individuals with PTSD. Convergence across a psychophysiological task, prepulse inhibition, and cognitive task, attentional blink, may provide direct and converging indices of impaired inhibitory functioning in PTSD. In the present study, PPI was examined using white noise that was preceded by a tone, and AB was examined using a presentation of letters in a stream of numbers. Each task was conducted separately and employed neutral stimuli. The present study had three main goals. The first goal of the present study was to examine PPI and AB in a sample of individuals with chronic PTSD, compared to a trauma-exposed, no PTSD group and a healthy individuals control group. If PTSD is characterized as an inhibition-related disorder, then individuals with PTSD should exhibit reduced PPI and an increased delay in recovering from the distractor, that is an AB deficit, compared to trauma-exposed and healthy individuals. The second goal was to examine the functional relationship between two proposed measures of inhibition, PPI and AB. If PPI and AB reflect similar inhibitory processes, then impairment in PPI will correspond to a similar impairment in AB, whereby decreased PPI (i.e., less processing of the prepulse) will be associated with decreased AB (i.e., low accuracy scores/poor performance on the AB task). Finally, to better characterize inhibitory deficits in PTSD, the association between reduced PPI/AB and PTSD symptoms of avoidance, reexperiencing, and hyperarousal was examined. Based on the observed association between reduced PPI and greater severity of PTSD, reexperiencing, and hyperarousal symptoms (Grillon, 1996), reduced PPI and AB should be associated with higher PTSD symptoms, particularly reexperiencing and hyperarousal.

1.2 Method

1.2.1 Participants

Sixty-seven (22 men, 45 women) individuals participated in this study. All participants were recruited through community advertisements and local referrals, seeking research participants with PTSD, trauma exposure and no PTSD, and psychiatrically healthy controls. To assess initial eligibility, a trained research assistant utilized a brief, adapted standardized telephone screening regarding general psychological functioning and trauma exposure and related symptoms (Posttraumatic Diagnostic Scale; PDS; Foa, Cashman, Jaycox, & Perry, 1997). General inclusion criteria included: being between the ages of 18 and 65 and proficient in reading, writing, and speaking English. General exclusion criteria included: a current diagnosis of schizophrenia or delusional disorder; medically unstable bipolar

disorder; depression with psychotic features or depression severe enough to require immediate psychiatric treatment (e.g., actively suicidal); current diagnosis of alcohol/substance dependence within the previous three months; or below hearing and visual acuity thresholds.

All participants reported normal or corrected-to-normal visual acuity and hearing thresholds below 20 dB at 1 kHz. Hearing threshold was determined by presenting sounds (20, 40, 60 dB) at 1 kHz in both ears and instructing the participant to raise his/her hand upon hearing the sounds through the headphones. For audiometric screening, a threshold of identification of the 60 dB at 1k Hz frequency was used. No one was excluded based on these criteria.

Specific inclusion and exclusion criteria for PTSD, No PTSD, and healthy controls are detailed below. Sample characteristics are presented in Table 1.

PTSD group (PTSD)—The PTSD group was comprised of 28 individuals (6 men, 22 women) that were exposed to a DSM-IV traumatic event and met current DSM-IV criteria for primary, chronic PTSD using the Posttraumatic Symptom Scale-Interview Version (PSS-I; Foa, Riggs, Dancu, & Rothbaum, 1993) and the Structured Clinical Interview (SCID-IV; First, Spitzer, Gibbon, & Williams, 1994), to determine primary diagnosis and assess comorbidity. This assessment was conducted by a doctoral level clinician. Participants met criteria for other current disorders: 61% for major depressive disorder; 12% for substance abuse; and 21% for anxiety disorders. Sixty-one percent ($n = 17$) of the participants reported being on psychotropic medications, 21% ($n = 6$) were on hormonal birth control, 64% ($n = 18$) were regular coffee drinkers, and 21% ($n = 6$) reported they were smokers.

Trauma-exposed group (No PTSD)—The trauma-exposed group consisted of 20 individuals (7 men, 13 women) who reported experiencing a DSM-IV traumatic event but did not meet criteria for current PTSD. This was assessed initially using the Posttraumatic Diagnostic Scale (PDS; Foa, Cashman, Jaycox, Perry, 1997). Lack of current diagnostic status for PTSD was confirmed via the PSS-I and SCID-IV. This assessment was conducted by a doctoral level clinician. One participant met criteria for a co-occurring Axis I disorder (i.e., major depressive disorder). No other current diagnostic comorbidity was present. Thirty percent ($n = 6$) reported taking psychotropic medications, 17% ($n = 3$) were on hormonal birth control, 75% ($n = 15$) were regular coffee drinkers, and 10% ($n = 2$) reported they were smokers.

No psychopathology control group (Control)—The control group was made up of 19 individuals (9 men, 10 women) who did not report a history of Criteria A trauma exposure on the PDS and no current DSM-IV psychopathology based on the SCID-IV. This assessment was conducted by a trained research assistant. Further, to assure a no psychopathology control group, participants were excluded if they reported score higher than 10 on the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock & Erbaugh, 1961) and higher than 40 on both the state and trait subscales on the State-Trait Anxiety Inventory (STAI; Spielberger, 1988). Twenty-one percent ($n = 4$) of the participants were on a psychotropic medication, 21% ($n = 4$) were on hormonal birth control, 47% ($n = 9$) were regular coffee drinkers, and no one reported smoking.

1.2.2 Materials

Attentional blink—A visual presentation of AB was used (Raymond et al., 1992). The AB task was comprised of sequences with one or two targets (T) embedded in a stream of 16 to 20 distractors (D) referred to as rapid serial visual presentation (RSVP). The target set (T1, T2) consisted of uppercase letters (ACEJKRTY), and the distractor set consisted of eight Arabic numerals (23456789). Two sequences were used. First, to assess initial attention, in single-target identification, T1 was the only target for identification within the RSVP sequence. Second, to assess AB, in two-target identification, T1 was separated from T2 by 1, 2, 3, 4, or 5 serial positions, which was defined as the lag length (L1 - L5). Lag length, or stimulus onset asynchrony (SOA), was set at either 30, 60, or 120 ms between the target and the distractor.

AB presentation was controlled by Eprime software v 1.0 (Psychology Software Tools, Inc.) and presented on a 17-inch Dell monitor. All stimuli were presented in size 48 Time New Roman font, measuring 10 mm wide and 10 mm tall in a white font against a black background. The response keys on the computer keyboard were labeled to aid with identification. All the stimuli within the RSVP sequence were displayed for 16 ms, followed by a 25–30 ms interstimulus interval (ITI). Generation of the targets and distractors was similar to the paradigm used by Cheung, Chen, Chen, Woo, and Yee (2002). The distractors in the RSVP sequence were arranged in a random order, under the constraint that the same distractor could not appear in the previous four serial positions in the RSVP sequence. The letters were randomly drawn from the target set, and designated target 1 (T1) and target 2 (T2). No letter could appear more than once in a block of four consecutive sequences, and a distractor always followed T2.

The overall task consisted of 124 sequences, with two separate versions. The first four sequences involved practice trials, and the remaining 120 sequences were randomly generated and used toward data collection. The 120 sequences were made up of six lags with 20 trials per lag.

Prepulse inhibition of startle—An auditory prepulse inhibition of startle paradigm was used (Braff & Geyer, 1990). The startle stimulus consisted of a 50 ms burst of 105 dB noise with a 0 instantaneous rise/fall time. The prepulses consisted of 25 ms, non-startling tones (75 dB, 1000 Hz, 4 ms rise/fall times) at 30 ms, 60 ms, and 120 ms interstimulus intervals before the onset of the startle stimulus. These prepulse intervals were used because 30 ms and 60 ms are thought to reflect automatic, involuntary processes (Graham, 1975), and the 120 ms prepulse interval is thought to indicate strategic, voluntary processes (Filion, Dawson, & Schell, 1993). Intensity levels of the startle probes and non-startling tones were calibrated with a sound level meter.

The series of startle stimuli trials were presented either alone or were preceded by prepulses. There were four types of startle stimuli trials: 50 ms 105 dB noise burst presented alone; 50 ms 105 dB noise burst, followed after 30 ms by a 25 ms 75 dB tone; 50 ms 105 dB noise, followed after 60 ms by a 25 ms 75 dB tone; and a 50 ms 105 dB noise, followed after 120 ms by a 25 ms 75 dB tone. The four types of startle stimuli trials were repeated 20 times each, for a total of 80. The order of the four trial types was randomized with the constraint

that the same type of trial could not occur more than twice in succession. The recording session was initiated by a startle-alone trial on the first and last trial. Between trials or intertrial intervals, a time ranging from 15 s and 35 s (mean 25 s) elapsed. Eighty startle trials consisted of two blocks of 40 each, over a period of 20–30 min.

Physiological recording of orbicularis oculi electromyogram (EMG) was controlled by Coulbourn Instruments Labline LLC (Model v15–17) and acquired by Windaq software D1–720 v.2.72. A set of 4 mm, silver/silver chloride sensors (EMG) were placed below the left eye, directly below the pupil and 13 mm apart to measure contraction of the orbicularis oculi muscle, and a ground electrode was placed on the center of the forehead. EMG was filtered with a bandwidth of 100–1000 Hz and rectified with a 60 Hz notch filter to eliminate 60 Hz interference.

1.2.3 Interviews and Self-Report Measures

Structured clinical interviews—The Structured Clinical Interview for the DSM-IV (SCID-IV; First et al., 1994) is a semi-structured diagnostic interview that assesses PTSD symptoms severity and current psychopathology and functioning to evaluate primary Axis I diagnostic status. The SCID-IV was used to determine primary PTSD as well as to confirm lack of diagnostic status for the Control group. A previous version of the SCID shows good agreement ($K=.84-.4$, $M=.61$) for all disorders across a large number of samples (Segal et al., 1994). Interrater reliability via recordings of diagnostic interviews was conducted for 10% of the sample, with both presence of current mood disorders ($K = .73$) and other current anxiety disorders ($K = .86$) being acceptable.

Posttraumatic Symptom Scale-Interview Version (PSS-I; Foa, et al., 1993) is a brief, semi-structured interview that evaluates the presence of DSM-IV criteria A trauma and severity of 17 PTSD symptoms as defined by DSM-IV. It yields a total severity score, diagnostic status, and cluster scores for reexperiencing, avoidance, and hyperarousal symptoms. It shows high interrater reliability ($rs = .93-.95$; Foa & Tolin, 2000). For the current study, interrater reliability was assessed via recording of the diagnostic interviews in 10% of the sample, yielding excellent reliability ($ICC = .95$) for total severity.

Self-report measures—Self-report instruments were collected across anxiety, depression, cognitive ability, dissociation as possible variables that may affect the relationship between inhibition and PTSD.

Posttraumatic Diagnostic Scale (PDS; Foa, Cashman, Jaycox, Perry, 1997) is a 49-item self-report measure that assesses DSM-IV Criteria A traumatic event status and subsequent PTSD symptoms. The measure yields both total severity and cluster scores of reexperiencing, avoidance, and hyperarousal. The measure was also used to assess trauma exposure in the No PTSD and Control groups. The total score shows fair convergent validity, sensitivity, and specificity of PTSD diagnoses with the SCID (Foa et al., 1997). In the present sample, internal consistency was excellent ($\alpha = .96$).

The Beck Depression Inventory (BDI; Beck & Steer, 1978) is a 21-item inventory that assesses cognitive and physical symptoms of depression. This instrument was used to

determine final exclusion for current depression in the Control group. The concurrent validity is also high, as demonstrated by agreement with clinician ratings ($r = .72$), and other depression scales ($r = .74$; Beck, Steer, & Garbin, 1988). The internal consistency in the present sample was excellent ($\alpha = .96$).

State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) is a measure that assesses anxiety as a temporary state (20 items) and as an enduring trait (20 items). The state subscale was used to assess participant's current level of anxiety, whereas trait anxiety was used to evaluate the participant's general level of anxiety. The state and trait subscales were used to evaluate final exclusion for current high levels of anxiety in the Control group. The STAI has high agreement with other measures of anxiety (e.g., Bieling, Antony, & Swinson, 1998). Internal consistency for the present sample was high for both state ($\alpha = .97$) and trait anxiety ($\alpha = .97$).

The Dissociative Experiences Scale (DES; Bernstein & Putnam, 1986) is a 28-item self-report inventory that indexes the frequency of dissociative experiences. DES was scored using the mean score. DES was used to evaluate participant's disturbances in awareness and cognition. It shows excellent convergent validity with other self-report and interview measures of dissociation and good construct validity ($r = .70$, Bernstein & Putnam, 1986). Internal consistency for the present sample was high ($\alpha = .91$).

The Shipley Institute of Living Scale (Shipley, 1967) is a 60-item questionnaire that assesses cognitive functioning in areas of verbal intelligence and abstract reasoning ability. Scores from the verbal intelligence and abstract reasoning subscales were used to calculate a composite score. The full scale demonstrates fair to good test-retest reliability ($r = .62 - .82$; Kaufman, 1990). In the present study, internal consistency across verbal intelligence and abstract reasoning was good ($\alpha = .76$).

Means and standard deviations across groups are presented in Table 2. As would be expected, there were differences across psychopathology measures with the three groups, BDI: [$F(2, 64) = 110.95, p < .001, \eta^2 = .78$]; STAI-S [$F(2,63) = 39.63, p < .001, \eta^2 = .56$]; STAI-T [$F(2,64) = 60.65, p < .001, \eta^2 = .65$]; DES [$F(2,62) = 13.42, p < .001, \eta^2 = .30$]. Post-hoc comparisons using the Tukey HSD test showed individuals with PTSD reported more depressive symptoms, state anxiety, trait anxiety, and dissociation compared to those who were trauma-exposed and had no psychopathology.

1.2.4 Design

For examination of attentional blink, the present study utilized a 3 (Group: PTSD, No PTSD, Control) x 5 (Attentional blink lags: 1, 2, 3, 4, 5) mixed design, with attentional blink lag as the within-subjects variable. For examination of prepulse inhibition, the present study utilized a 3 (Group: PTSD, No PTSD, Control) x 3 (Lead Interval: 30 ms, 60 ms, 120 ms) mixed design, with lead interval as the within-subjects variable. The primary dependent variables were percent accuracy on AB and percent inhibition of startle response on PPI.

1.2.5 Procedure

Upon arrival, participants were seated in a sound-attenuated room. After obtaining informed consent, participants were administered appropriate structured interviews (SCID-IV; PSS-I) and completed self-report questionnaires (PDS, BDI, STAI-T, DES, Shipley). Next, the participant's vision and hearing were assessed after fitting the individual with Bose Triport headphones (Model TP-1A).

The order of administration of the PPI and AB tasks was counterbalanced. To set up the AB task, participants sat in a dimly lit room at a viewing distance of 35 cm away from the monitor. Next, participants were instructed to identify the letters and ignore the numbers from a stream presented in rapid succession. Participants were also told that a minimum of one letter and a maximum of two letters would be presented. Following the stream of letters and numbers, participants entered the target letters on the keyboard. If no second target was presented, participants pressed a key labeled 'NO' on the keyboard to ensure that participants were always entering two responses. Participants were able to control the pace of trials by pressing the space bar to initiate the next RSVP trial. Participants started with a practice block of four trials. Participants were also given a 1 min break halfway through the AB task.

For the PPI task, participants were oriented to psychophysiological monitoring procedures. Next, physiological monitoring sensors were attached. Once headphones were on the participants, a single startle trial was delivered through the headphone to orient them to the sound. After checking up on the participant, they were instructed on the task. Specifically, they were told they would hear soft and loud tones over the headphones and they were instructed not to say or do anything when hearing the sounds and to direct their attention to the silent video until the experimenter returned to the room. A silent video that showed various scenic panoramas and ran for the duration of the task was used to help improve participant attention (Ornitz & Pynoos, 1989) as the tones were presented binaurally through headphones.

After completion of both the AB and PPI, participants were thoroughly debriefed and compensated \$20/hour for their time.

1.3 Data Reduction and Data Analysis

Attentional blink

Single target trials and dual target trials were scored based on standardized scoring procedures (Raymond et al., 1992). For single target trials, percent accuracy for the first target was calculated. For dual target trials, the percent accuracy of T2 identification across lags on trials in which T1 was correctly identified was used to assess the main AB effect, reflecting the probability of T2 identification given accurate identification of T1. Accurate identification was defined as correct responding with the correct letters and order in the RSVP out of number of trials in the lag. For example, if T1 was "A" and T2 was "J", the correct responses were "A then J" and not "J then A".

Prepulse inhibition

The EMG responses in each type of trial were averaged across the 120 trials using Windaq Waveform Browser v. 2.22 (Dataq Instruments, OH). Startle magnitude on the no prepulse trials, or startle trials only, served as a reference and the startle magnitude on the prepulse trials, where the startle trials were preceded by prepulses was reduced. Startle and prepulse trials are used to compute percent startle modulation scores (Braff, Geyer, & Swerdlow, 2001). Startle responses were measured by the peak amplitude occurring 20 –120 ms after stimulus onset, relative to a 50 ms average baseline preceding probe onset (Balaban, Losito, Simon, & Graham, 1986). The baseline window was determined after calculating the mean of EMG during the interval of 50 ms before the stimulus onset. Although both percent and arithmetic difference scores have been utilized to obtain a full assessment of PPI (Braff, et al., 2001), proportion of difference is the method least affected by differences in control reactivity and, thus, was used (Blumenthal, et al., 2005). Prepulse inhibition magnitudes were defined by percent change scores from baseline ITI startle: $[(\text{mean prepulse startle} - \text{mean ITI startle}) / \text{mean ITI startle}] \times 100$. A negative prepulse inhibition score indicates that eyeblink activity was reduced in the paired stimulus condition, while a positive score indicates that eyeblink activity was increased.

Data screening

The assumptions of linearity and homogeneity of variance were met, and skewness and kurtosis were adequate. Across both AB and PPI, univariate outliers were screened to reduce outlier status. Outliers were detected using z-scores where values that fell outside the value range of + 3.94 (Field, 2008). Following recommendations by Tabachnick and Fidell (2001) that covariates should be correlated with outcome variables, demographic factors of gender, age, medication status, cognitive functioning, and smoking (“Do you smoke?”, “How many times have you smoked today?”) were examined as possible covariates. Covariates for AB were both age and number of times smoked on testing day, consistent with the association of attention and cognitive performance with age (Bornstein, 1983) and acute smoking (Evans & Drobos, 2009; Vrana, Calhoun, McClernon, Dennis; Lee, & Beckham; 2013). No covariates were identified for PPI. Accordingly, main analyses for AB used age and number of times smoked on testing day as covariates and main analyses for PPI used no covariates. To test the posthoc hypothesis of depression potentially driving the observed effects, depression (BDI) was added as a covariate to the analysis. For either AB or PPI, depression did not emerge as a significant covariate ($ps > .16$).

1.4 Results

1.4.1 Attentional Blink

Table 3 summarizes the means and standard deviations for percent accuracy on the single and dual target trials across groups. Repeated measures, analysis of covariance (ANCOVA) were conducted on the multiple outcome variables of AB (T1, T2, T3, T4, T5) across groups (PTSD, Trauma-exposed, Control), covarying for current age and number of times smoked.

Single target identification—Initial attention was examined by assessing performance on reporting a single target in the visual stream. There were no differences across groups on accuracy of single target identification within RSVP sequences.

Attentional blink: Dual trial identification—As can be seen in Figure 1, repeated measures (Group: PTSD, no PTSD, Control X Lag: 1, 2, 3, 4, 5) ANCOVAs revealed a Group x Lag quadratic effect, $F(2, 62) = 3.26, p = .05$. Breaking down this effect by group, there was a quadratic effect of time only for the Control group, $F(1, 17) = 7.63, p = .01$. Only the control group evidenced the expected quadratic AB pattern of responses, with differences between Lag 1 and 2 ($d = 1.15$), Lag 1 and 3 ($d = 0.72$), Lag 1 and 4 ($d = 0.49$) but not between Lag 1 and 5 ($d = 0.05$). This quadratic effect was not significant for either the PTSD, $F(1, 25) = 2.49, p = .13$ (Lag 1 & 2: $d = .96$; Lag 1 & 3: $d = .79$; Lag 1 & 4: $d = .47$, Lag 1 & 5: $d = 0.33$), or no PTSD group, $F(1, 17) = 0.81, p = .38$ (Lag 1 & 2: $d = 1.77$; Lag 1 & 3: $d = 1.55$; Lag 1 & 4: $d = 0.92$; Lag 1 & 5: $d = 0.42$). Thus, for individuals with trauma exposure (PTSD, trauma exposed No PTSD), the expected AB pattern of responding was not found.

1.4.2 Prepulse Inhibition

Table 3 also shows the means for baseline startle responses and percent PPI across lead intervals and groups.

Baseline startle—A set of one-way ANOVA was conducted to compare PTSD, No PTSD, and Control groups on baseline startle responses and PPI. Specifically, as can be seen in Table 3, there were no differences across groups on startle responses at baseline.

Effects of lead stimulus—To examine the effects of short-lead interval (30, 60, 120 ms) on PPI, a multivariate analysis was conducted comparing PTSD, No PTSD, and Controls. As can be seen in Table 3, for the 30-ms interval, there was a main effect of Group, $F(2, 64) = 4.09, p = .02$, with individuals with PTSD showing less inhibition than the Control group ($d = 0.80$) and a trend toward less inhibition than the trauma-exposed No PTSD group ($p = .05, d = 0.59$). For the 60-ms interval, there was also a main effect of Group, $F(2, 64) = 3.16, p = .05$, with individuals with PTSD showing less inhibition than both the No PTSD ($d = 0.63$) and the Control group ($d = 0.62$).

For the 120-ms lead interval, there was no effect of Group, $F(2, 64) = 1.27, p = .29$, with individuals with PTSD showing no difference from either the No PTSD ($d = 0.01$) and the Control group ($d = 0.48$). See Figure 2 for the magnitude of PPI represented by percent change from mean baseline startle response magnitude across groups. Taken together, this suggests that PTSD psychopathology, not just trauma exposure, had negative effects on PPI, specifically early stages of stimulus processing but not later stages.

1.4.3 Association between AB and PPI

The relationship between these measures of inhibition was examined in a series of Pearson correlations. As can be seen in Table 4, there was no strong relationship between AB and PPI. Specifically, less inhibition in PPI was marginally associated with greater accuracy on

Lag 1 of AB, $r = -.21$, $p = .08$, potentially suggesting that less inhibitory processes are necessary in processing a relatively easy task of two letters placed right after each other.

1.4.4 Association Among Psychopathology, AB, and PPI

The individual difference variables, PTSD severity (total, cluster), depression, trait anxiety, and dissociation were examined with a series of Pearson correlations with AB and PPI indices, using Holm step down procedures to control for multiple comparisons.

PTSD symptoms—As shown in Table 5, for AB, none of the associations reached significance, though there was a trend toward having higher levels of reexperiencing symptoms being associated with less accuracy on identification of the second target at Lag 2. For PPI, higher PTSD severity was associated with reduced inhibitory processing for automatic processing at 30 ms, with similar trends being seen for re-experiencing and avoidance symptoms. Finally, there were also trends for reexperiencing being associated with impairments in strategic processes up to 120 ms.¹

Depression, anxiety, and dissociation—As seen in Table 5, there were no strong associations among these measures of psychopathology, AB and PPI.

1.5 Discussion

Compared to trauma-exposed and healthy individuals, individuals with chronic PTSD exhibited impairment in attending to relevant from irrelevant information in prepulse inhibition of startle responses, potentially implicating a faulty inhibitory mechanism that facilitates intrusion of irrelevant sensory information and increases demands on attentional allocation. The faulty information processing in these individuals was associated with PTSD severity. Consistent with Grillon et al. (1996), specifically, greater severity of PTSD was associated with reduced inhibition in PPI, pointing to the chronic nature of the disorder in potentially weakening inhibitory processes. This dysfunction in inhibition was also evidenced in attention on the attentional blink task. Although healthy individuals exhibited the typical u-shaped pattern showing recovery from impairment in attention in AB, both PTSD and trauma-exposed individuals did not show this pattern, suggesting a role of both trauma exposure and subsequent PTSD in impairment in attention. Unlike Cornwall et al. (2006), there was only weak evidence of a functional relationship between AB and PPI, with reduced inhibition associated with greater accuracy in the interval before the AB effect. Taken together, findings from both modalities potentially point to evidence of a faulty inhibitory mechanism underlying the information processing deficits in PTSD or trauma exposure in general.

The PPI deficits observed in PTSD are consistent with the burgeoning literature on inhibitory dysfunction in PTSD (e.g., McFarlane, Weber, & Clark, 1993; Vasterling, Brailey, Constans, & Sutker, 1998); and, in contrast, with findings in depression and ADHD

¹To further examine the role of PTSD severity, we reran these correlations including both the PTSD and no PTSD groups ($n = 48$). Including the trauma exposed, no PTSD group attenuated observed correlations, with none of the associations approaching significance even before family-wise correction.

where no alterations are consistently found (Kohl et al., 2013). Specifically, the differences were evident in the 30 and 60 ms lead intervals or automatic processes but not the 120 ms lead interval or voluntary, controlled processes. This is in accord with findings by Grillon et al. (1996) using PPI and Kanagaratnam and Asbjornsen (2007) using a Stroop measure on automatic processing. Thus, individuals with PTSD may be deficient in automatic, early sensory processing compared to trauma-exposed and healthy individuals. This pattern of findings is consistent with sensorimotor gating abnormalities associated with impaired mental flexibility and perceptual disorganization (Braff & Freedman, 1999).

Relative to healthy controls, both PTSD and trauma-exposed individuals did not exhibit the u-shaped pattern typically observed in AB, suggesting trauma exposure is associated with impairment in this form of attention. That is, trauma exposed individuals with and without PTSD did not recover from an impairment of attention in the same way as non-trauma exposed individuals. Interestingly, impaired target detection in AB has been related to anxiety, but not depression, positive affect, or negative affect (e.g., Alderman et al., 2015; Van Dam, Earleywine, & Altarriba, 2012). This observed impairment in attention is consistent with a growing animal literature that suggests the deleterious effects from trauma exposure alone on cognitive functioning (e.g., George, Rodriguez-Santiago, Riley, Abelson, Floresco, & Liberzon, 2015). The localization of this impairment to trauma exposure rather than PTSD per se has also been found on attentional neuropsychological measures and sustained attentional tasks (e.g., Koenen, Driver, Oscar-Berman, Wolfe, Folsom, Huang, et al. 2001; Stein, Kennedy, & Twamley, 2002). One explanation for varying effects across trauma exposure and PTSD may be that individuals with PTSD may have simply experienced a higher dose of trauma exposure (e.g., McNally, 2003; Kanagaratnam & Asbjornsen, 2007; Mollica, McInnes, Poole, & Tor, 1998; Neuner, Schauer, Karunakara, Klaschik, Robert & Elbert, 2004). Indeed, the absence of strong correlations between AB and PTSD symptomatology and differential pattern of trauma exposure across the PTSD and no PTSD groups is further consistent with this interpretation for AB.

Given the usage of neutral stimuli, the converging data from PPI and AB suggests that cognitive processing deficits may be from a more fundamental inhibitory deficit rather than a dysfunction in processing trauma-specific stimuli alone. Although both PPI and AB show evidence for inhibitory effects, this study did not find an association between these paradigms. This is in contrast to Cornwell et al. (2006) who found initial evidence for an underlying association between PPI and AB. This may be due to differences in sample (clinical vs. non-clinical), task characteristics (task-based vs. passive PPI paradigm), or methods (combined task vs. separate tasks). Nevertheless, this discrepancy argues for further understanding the underlying constructs of these tasks and tighter terminology when defining specific cognitive processes (Friedman & Miyake, 2004; Horner & Hamner, 2002). The divergent findings across PPI and AB point to PTSD being more closely linked to a dysfunction in early sensory gating or lower level attentional processes (e.g., Grillon et al., 1996) and trauma exposure being more associated with deficits in higher-level attentional processes (e.g., Stein, Kennedy, & Twamley, 2002). Some have argued that PPI and AB differ in function such that PPI is a protective mechanism that protects limited capacity systems from being overloaded with incoming sensory information (e.g., Graham, 1979) and AB represents a limitation in our attentional system from processing multiple stimuli

(Raymond et al., 1992; Raymond, & Arnell, 1994).² Indeed, this distinction between paradigms is consistent with the overall pattern of findings and a review of executive functions in PTSD that reported “subtle” deficits in executive control functions of inhibiting automatic responses and regulating attention in PTSD (Aupperle, Melrose, Stein, & Paulus, 2012).

A couple of limitations should be noted. First, a comparison group to isolate the inhibitory effects from the presence of general psychopathology was not included, such as might be seen in obsessive-compulsive disorder or depression where intrusive thoughts are also present. Related to this, it is still unknown to what extent the PPI findings are specific to PTSD or affected by the presence of co-occurring disorders, such as depression. Indeed, symptom heterogeneity in PTSD common is PTSD (e.g., Zoellner, Pruitt, Farach, & Jun, 2014), and depression and PTSD commonly co-occur (e.g., Rytwinski et al., 2013). In the present study, secondary symptomatology measures (depression, anxiety, dissociation) were only modestly associated with AB or PPI. When depression was added as a covariate in the analyses, it was not significant. Nevertheless, the role of altered information processing due to these factors cannot be eliminated without additional controls. In addition, the trauma-exposure effects seen in AB may reflect residual impairments associated with a prior history, but not current presence, of psychopathology. Related, a prior diagnosis could potentially affect current inhibitory processes in AB and PPI, however, the No PTSD and no psychopathology control groups consistently separated themselves from the PTSD group on psychopathology measures and on AB and PPI tasks, arguing that they did serve as no psychopathology controls. Finally, trauma-specific content during the AB or PPI tasks was not examined; and thus, the present study was not able to ascertain differential effects between content independent and dependent inhibitory deficits. Indeed, these attentional deficits in PTSD extend to AB paradigms that employ trauma stimuli (Amir, Taylor, Bomyea, & Badour, 2009; Schonenberg & Abdelrahman, 2013; Olatunji, Armstrong, McHugo, & Zald, 2013).

Taken together, the findings underscore the importance of content-independent inhibitory deficits in PTSD and trauma exposure in general. There is a convergence across PPI and AB paradigms that a general inhibitory deficit is present and may be associated with the inability to regulate symptoms in PTSD. Future research needs to examine these deficits over time, using both prospective pre-trauma exposure designs as well as treatment designs to differentiate if this is an underlying mechanism of the disorder.

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Highlights

- Inhibitory deficits such as seen in prepulse inhibition and attentional blink may underlie cognitive abnormalities in PTSD
- Deficits in prepulse inhibition were more prevalent in trauma-exposed individuals with PTSD compared to those without PTSD and healthy controls
- Deficits in attentional blink were more prevalent in both trauma-exposed with and without PTSD compared to healthy controls
- Prepulse inhibition and attentional blink were not strongly associated
- These findings suggest a general faulty inhibitory mechanism associated with trauma exposure and PTSD

Figure 1.
Dual-Target Performance in PTSD, Trauma-exposed, and Healthy Controls.

Figure 2. Percent change of PPI in PTSD, Trauma-exposed, and Healthy Controls. Error bars reflect standard errors.

Table 1

Sample Characteristics

	PTSD (<i>n</i> = 28) <i>M</i> (<i>SD</i>)	No PTSD (<i>n</i> = 20) <i>M</i> (<i>SD</i>)	Control (<i>n</i> = 19) <i>M</i> (<i>SD</i>)
Age (years)	36.79 (12.88)	32.40 (13.65)	29.05 (13.87)
Education (years)	15.29 (3.47)	16.38 (2.60)	15.72 (1.99)
Gender (% female)	78.6	65.0	52.6
Criteria A Event			
Sexual Assault (%)	46.4	11.2	
Nonsexual Assault (%)	39.3	22.3	
Motor Vehicle Accident (%)	7.1	27.8	
Natural Disaster (%)	0.0	5.6	
Other (%)	7.1	33.3	
Time Since Event (years)	15.03 (13.98)	11.61 (9.39)	
Background			
Caucasian (%)	67.9	78.9	84.2
African-American (%)	17.9	5.3	0.0
Asian-American (%)	7.1	5.3	10.5
Other (%)	7.1	10.5	5.3
Cognitive Ability (Shipley)	61.54 (15.32)	63.63 (9.09)	65.82 (7.06)

Table 2

Psychopathology Measures Across Groups

	PTSD (<i>n</i> = 28) <i>M</i> (<i>SD</i>)	No PTSD (<i>n</i> = 20) <i>M</i> (<i>SD</i>)	Control (<i>n</i> = 19) <i>M</i> (<i>SD</i>)
PTSD Severity (PSS-SR)	29.07 (7.56)		
Reexperiencing	7.96 (2.78)		
Avoidance	11.50 (3.68)		
Hyperarousal	9.61 (2.18)		
PTSD (PDS)	30.43 (8.49)	1.73 (1.87)	
Depression (BDI)	27.05 (9.10) _a	4.55 (4.66) _b	1.42 (2.24) _c
Trait Anxiety (STAI-T)	59.93 (11.08) _a	36.93 (10.20) _b	30.74 (6.36) _c
Dissociation (DES)	14.01 (10.73) _a	4.86 (4.76) _b	3.40 (3.67)

Note. Differing subscripts across rows reflect significant differences between groups ($p < .05$). PSS-SR = Posttraumatic Symptom Scale-Self-Report Version; BDI = Beck Depression Inventory; STAI-T = State-Trait Anxiety Inventory; DES = Dissociative Experiences Scale.

Table 3

Summary of AB and PPI Means Across Groups

	PTSD (<i>n</i> = 28) <i>M</i> (<i>SD</i>)	No PTSD (<i>n</i> = 20) <i>M</i> (<i>SD</i>)	Control (<i>n</i> = 19) <i>M</i> (<i>SD</i>)
Attentional Blink			
Single Target Only	.85 (.24)	.86 (.19)	.84 (.22)
T2 Interval			
Lag 1	.93 (.09)	.95 (.08)	.95 (.04)
Lag 2	.77 (.19)	.69 (.25)	.79 (.14)
Lag 3	.79 (.21)	.75 (.23)	.88 (.08)
Lag 4	.87 (.13)	.85 (.17)	.91 (.08)
Lag 5	.89 (.12)	.91 (.15)	.96 (.08)
Prepulse Inhibition (%)			
Baseline startle (<i>μV</i>)	33.96 (44.66)	10.37 (14.11)	9.40 (6.46)
Lead Stimulus (<i>μV</i>)			
30 ms (%)	−28.98 (23.93)	−43.45 (25.13)	−46.92 (26.01)
60 ms (%)	−32.36 (25.91)	−48.71 (25.87)	−48.96 (27.81)
120 ms (%)	−31.77 (30.93)	−32.29 (39.28)	−46.31 (29.12)

Note. Unadjusted means are presented.

Table 4

Pearson Coefficients between Measures of Inhibition

	1.	2.	3.	4.	5.	6.	7.
AB							
1. Lag 1							
2. Lag 2		.29*					
3. Lag 3		.24	.75*				
4. Lag 4		.01	.51*	.72*			
5. Lag 5		.02	.42*	.60*	.86*		
PPI (%)							
6. 30 ms (%)	-.04	.18	-.07	.02	-.09		
7. 60 ms (%)	-.21	.14	-.06	.09	.05	.75*	
8. 120 ms (%)	-.18	-.11	-.01	.10	.03	.65*	.71*

* $p < .05$.

Table 5

Pearson Coefficients of AB, PPI, and Psychopathology

	PTSD Severity (PSS-SR) [†]			Anxiety (STAI-T)	Dissociation (DES)
	Total	Reexp.	Avoid.	Depression (BDI)	
AB (%)					
Lag 1	-.26	-.22	-.21	-.18	-.22
Lag 2	-.22	-.44	-.07	-.07	-.04
Lag 3	-.07	-.21	-.04	.06	-.19
Lag 4	-.08	-.19	-.11	.10	-.14
Lag 5	.11	-.09	.09	.23	-.14
PPI (%)					
30 ms (%)	-.53*	-.47	-.44	.17	.22
60 ms (%)	-.29	-.45	-.10	-.17	.27
120 ms (%)	-.33	-.48	-.22	-.10	.10

n = 28 for PTSD sample only.* Adjusted *p* < .05 based on Holm-Step Down procedure, controlling for family-wise error.