Journal of Anxiety Disorders 37 (2016) 94–103

Contents lists available at ScienceDirect

Journal of Anxiety Disorders

An analysis of inhibitory functioning in individuals with chronic posttraumatic stress disorder

Aileen M. Echiverri-Cohen*, Lori A. Zoellner, William Ho, Jawad Husain[1]

Department of Psychology, University of Washington, Seattle, Washington, USA

ARTICLE INFO

Article history:
Received 22 March 2015
Received in revised form
29 November 2015
Accepted 3 December 2015
Available online 10 December 2015

Keywords:
Inhibition
Attentional blink
Prepulse inhibition
Posttraumatic stress disorder

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.

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, 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, Southwick, Johnson, Yehuda, & Charney, 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 et al., 1998, 2000; MacDonald, Cohen, Stenger, & Carter, 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 over-activated 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, Elzinga, Schmahl & Vermetten, 2011).

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 (Cornwell, Echiverri, & 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

* Corresponding author at: Harbor-UCLA Medical Center, 1000 W. Carson St., Torrance, CA 90502, USA.
E-mail addresses: aileen2@uw.edu (A.M. Echiverri-Cohen), zoellner@uw.edu (L.A. Zoellner), willh21@uw.edu (W. Ho), jawadh@bu.edu (J. Husain).
[1] Current address: Boston University School of Medicine, USA.

http://dx.doi.org/10.1016/j.janxdis.2015.12.002
0887-6185/

processing and voluntary, controlled, attentional processing. PPI has been shown to follow different time courses, such that automatic processing occurs before 120 ms (Wynn, Dawson & Schell, 2004) 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., Giakoumaki, 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 et al., 1996). A growing number of studies report no differences in PPI across PTSD and control groups (Butler et al., 1990; Grillon, Morgan, Davis, & Southwick, 1998b; Holstein, Vollenweider, Jancke, Schopper, & Csomor, 2010; Morgan, Grillon, Lubin, & Southwick, 1997; Lipschitz 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 and 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, Shapiro, & Arnell, 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; Weichselgartner and 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 magnetoencephalography (EEG and 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 distracters. 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, Breitmeyer, Nuechterlein, & Green, 2006); attention deficit hyperactivity disorder (Li, Lin, Chang, & Hung, 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.

2. Method

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