Journal of Psychiatric Research 63 (2015) 75–83

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

Brain and behavioral evidence for altered social learning mechanisms among women with assault-related posttraumatic stress disorder

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ARTICLE INFO

Article history:
Received 19 September 2014
Received in revised form
30 January 2015
Accepted 5 February 2015

Keywords:
PTSD
Assault
fMRI
Reinforcement learning
Trust
Social deficits

ABSTRACT

Current neurocircuitry models of PTSD focus on the neural mechanisms that mediate hypervigilance for threat and fear inhibition/extinction learning. Less focus has been directed towards explaining social deficits and heightened risk of revictimization observed among individuals with PTSD related to physical or sexual assault. The purpose of the present study was to foster more comprehensive theoretical models of PTSD by testing the hypothesis that assault-related PTSD is associated with behavioral impairments in a social trust and reciprocity task and corresponding alterations in the neural encoding of social learning mechanisms. Adult women with assault-related PTSD (n = 25) and control women (n = 15) completed a multi-trial trust game outside of the MRI scanner. A subset of these participants (15 with PTSD and 14 controls) also completed a social and non-social reinforcement learning task during 3T fMRI. Brain regions that encoded the computationally modeled parameters of value expectation, prediction error, and volatility (i.e., uncertainty) were defined and compared between groups. The PTSD group demonstrated slower learning rates during the trust game and social prediction errors had a lesser impact on subsequent investment decisions. PTSD was also associated with greater encoding of negative expected social outcomes in perigenual anterior cingulate cortex and bilateral middle frontal gyri, and greater encoding of social prediction errors in the left temporoparietal junction. These data suggest mechanisms of PTSD-related deficits in social functioning and heightened risk for re-victimization in assault victims; however, comorbidity in the PTSD group and the lack of a trauma-exposed control group temper conclusions about PTSD specifically.

1. Introduction

There have been considerable efforts to understand the cognitive and neural mechanisms mediating posttraumatic stress disorder (PTSD) symptoms in order to boost treatment efficacy and ameliorate the poor quality of life associated with PTSD. Neurocircuitry models of PTSD (Rauch et al., Aug 15 20 06; Shin et al., Jul 2006; Admon et al., Jul 2013; Pitman et al., Nov 2012) have focused on identifying the neural mechanisms that mediate the clinical and behavioral observations of hypervigilance for threat and impaired fear extinction/fear inhibition. These models have ample empirical support and powerfully explain critical phenomena among PTSD populations. For example, hyperactive amygdala (Patel et al., Oct 2012; Rauch et al., May 1 2000) and insular cortex responses (Aupperle et al., 2012) during threat processing and anticipation explain attentional bias towards threat (Cisler et al., Jul 2011) and heightened interoceptive monitoring (Aupperle et al., 2012); altered structure and function of the hippocampus (Pitman et al., Nov 2012; Dannlowski et al., Feb 15 2012; Gilbertson et al., Nov 2002; Milad et al., Dec 15 2009; Admon et al., Aug 18 2009) explain the impaired ability to extinguish learned fear responses (Milad et al., Dec 15 2009; Wessa and Flor, Nov 2007; Jovanovic et al., Jul–Aug 2013; Norrholm et al., Mar 15 2011; Fani et al., Mar 2012; Milad et al., Jun 2008); weaker recruitment of perigenual anterior cingulate cortex (ACC) (Shin et al., Dec 15 2001; Shin et al., Mar 2005) explains observed deficits in emotion regulation (Moore

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http://dx.doi.org/10.1016/j.jpsychires.2015.02.014
0022-3956/

et al., Sep 2008; Tull et al., Sep 2007). While these neurocircuitry models represent mechanisms of hypervigilance for threat, fear extinction, and emotion regulation, they do not account for observed PTSD-related deficits in social domains.

A less widely-known literature (Messman-Moore and Brown, Jun 2006; Messman-Moore et al., Mar 2013; Walsh et al., Oct 2012; Yeater et al., Feb 2011; Yeater and Viken, Aug 2010) demonstrates significant deficits in risk perceptions for social situations among violence victims and individuals with PTSD. For example, one study found that the latency with which victimized women decided to escape hypothetical risky social situations escalating towards rape significantly predicted subsequent revictimization (Messman-Moore and Brown, Jun 2006). A related line of research has demonstrated both among adolescents (Cisler et al., Oct 2011) and adults (Cougle et al., May 2009) that greater baseline histories of assault exposure and PTSD symptoms prospectively predict increased rates of revictimization. These data suggest that 1) violence victims have *lower* danger perceptions of risky social situations, and 2) assaultive violence exposure and PTSD severity predict heightened risk for future victimization. Critically, both of these observations cannot be explained by existing neurocircuitry models of PTSD or trauma exposure. For example, given the known findings of amygdala hyper-reactivity and attentional bias towards threat, one would predict greater risk perceptions in social situations when in fact the opposite is observed.

We previously demonstrated among adolescent girls that assaultive violence exposure is associated with less behavioral slowing as well as decreased ACC and bilateral anterior insula responses to unexpected negative social behavior during a social contingency learning task (Lenow et al., Jul 30 2014). These preliminary data supported a hypothesis of altered social learning mechanisms among adolescent assault victims and ostensibly suggest mediating mechanisms to explain their decreased social risk perceptions and increased risk for revictimization. Here, we sought to elaborate this model by investigating the neural and cognitive mechanisms of altered social learning among adult women with assault-related PTSD. We assessed social learning behavior outside of an fMRI context using the trust game, a widely used neuroeconomic game that quantifies social trust based on monetary exchanges with another player. Multi-trial versions of the trust game (Belli et al., Oct 2012; King-Casas et al., Aug 8 2008; Krueger et al., Dec 11 2007; Unoka et al., Aug 2009) enable the study of dynamic interactions in social dyads (e.g., characterizing how one player responds when their investments are not reciprocated). We also characterized and compared social and non-social learning mechanisms during fMRI using two-arm variants of commonly used bandit tasks (Daw et al., Jun 15 2006; Behrens et al., Nov 13 2008; Behrens et al., Sep 2007). In these tasks, we manipulated the reward structure of task responses and used computational modeling to probe the neural correlates of the task components of value expectation, prediction errors, and volatility (i.e. uncertainty) (Behrens et al., Sep 2007; Rushworth and Behrens, Apr 2008). To isolate a hypothesized unique relationship between assault-related PTSD and neural encoding of these component mechanisms during social learning, we modeled these same components in a non-social learning task. This methodology and analytic approach enabled testing the hypothesis that assault-related PTSD is associated with altered behavioral and neural correlates of social learning. However, it is important to note that our control group included only women with no history of trauma or PTSD; accordingly, inferences cannot be derived regarding specificity of the findings for PTSD specifically (vs just assault exposure) or for assault specifically (versus general trauma exposure).

2. Methods

2.1. Participants and assessment

Forty adult women, aged 20–53, were enrolled in the study. Five additional women were screened, but were ineligible due to the presence of a psychotic disorder (among a woman with PTSD), a current mental health disorder (among control women), or assault exposure without a current diagnosis of PTSD. The PTSD sample was comprised of 25 adult women and the control sample was comprised of 15 women. Table 1 provides demographic and clinical characteristics of the sample. Inclusion criteria for the PTSD group were a history of directly experienced assault exposure and a current diagnosis of PTSD; exclusion criteria were the presence of psychotic disorders, a primary substance use disorder, or internal metal. Control participants were included based on female sex and

Table 1
Clinical and demographic characteristics of the sample.

Variable	PTSD (n = 25)		Control (n = 15)		*p* Value group difference
	Mean (or frequency)	*SD*	Mean (or frequency)	*SD*	
Age	34.7	8.3	30.87	7.1	.14
Ethnicity	64% Caucasian 32% African-American 4% Other	–	67% Caucasian 27% African-American 7% Other	–	.5
Education	8% not graduate high school 28% graduate high school or GED 64% some college or more	–	0% not graduate high school 13% graduate high school or GED 87% some college or more		.25
Days since last menstruation[a]	15.5	10.0	12.7	11.95	.48
Current Job	40% unemployed	–	7%		.02
PCL score	55.7	16.6	20.00	3.5	<.01
BDI-II score	22.8	14.1	2.4	2.3	<.01
Number of total direct assaults	6.3	2.6	0	0	<.01
Number of physical assaults from non-caregiver	2.4	1.5	–	–	–
Number of physical assaults from caregiver	1.6	1.5	–	–	–
Number of sexual assaults	2.4	1.4	–	–	–
Current Major Depressive Disorder	44%	–	0	–	.01
Current Generalized Anxiety Disorder	52%	–	0	–	<.01
Current PTSD	100%	–	0	–	<.01
Current Marijuana Dependence	4%	–	0	–	.43
Current Alcohol Dependence	16%	–	0	–	.10

[a] Refers to days since menstruation among women who regularly menstruate; 5 PTSD women and 1 control women either were not menstruating (e.g., menopause) or had irregular cycles (>80 days since last menstruation).