Potentiated Amygdala Response to Repeated Emotional Pictures in Borderline Personality Disorder

Supplemental Information

Table S1. Clinical Self-Report Ratings in Healthy Control, Borderline Personality Disorder, and Schizotypal Personality Disorder Groups

Scale	Healthy Controls			Borderline PD Patients			Schizotypal PD Patients			Healthy Controls vs. BPD Patients	BPD Patients vs. SPD Patients	Healthy Controls vs. SPD Patients		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	One Way 3-group ANOVA's, followed up by t tests: F, t, p-va				
Affective Intensity Measure	30	3.32	0.44	32	3.85	0.63	28	3.40	0.47	<i>F</i> (2,87) = 9.03, <i>p</i> < 0.001				
										t(60) = -3.78,	t(58) = 3.07,	NS		
										<i>p</i> < 0.001	<i>p</i> < 0.01			
Affective-Lability Scale	30	0.42	0.38	33	1.63	0.60	28	0.99	0.70	<i>F</i> (2,88) = 35.20, <i>p</i> < 0.01**				
										t(61) = -9.46,	t(59) = 3.83,	t(56) = -3.92,		
										<i>p</i> < 0.01***	<i>p</i> < 0.001	<i>p</i> < 0.001		
Barratt Impulsivity Scale	30	42.26	8.28	33	65.50	12.67	28	56.18	12.79	<i>F</i> (2,88) = 32.60, <i>p</i> < 0.01**				
										t(61) = -8.53,	t(59) = 2.85,	t(56) = -4.96,		
										<i>p</i> < 0.01***	<i>p</i> < 0.01	<i>p</i> < 0.01**		
Buss-Perry Aggression	30	42.96	6.55	33	66.17	11.86	28	53.40	11.22	<i>F</i> (2	2,88) = 41.01, <i>p</i> < 0.01 ³	**		
Questionnaire										t(61) = -9.48,	t(59) = 4.29,	t(56) = -4.37,		
										<i>p</i> < 0.01***	p < 0.01*	<i>p</i> < 0.01*		
Childhood Trauma	26	41.69	6.29	32	62.86	16.01	27	59.22	18.82	$F(2,82) = 15.95, p < 0.01^{**}$		**		
Questionnaire										t(56) = -6.35,	NS	t(51) = -4.51,		
										<i>p</i> < 0.01***		<i>p</i> < 0.01*		
Dissociative Experiences Scale	29	4.95	3.99	31	22.13	15.47	26	17.52	14.78	<i>F</i> (2	<i>F</i> (2,83) = 14.82, <i>p</i> < 0.01**			
										t(58) = -5.80,	NS	t(53) = -4.41,		
										<i>p</i> < 0.01***		p < 0.01*		

ANOVA, analysis of variance; BPD, borderline personality disorder; NS, non significant; PD, personality disorder; SPD, schizotypal personality disorder. **p* < 0.0001

^{**}*p* < 0.00001

****p* < 0.000001

Table S2. Brain regions in whole-brain analysis showing significant between-group differences in activation during unpleasant pictures. All regions in this table are significant, p < 0.05, corrected. We report the highest *Z*-score and the corresponding Talairach coordinates for that voxel within the region. For the amygdala clusters, we report the cluster size within the amygdala. For all other clusters, we report the contiguous cluster size.

		Cluster		Talaira	Talairach coordinates		
		Size	Z-		(mm)		
	Region	(voxels)	score	Х	Y	Z	
	SPD patients – Controls:						
	Left amygdala	34	2.49	-30	-2	-16	
Novel	Right amygdala	24	3.16	32	2	-16	
	SPD patients – BPD patients:						
	Left amygdala	84	3.30	-30	-6	-16	
	Right amygdala	58	2.96	24	-2	-12	
	BPD patients – Controls:						
	Right amygdala	54	3.51	32	2	-16	
	Left fusiform gyrus (BA 37)	924	4.13	-48	-56	-8	
	SPD patients – Controls:						
	Left amygdala	36	3.45	-30	0	-16	
Repeated	Right amygdala	37	3.71	30	2	-16	
	Right dorsolateral prefrontal cortex (BA 10)	3468	4.75	30	50	10	
	Right inferior parietal cortex (BA 40)	2308	2.28	-34	-42	38	
	Left fusiform gyrus (BA 37)	919	3.80	-16	-54	-26	
	BPD patients – Controls:						
	Left parahippocampal gyrus (BA 27)	2118	4.09	-6	-28	-8	
	Right fusiform gyrus (BA 37)	991	3.27	24	-50	-24	
	Right anterior cingulate (BA 24)	824	3.64	6	6	48	
Repeated – Novel	Right inferior frontal gyrus (BA 44)	804	3.72	36	2	30	
	BPD patients – SPD patients:						
	Left amygdala	28	2.61	-20	-2	-14	
	Right amygdala	52	3.32	30	-6	-22	
	Right dorsolateral prefrontal cortex	832	3.95	28	60	14	
	(BA 10)						

BA, Brodmann area; BPD, borderline personality disorder; SPD, schizotypal personality disorder.



Figure S1. Amygdala tracing methods. We employed our published methods for tracing the amygdala on each study participant's structural MRI scan (see 1). (A) Coronal magnetic resonance imaging (MRI): anterior-posterior dimension of amygdala. At this mid-section, the amygdaloid complex is roughly elliptical in shape, and anatomical margins are defined by the cornu ammonis and the white matter of gyrus ambiens in the medial aspect, the cornu inferius of the lateral ventricle in the ventral aspect, the temporal lobe white matter laterally, and the gyrus semilunaris in the dorsal aspect. (B) Using an edge contrast-enhancing technique (gradient filter) (1), we were able to better visualize the dentate gyrus of the hippocampus and boundaries between the hippocampus and the amygdala. Tracing procedure: the white line produced by the gradient filter is identified by mouse and the program finds the local maximum for the edge. Outlining of the amygdala began at its largest extent (approximately the center in the antero-posterior dimension) where clear boundaries between gray matter and surrounding white matter are visible and extended to the anterior and anterior ends of the amygdaloid complex. The posterior portions of the amygdaloid complex were outlined by using the ventricular recess, hippocampus, and gyrus semilunaris as reference points. Anteriorly, the amygdaloid complex gray matter is more heterogeneous and hard to identify. We outlined from the mid-section forward using gradient filtering and excluded the entorhinal cortex, which may include the inferior amygdala. The outlining ended at the first coronal MRI section on which there was visible white matter between the amygdala, ambiens, and white matter of the entorhinal cortex. This procedure may have omitted the very anterior end of the amygdaloid complex, but it had the advantage of excluding other extraneous structures from our analysis. (C) Traced amygdala is shown. The amygdala region-of-interest edges were coregistered to the echo planar image (EPI) for each participant (described in Methods) and the mean blood

oxygen level-dependent (BOLD) activation levels were determined for time epochs and conditions.

Scanning parameters: The T2 involved a Turbospinecho sequence (TE = 99 msec, TR = 5760, slice thickness = 3 mm/skip 1 mm, field of view (FOV) = 21 cm, matrix 256 x 256, 32 slices).

EPI images were acquired with a BOLD-EPI sequence (42-axial slices, 2.5 mm thick, skip = 0.8 mm (33%), TR = 3000 msec, TE = 27 msec, flip angle = 85° , FOV = 210 mm, matrix = 64 x 64).

For high-resolution-structural-images that allowed accurate anatomical tracing of the amygdala, we acquired T1-weighted structural magnetization-prepared rapid gradient echo (MP-RAGE) imaging (208 slices for whole brain; axial acquisition, 0.82 mm slice thickness, TR = 2500 msec, TE = 4.38 msec, TI = 1100 msec, flip angle = 8°, FOV = 210 mm, matrix size = 256 x 256 x 208).



Figure S2. Scatterplots show the correlational analysis between amygdala activation during the repeated unpleasant pictures and dissociative symptoms in borderline personality disorder (BPD) patients (Top graph) and schizotypal personality disorder (SPD) patients (Bottom graph). Among both patient groups, greater blood oxygen level-dependent (BOLD) activation during the repeated unpleasant pictures was associated with less severe dissociative symptoms.

International Affective Picture System (IAPS) Library Pictures

<u>Pleasant pictures</u>: 2154, 2310, 2224, 7508, 1710, 8470, 4623, 4626, 1340, 2339, 2332, 4533, 5831, 2303, 8499, 8300, 8600, 4645, 2150, 4603, 2306, 8380, 8420, 8210, 2040, 2345, 1920, 2398, 2209, 2550, 8502, 8370.

<u>Neutral pictures</u>: 7217, 2480, 2397, 7205, 7504, 2038, 2191, 2372, 7041, 2593, 2570, 9210, 2635, 7052, 2485, 5395, 7150, 2516, 7025, 7493, 2575, 2235, 2305, 7002, 2580, 7185, 2487, 2357, 2440, 7057, 2579, 7180.

<u>Unpleasant pictures</u>: 6561, 3180, 2205, 2455, 9426, 9429, 6836, 6250.1, 6821, 9440, 9430, 4621, 9424, 9220, 2053, 6560, 2700, 6838, 6315, 6562, 3230, 6840, 6370, 2490, 9007, 9417, 3300, 3181, 2694, 6212, 9050, 8485.

Supplemental Reference

1. Haznedar MM, Buchsbaum MS, Wei TC, Hof PR, Cartwright C, Bienstock CA, *et al.* (2000): Limbic circuitry in patients with autism spectrum disorders studied with positron emission tomography and magnetic resonance imaging. *Am J Psychiatry* 157:1994-2001.