

Supplementary Information

European Archives of Psychiatry and Clinical Neuroscience

Analysis of brain volumetry and functional connectivity during resting state in patients with Borderline Personality Disorder

Vera Flasbeck*, Björn Enzi, Georg Juckel, Martin Brüne

Corresponding author: Vera Flasbeck (email: vera.flasbeck@rub.de)

Ruhr University Bochum, LWL University Hospital Bochum, Department of Psychiatry, Psychotherapy and Preventive Medicine, Bochum, Germany

Extended Methods

Study procedure

The data reported here are part of a larger study on empathy for pain during fMRI scanning in patients with BPD presented previously [25]. After a brief screening for in-and exclusion criteria, sessions were scheduled to align with menstrual cycle phase or hormonal contraceptive use. For MRI safety, all participants were required to be free of MRI-unsafe metals and have tattoos without iron-oxide ink. The fMRI scanning consists of the T1-weighted anatomical scan, followed by fMRI recording while performing an empathy task and the resting state fMRI scanning. Additional assessments included a pressure-pain test (following scanning) and collection of saliva samples (data not shown here). Participants were compensated either with 30 € or 2.5 test subject hours (for psychology students, n=16 in the control group).

VBM and Functional connectivity quality control details

During quality control of VBM preprocessing, one patient was excluded due to a quartic mean Z-score of 2.65, all other scans had scores < 2.

During preprocessing of rs-fMRI functional connectivity, the effective degrees of freedom of the BOLD signal after denoising ranged from 8.2 to 40.7 (average 35.1) across all subjects.

Extended Results

Table S1: Demographic characteristics and psychometric questionnaire results of control participants and patients with BPD.

	HC group (n=54)	BPD group (n=49)	Statistics
Age (mean (SD)) ¹	24.3 (4.3)	24.8 (5.0)	$t(101)=-0.53, p=0.599, d=-0.10$
BMI ¹	22.7 (2.3)	25.8 (7.7)	$t(55.7)=-2.70, p=0.009, d=-0.56$
IQ* ¹	101.8 (12.2)	98.4 (11.0)	$t(101)=1.48, p=0.143, d=0.29$
Menstrual cycle day (mean (SD)) ¹	10.3 (4.5)	9.2 (4.3)	$(t(59)=0.993, p=0.325, d=0.255)$
Handedness* ¹ (mean (SD); frequency left/right/both)	74.7 (43.5); 49/4/1	60.6 (48.0); 41/6/2	$t(101)=1.57, p=0.120, d=0.31$
hormonal contraception ² (yes/no)	19/35	13/36	$\chi^2(1)=0.898, p=0.343$
Mother language ² (German/other/German+other)	37/10/5	44/3/2	$\chi^2(2)=5.58, p=0.062$
Marital status ² (single/divorced/relationship living together, relationship living apart/married)	32/0/10/11/1	30/1/8/10/0	$\chi^2(4)=2.10, p=0.718$
Education ² (Certificate of Secondary Education/General Certificate of Secondary Education/higher education entrance qualification/university degree/other)	0/1/36/17/0	5/15/25/2/2	$\chi^2(4)=32.91, p<0.001$
Nicotine use ² (no/low/high consumption)	51/3/0	21/9/19	$\chi^2(2)=34.34, p<0.001$
Psychometric questionnaires (mean (SD); median)³			
BSL-23 mean	0.2 (0.2); 27.6	2.2 (0.6); 78.9	$U=3.0, Z=-8.72, p<0.001$
CTQ emotional abuse	8.0 (3.7); 30.9	18.2 (5.5); 75.3	$U=182.0, Z=-7.56, p<0.001$
CTQ physical abuse	5.5 (1.9); 39.4	8.4 (4.5); 65.9	$U=644.5, Z=-5.31, p<0.001$
CTQ sexual abuse	5.2 (0.9); 42.8	9.3 (6.1); 62.8	$U=793.5, Z=-4.58, p<0.001$
CTQ emotional neglect	8.6 (3.9); 36.5	16.8 (4.4); 74.2	$U=233.0, Z=-7.22, p<0.001$
CTQ physical neglect	6.4 (2.5); 36.5	9.8 (3.8); 69.1	$U=484.0, Z=-5.70, p<0.001$
Total number of DSHI-items answered with yes	0.47 (0.99); 27.5	6.96 (2.91); 77.5	$U=24.5, Z=-8.81, p<0.001$

*Multiple Choice Vocabulary Intelligence Test; *Laterality quotient; ¹ differences between groups calculated by t-tests; ² differences regarding frequencies between groups calculated by chi-squared test; ³ differences between groups calculated by Mann-Whitney U tests.

BDI = Beck Depression Inventory; BSL-23 = Borderline Symptom List 23; CTQ = Childhood trauma questionnaire; DSHI = Deliberate-Self-Harm Inventory

VBM

The whole-brain voxel-based morphometry analysis of group differences showed significant grey matter reductions in patients with BPD compared to the controls group (see Table S2), when controlling for age, BMI and total intracranial volume. The contrast BPD > HC did not show any significant findings as well.

Table S2 Results from whole-brain VBM analysis using a *t*-test between patients with BPD and healthy controls, controlling for total intracranial volume, BMI and age. Data for the contrast HC > BPD are shown.

Brain region	Total cluster size (k)(extent region)	MNI (at peak), x, y, z	<i>t</i>	<i>Z</i>	<i>p</i> _{FWE} (peak)
Right superior frontal gyrus	154 (84)	20 29 47	6.184	5.659	<0.001
Right middle frontal gyrus	(70)	27 26 47	5.756	5.321	0.007
Left middle/superior frontal gyrus	59 (36/23)	-20 3 51	5.569	5.171	0.015
Left inferior frontal gyrus, pars triangularis/pars opercularis	11 (4/3)	-60 17 5	5.492	5.108	0.020
Left insula	15 (15)	-42 12 -3	5.430	5.058	0.025

Significant effects at $pFWE_{peak} < 0.05$ ($k \geq 10$). Displayed clusters also meet $pFWE_{cluster} < 0.05$.

When including age, BMI, TIV and additional education level and/or nicotine use, no suprathreshold clusters were found.

Functional connectivity

Inclusion of the additional covariates age, BMI, education level and nicotine use revealed one significant group difference for the connectivity of the right middle frontal gyrus with the right precentral gyrus (total cluster size 234 voxel at coordinate 50 -8 52, with $t = 4.52$, $\beta = 0.25$, $pFWE_{peak} = 0.013$, Fig. S1).

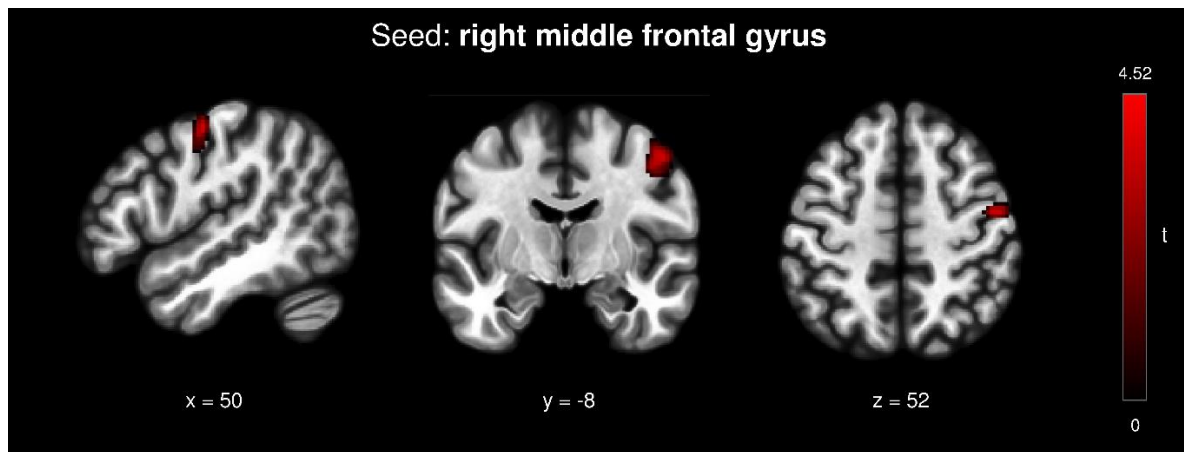


Fig. S1 Brain maps including t-values indicating significant different functional connectivity with the right middle frontal gyrus in patients with BPD vs. controls, controlling for age, BMI, education level and nicotine use.

Table S3 Significant results from correlation analyses between rs-FC of selected seeds with psychometric questionnaires in the whole sample and patients with BPD controlled for age, BMI, education level and nicotine use.

Seed region	Cluster size (k)	Brain region	MNI (at peak), x, y, z	p_{FDR} (cluster)	t	Effect size (beta)	direction
Childhood Trauma Questionnaire (total score)							
Whole sample							
Right superior frontal gyrus	313	Right cerebellum crus I/II	12 -88 -32	0.0039	4.59	0.0	positive
	191	bilateral frontal pole	2 68 14	0.026	4.61	0.01	positive
BPD group							
Right superior frontal gyrus	304	Right supplementary motor cortex	8 0 62	0.0015	-5.92	-0.01	negative
	221	Right lateral occipital cortex (superior division)/	36 -56 32	0.0056	5.00	0.01	positive
	151	Right frontal pole	10 62 36	0.0238	5.29	0.01	positive
	143	Right frontal pole	18 68 10	0.0238	5.32	0.01	positive
Right middle frontal gyrus	201	Left superior/middle frontal gyrus	-20 16 40	0.0006	-5.89	-0.01	negative
Borderline symptom list (mean)							
Whole sample							
Right middle frontal gyrus	165	Left orbitofrontal cortex	-32 22 -20	0.0381	5.17	0.1	positive
Deliberate-Self-Harm Inventory							
Whole sample							
Right middle frontal gyrus	600	Right pre and postcentral gyri	50 -4 44	0.00001	5.12	0.04	positive

Significant effects shown for $p_{FDR} < 0.05$ on cluster level. Only regions contributing most to the clusters are listed.