PERGAMON

Available online at www.sciencedirect.com
SCIENCE DIRECT®

Journal of Psychiatric Research 37 (2003) 109–115

JOURNAL OF PSYCHIATRIC RESEARCH

www.elsevier.com/locate/jpsychires

Positron emission tomography in female patients with Borderline personality disorder

F.D. Juengling[a,1], C. Schmahl[b,1], B. Heßlinger[b], D. Ebert[b], J.D. Bremner[c], J. Gostomzyk[d], M. Bohus[b,*], K. Lieb[b]

[a]*Department of Nuclear Medicine, PET group, University of Freiburg Medical School, Hugstetterstr. 55, D-79106 Freiburg, Germany*
[b]*Department of Psychiatry and Psychotherapy, University of Freiburg Medical School, Hauptstr. 5, D-79104 Freiburg, Germany*
[c]*Departments of Psychiatry and Behavioral Sciences and Radiology, and Center for Positron Emission Tomography, Emory University School of Medicine, Atlanta, GA, and Atlanta VAMC, Decatur, GA, USA*
[d]*Department of Psychiatry, University Hospital Ulm, Leimgrubenweg 12-14, 89075 Ulm, Germany*

Received 2 May 2002; received in revised form 19 July 2002; accepted 14 October 2002

Abstract

The pathology of Borderline personality disorder (BPD) is poorly understood and its biological basis remains largely unknown. One functional brain imaging study using [^{18}F]Deoxyglucose-PET previously reported frontal and prefrontal hypometabolism. We studied brain metabolism at baseline in 12 medication-free female patients with BPD without current substance abuse or depression and 12 healthy female controls by [^{18}F]Deoxyglucose-PET and statistical parametric mapping. We found significant frontal and prefrontal hypermetabolism in patients with BPD relative to controls as well as significant hypometabolism in the hippocampus and cuneus. This study demonstrated limbic and prefrontal dysfunction under resting conditions in patients with BPD by FDG-PET. Dysfunction in this network of brain regions, which has been implicated in the regulation of emotion, may underlie symptoms of BPD.

Keywords: Borderline Personality Disorder; Positron Emission Tomography; Limbic system; Prefrontal Cortex

1. Introduction

Borderline personality disorder (BPD) is a persistent and severe mental disorder characterized by patterns of instable interpersonal relationships, self-image, affects, and marked impulsivity that begins in early adulthood and is present in a variety of different contexts throughout adult life (American Psychiatric Association, 2000). Most researchers currently agree that a dysfunction of the emotional regulation system is a core component of the disorder (Linehan, 1993; Silk, 2000; Corrigan et al., 2000; Herpertz et al., 1999; Stiglmayr et al., 2001). Currently, the etiology of BPD is poorly understood and its biological basis remains largely unknown. Preclinical research has revealed a network of regions involved in emotional regulation including prefrontal cortex, hippocampus, and amygdala (Davidson et al., 1999). The amygdala play a decisive role in the regulation of fear (Davis, 2001) and the hippocampus is involved in fear responses to the context of a stressful situation (Phillips and Le Doux 1992). Prefrontal cortex also regulates emotion and stress responses, including impulse control, inhibition of responses to external stimuli, and extinction of fear responses.

The crucial function of these brain regions in the expression and modulation of emotion and impulsivity in both animals and humans has led to the hypothesis that dysfunctions in these regions may underlie some of the psychopathological symptoms seen in patients with BPD. One functional brain imaging study employing [^{18}F]Deoxyglucose positron emission tomography (FDG-PET) under resting conditions revealed decreased metabolism in premotor and prefrontal areas, the anterior part of the cingulate cortex, and the thalamic, caudate and

* Corresponding author. Tel.: +49-761-270-6822; fax: +49-761-270-6619.
E-mail address: martin_bohus@psyallg.ukl.uni-freiburg.de (M. Bohus).
[1] Both authors contributed equally to this work.

0022-3956/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0022-3956(02)00084-5

lenticular nuclei, in BPD patients as compared to controls (De la Fuente et al., 1997). In a pilot fenfluramine challenge study in five BPD patients and eight controls, Soloff et al. (2000) found greater FDG uptake in response to fenfluramine in medial and orbital regions of right prefrontal cortex (area 10), left middle and superior temporal gyri, left parietal lobe, and left caudate body in the control participants. There were no areas in which patients with BPD had greater relative regional uptake than controls. Herpertz et al. (2001) found elevated fMRI BOLD signals in the amygdala and prefrontal cortex of patients with BPD but not of controls during the presentation of emotionally aversive pictures of the International Affective Pictures System (IAPS).

In the present study, we compared brain metabolism in patients with BPD in comparison to normal controls using FDG-PET under resting conditions. Since there is only one published study to date investigating baseline brain metabolism in BPD, we aimed at replicating the results of De la Fuente et al. (1997). Based on the preclinical studies and preliminary PET studies in BPD cited above we hypothesized alterations in function in prefrontal cortex, anterior cingulate, and hippocampus in BPD.

2. Methods

2.1. Patients

Twelve female patients fulfilling DSM-IV as well as DIB-R (Zanarini et al., 1989a) criteria for BPD (score $\geqslant 8$) were recruited at the Department of Psychiatry and Psychotherapy/University of Freiburg Medical School. All patients had been referred to participate in an inpatient treatment program for BPD. All patients had been free of psychotropic medication for at least 4 weeks. Diagnosis of BPD was assessed using the appropriate segment of the Structured Clinical Interview for DSM-IV Personality Disorders (First et al., 1995). Axis I disorders were assessed by use of the structured clinical interview for DSM-IV Axis I Disorders (Spitzer et al., 1995) or by use of the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998). Patients with a lifetime diagnosis of schizophrenia, bipolar I disorder, alcohol or drug abuse within the past 6 months, or current anorexia or major depression were excluded. Four patients had current comorbid dysthmia, two panic disorder, two agoraphobia, three social phobia, three obsessive-compulsive disorder, three posttraumatic stress disorder (PTSD), and two bulimia. In addition to the interview, depression was self-assessed by the patients using Beck's Depression Inventory (Beck et al., 1961). Only patients who had successfully finished regular schooling in the German system were included. PET measurements in patients with BPD were compared to 12 healthy female controls who were recruited by newspaper advertisement. The controls were free of lifetime psychiatric disorders and reported no psychiatric disorders in their first degree relatives. Mean age in the patient group was 25 ± 4 years (range 18–32 years), mean age in the control group was 30 ± 9 years (range 18–39 years). There was no significant group difference in mean age between patients and controls (two tailed t-test; $P = 0.131$). Written informed consent was obtained before participation in the study. The experiments were performed in accordance with the Helsinki Declaration of 1975. The protocol was approved by the local Ethical Committees.

2.2. Positron emission tomography

The PET procedure was performed according to previously defined standards (Juengling et al., 1999; Juengling et al., 2000). In brief, the patients were allowed to rest for at least 10 min before injection of 200 ± 20 MBq 18-FDG and during the uptake period for another 20 min in an acoustically isolated and dimmed room. The patients were then transferred to the scanner (Siemens CTI ECAT EXACT tomograph, 10.8 cm FOV, 6.8 mm FWHM), where the patients' heads were positioned according to the orbitomeatal line. The control group was measured on the same type and model of the named PET-scanner at a later time point.

Image acquisition was started 30 min after injection. Six dynamic frames of 5 min duration each were acquired. Images were then reconstructed using filtered back-projection by Shepp-Logan filter (cut-off 0.35 cycles/pixel). Attenuation correction was performed using the standard mathematical algorithm implemented in ECAT software. The dynamic frames were then checked for motion artifacts and summed up to generate a single dataset of 31 transaxial planes.

Table 1
Hypometabolic areas in patients with BPD as compared to controls[a]

Anatomical structure	Hemisphere	$x\ y\ z$ – Talairach coordinates[b] (center)	Maximum Z-score	Extent of difference to NDB (%)
Hippocampus	Left	32 –10-16	5.14	−10.7%
Cuneus (BA 19)	Left	30 –67 20	6.13	−14.4%

[a] Given are the anatomical structure, the putative areas of Brodman, the Talairach coordinates of the localization of the maximum Z-score of each cluster (in x-, y-, z-direction) and the values of the maximum Z-scores and percentage of difference in regional activity as compared to the normal data base.

[b] Image orientation is according to radiological convention, i.e. negative x-coordinates correspond to the right hemisphere.

For Statistical Parametric Mapping (SPM), image data were converted to ANALYZE format, and automated spatial normalization was then performed using SPM99 in order to realign the dataset to a common 3-D stereotaxic space using the Montreal Neurological Institute (MNI) template (Friston, 1995). Prior to voxel-based statistical analysis, images were smoothed using a 10×10×10 mm Gaussian kernel. The global cerebral metabolic rate for glucose (gCMRGlc) was normalized to a mean of 50 μmol/100 ml/min by a group-wise analysis of covariance (ANCOVA). The normalized FDG-PET data of the patients were compared to a normal data base constituted from 12 healthy female subjects without morphological or neurological pathology by computing a pixel by pixel *t*-statistics for detection of aprioric hypo- or hypermetabolic areas (Signorini et al., 1999; Juengling et al., 1999).

The applied activity of injected FDG and the time delay between injection and start of acquisition were defined as confounding covariates. Only those voxel clusters were kept that exceeded *t*-values corresponding to $P < 0.0005$ in a single test and a minimal cluster size of 108 voxels corresponding to $P < 0.05$ based on extent threshold. An image of unpaired t-values was then calculated with each voxel consisting of the difference in mean metabolic activity divided by local variance between patients and normals. The *t*-statistics was transformed to a normal statistics yielding a *Z*-score for each pixel (Holmes, 1994). For visualization of the *Z*-score statistics, the *Z*-score voxel clusters were projected onto the standard MRI data set provided by SPM99, using the SPM projection routine. For anatomical identification, the coordinates derived from the MNI template were transformed using the appropriate algorithm (cf. http://www.mrc-cbu.cam.ac.uk/imaging/mnispace.html) to comply with the original grid by Talairach and Tournoux (1988). The extent of difference in regional activity measured in spherical volumes of interest (8 mm radius) centered on the Talairach coordinates of each Z-score voxel cluster in the patient group and corresponding volumes of interest in the normals.

3. Results

The group comparison of the patient data and the control group identified regions that showed statistically significant differences in glucose metabolism in distinct cortical and subcortical areas. A statistically significant ($P < 0.0005$) hypometabolism was found in the left cuneus and in the left hippocampus (Fig. 1, Fig. 2). A significant hypermetabolism ($P < 0.0005$) was found in the left and right anterior cingulate, the superior frontal gyrus bilaterally, the right inferior frontal gyrus and the opercular part of the right precentral gyrus (Fig. 3). The Talairach space localizations of the centers of significant voxel clusters and the maximum *Z*-scores each are summarized in Tables 1 and 3.

4. Discussion

This study investigated cerebral glucose metabolism in patients with BPD using FDG-PET. Twelve female patients with DSM-IV as well as DIB-R criteria for BPD and self-mutilating behavior were scanned under resting conditions. Brain scans were compared to 12 female controls.

Statistical parametric mapping analysis revealed that glucose metabolism was significantly *increased* in patients with BPD compared to controls in the anterior cingulate, the superior frontal gyrus bilaterally, the right inferior frontal gyrus and the opercular part of the right precentral gyrus and *decreased* in the left cuneus as well as in the left hippocampus.

In contrast to expectations, we could not replicate the findings of De la Fuente et al. (1997), who found frontal and anterior cingulate hypometabolism in their series of 10 patients with BPS. Both studies excluded current major depression and scores on rating scales for depression were in a comparable range (De la Fuente et al. : HDRS 27, our study: BDI 20.7).

However, there were differences between the patient group and controls in the study of De la Fuente with regard to gender homogeneity. In addition, six patients in the study of De La Fuente were recent abusers of benzodiazepines and/or alcohol and had to undergo withdrawal prior to the investigation within 10 days. In contrast, our patients did not fulfill diagnostic criteria for substance abuse within 6 months prior to the investigation and did not undergo withdrawal prior to the study. Thus, a possible explanation for differences in prefrontal metabolism might be the fact that recent withdrawal affected prefrontal metabolism. Another possible explanation for these differences in prefrontal metabolism might be the fact that BPD is not a uniform disorder but rather can be divided into different subgroups. Furthermore, in interpreting results of baseline imaging studies it has to be considered that individual differences in confounding variables such as anxiety or dissociation can have strong influence on brain metabolism. These variables were not controlled for in our study which was also the case for the study of De la Fuente et al. Also, differences in frontal and prefrontal metabolism between patients and controls as found in the present study may be attributable at least in part to comorbid psychiatric disorders in our patient group, since e.g. OCD has been associated with frontal hypermetabolism (Baxter et al., 1987) and hypermetabolism in the anterior cingulate (Sedo et al., 1989). A subgroup analysis, however, excluding patients with concurrent

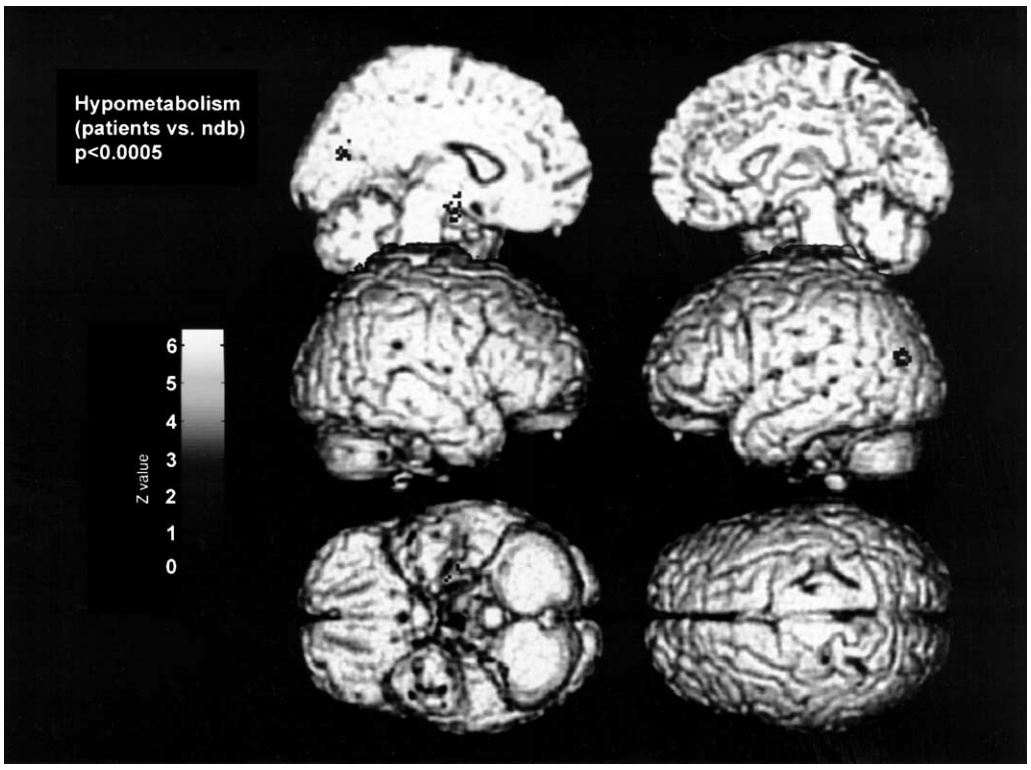

Fig. 1. Maximum intensity projections (MIP) of *Z*-scores of significantly hypometabolic areas onto surface-rendered standard 3-D MRI in patients with BPD as compared to controls. *Z*-scores are indexed by the color-bar.

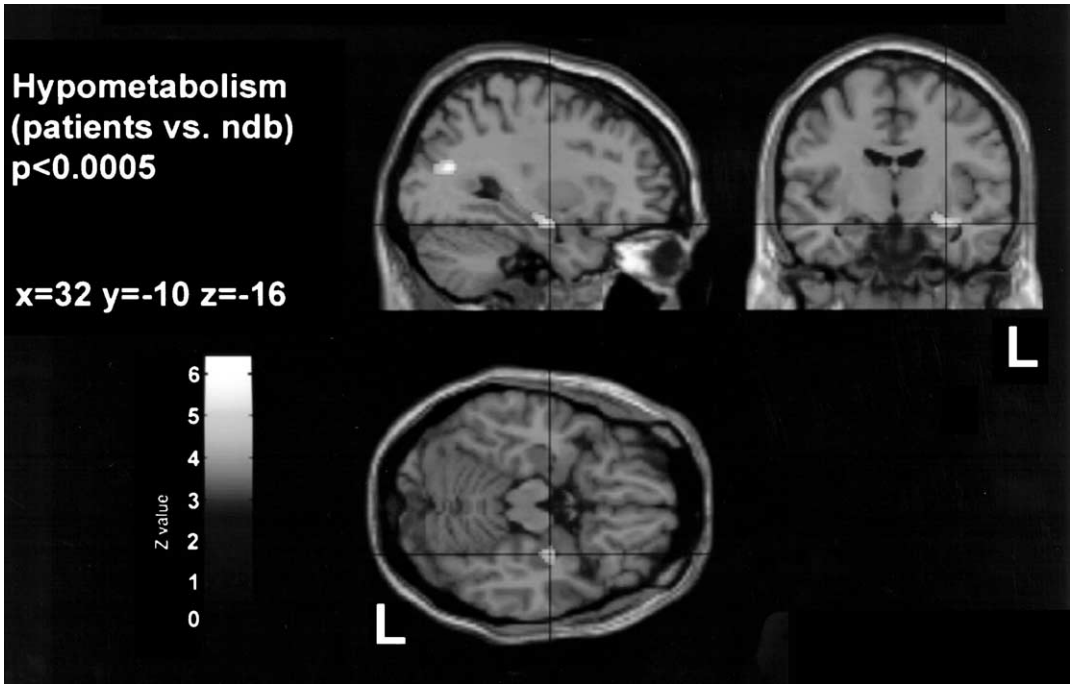

Fig. 2. Slice sections (in sagittal, coronal and axial view) of SPM *Z*-score projections of hypometabolism in patients with BPD as compared to controls onto the standard MRI data set. The area of maximum Z-score in the hippocampus (Talairach coordinates 32 –10 –16) is marked by the crosshair.

diagnosis of OCD, confirmed the findings in the anterior cingulate and frontolateral areas, except for the inferior frontal gyrus, while these findings reached only a *P*-value of <0.001 in this subgroup-analysis (Table 3).

Besides its different roles in emotion regulation, the anterior cingulate cortex plays a role in the affective-motivational component of pain (Davis, 2000; Treede et al., 1999), which was suggested to be involved in antinociceptive processes in patients with BPD

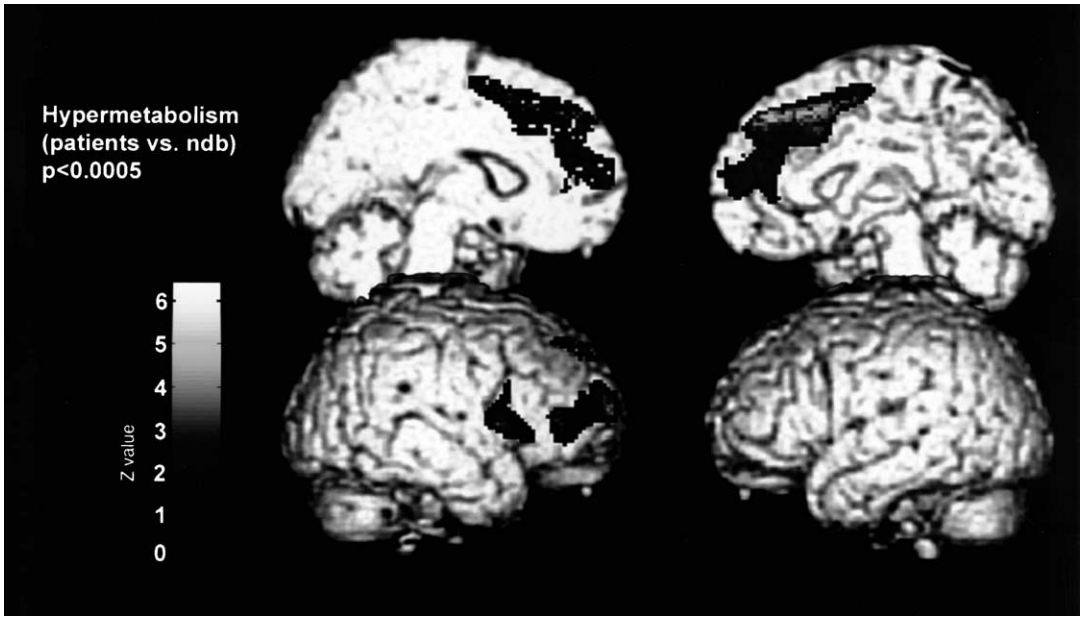

Fig. 3. Maximum intensity projections (MIP) of *Z*-scores of significantly hypermetabolic areas onto surface-rendered standard 3-D MRI in patients with BPD as compared to controls. *Z*-scores are indexed by the color-bar.

Table 2
Hypermetabolic areas in patients with BPD as compared to matched controls[a]

Anatomical structure	Hemisphere	*x y z* Talairach coordinates[b] (center)	Maximum *Z*-score	Extent of difference to NDB (%)
Anterior cingulate (BA 32)	Left	2 42 16	4.63	+5.6%
	Right	−2 10 45	5.58	+7.7%
G. frontalis sup. (BA 8)	Left	2 25 43	5.81	+7.4%
G. frontalis sup. (BA 10)	Right	−28 65 10	6.49	+8.7%
G. frontalis inf. (BA 45)	Right	−47 39 2	4.63	+7.1%
G. precentralis pars opercularis (BA 44)	Right	−57 6 7	5.23	+5.1%

[a] Given are the anatomical structure, the putative areas of Brodman, the Talairach coordinates of the localization of the maximum *Z*-score of each cluster (in *x*-, *y*-, *z*-direction) and the values of the maximum *Z*-scores and percentage of difference in regional activity as compared to the normal database.

[b] Image orientation is according to radiological convention, i.e. negative *x*-coordinates correspond to the right hemisphere.

Table 3
Hypermetabolic areas in patients with BPD excluding patients with comorbid OCD as compared to matched controls[a]

Anatomical structure	Hemisphere	*x y z* Talairach coordinates[b] (center)	Maximum *Z*-score	Extent of difference to NDB (%)
Anterior cingulate (BA 32)	Left	4 37 18	4.63	+5.0%
	Right	−5 21 30	4.40	+5.4%
G. frontalis sup. (BA 8)	Left	2 33 41	4.97	+8.2%
G. frontalis sup. (BA 10)	Right	−26 65 8	4.25	+6.7%
G. precentralis pars opercularis (BA 44)	Right	−55 6 5	4.08	+4.3%

[a] Given are the anatomical structure, the putative areas of Brodman, the Talairach coordinates of the localization of the maximum *Z*-score of each cluster (in *x*-, *y*-, *z*-direction) and the values of the maximum *Z*-scores and percentage of difference in regional activity as compared to the normal database.

[b] Image orientation is according to radiological convention, i.e. negative *x*-coordinates correspond to the right hemisphere.

(Schmahl et al., submitted for publication). Thus, anterior cingulate activation found in the present study is in good agreement with the pathologically reduced sensitivity to pain seen in BPD (Bohus et al., 2000).

We found hypometabolism in left hippocampus. Preclinical studies revealed that stress is associated with toxicity to the hippocampus, possibly acting through stress-induced glucocorticoid release (McEwen et al., 2001; Sapolsky, 1990). Childhood sexual and physical

abuse represents a severe stressor and a history of childhood abuse was found in 29–71% of BPD patients (Links et al., 1988, Herman et al., 1989, Zanarini et al., 1989b, Ogata et al., 1990, Westen et al., 1990). Stress-induced toxicity to hippocampal neurons has been hypothesized as the mechanism underlying hippocampal volume reduction in Posttraumatic Stress Disorder (Bremner et al., 1995; Bremner et al., 1997; Gurvits et al., 1996; Stein et al., 1997). Recently, reduced hippocampal as well as amygdala volume was also found in patients with BPD and a history of childhood abuse (Driessen et al., 2000). While this reduction in grey matter volume may lead to a reduction in glucose metabolism per se, a partial volume correction would be necessary to differentiate between atrophy-related changes and additional functional impairment. As no volume-rendering MRI was aquired in our patients, an appropriate partial volume correction could not be performed, thus limiting the interpretation of the hippocampal hypometabolism observed in our study.

While the hippocampus has also been shown in preclinical studies to play a critical role in emotion regulation especially related to environmental context (Kim and Fanselow, 1992; Phillips and LeDoux, 1992), therefore these findings taken together with those of the present study suggest that hippocampal dysfunction may underly symptoms of BPD.

In our patients, the cuneus showed ipsilateral hypometabolism as well. Although it is well known that afferent as well as efferent circuitries interconnect hippocampus and cuneus (Room et al., 1986; Swanson et al., 1982), the significance of this finding remains unclear.

As a specific strength of the present study it may be noted that the patient group as well as the control group were exclusively female and matched for age.

Several limitations should be considered in interpreting our findings. First, the influence of lifetime psychiatric conditions in the patients group can not be ruled out although we excluded patients with current depression and alcohol and drug abuse. The same holds true, however, for the study of De la Fuente et al. (1997). Second, when comparing a group of hospitalized patients with controls, several factors such as hospitalization stress or different emotional reaction to the experimental session may contribute to the observed findings. Furthermore, we did not assess clinically important factors such as impulsivity and self-injuries at the time of the investigation. Also smoking habits, which can influence brain physiology, were not assessed.

In conclusion, this study of BPD patients demonstrated limbic and prefrontal dysfunction in terms of metabolic impairment under resting conditions using FDG-PET and statistical parametric mapping. Further studies may use challenge paradigms to further assess the neural circuitry underlying emotion dysregulation in patients with BPD.

Acknowledgements

This research was supported by a grant from the Ministery of Baden-Wuerttemberg and the Borderline Personality Disorder Research Foundation (BPDRF, New York)

References

American Psychiatric Association. Diagnostic and Statistical manual of Mental Disorders. 4th ed., text revision. Washington, DC: American Psychiatric Press; 2000.

Baxter Jr LR, Phelps ME, Mazziota JC, Guze BH, Schwartz JM, Selin CE. Local cerebral glucose metabolic rates in obsessive-compulsive disorder. A comparison with rates in unipolar depression and in normal controls. Archives of General Psychiatry 1987;44:211–8.

Beck AT, Ward DH, Mendelson M, Mock J, Erbaugh JK. An inventory for measuring depression. Archives of General Psychiatry 1961; 4:561–71.

Bohus M, Limberger M, Ebner U, Glocker F, Wernz M, Lieb K. Pain perception during self-reported distress and calmness in patients with borderline personality disorder and self-mutilating behavior. Psychiatry Research 2000;95:251–60.

Bremner JD, Randall P, Scott TM, Bronen RA, Seibyl JP, Southwick Sm, Delaney RC, McCarthy G, Charney DS, Innis RB. MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder. American Journal of Psychiatry 1995;152:973–81.

Bremner JD, Randall P, Vermetten E, Staib L, Bronen RA, Mazure C, Capelli S, McCArthy G, Innis RB, Charney DS. Magnetic resonance imaging-based measurement of hippocampal volume in posttraumatic stress disorder related to childhood physical and sexual abuse—a preliminary report. Biological Psychiatry 1997;41:23–32.

Corrigan FM, Davidson A, Heard H. The role of dysregulated amygdalic emotion in borderline personality disorder. Medical Hypotheses 2000;54:574–9.

Davidson RJ, Abercrombie H, Nitschke JB, Putnam K. Regional brain function, emotion and disorders of emotion. Current Opinion in Neurobiology 1999;9:228–34.

Davis KD. The neural circuitry of pain as explored with functional MRI. Neurological Research 2000;22:313–7.

Davis M. The role of the amygdala in conditioned and unconditioned fear and anxiety. In: Aggleton J, editor. The Amygdala. New York: Oxford University Press; 2001. p. 211–87.

De la Fuente JM, Goldmanm S, Stanus E, Vizuette C, Morlán I, Bobes J, Mendlewicz J. Brain glucose metabolism in borderline personality disorder. Journal of Psychiatric Research 1997;31:531–41.

Driessen M, Herrmann J, Stahl K, Zwaan M, Meier S, Hill A, Osterheider M, Petersen D. Magnetic resonance imaging volumes of the hippocampus and the Amygdala in women with borderline personality disorder and early traumatization. Archives of General Psychiatry 2000;57:1115–22.

First MB, Spitzer RL, Gibbon M, Williams JBW, Benjamin LB. The Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II). Journal of Personality Disorders 1995;9:83–91.

Friston KJ, Ashburner J, Poline JB, Frith CD, Heather JD, Frackowiak RSJ. Spatial registration and normalisation of images. Human Brain Mapping 1995;2:165–89.

Gurvits TV, Shenton ME, Hokama H, Ohta H, Lasko NB, Gilbertson MW, Orr SP, Kikinis R, Jolesz FA, McCarley RW, Pitman RK. Magnetic resonance imaging study of hippocampal volume in chronic, combat related posttraumatic stress disorder. Biological Psychiatry 1996;40:1091–9.

Herman JL, Perry JC, van der Kolk BA. Childhood trauma in borderline

personality disorder. American Journal of Psychiatry 1989;146:490–5.

Herpertz SC, Kunert HJ, Schweger UB, Sass H. Affective responsiveness in borderline personality disorder: a psychophysiological approach. American Journal of Psychiatry 1999;156:1550–6.

Holmes AP. Statistical issues in functional brain mapping. University of Glasgow, Dept. of Statistics: PhD thesis 1994.

Juengling FD, Kassubek J, Moser E, Nitzsche EU. Precise localization of dysfunctional areas in vertebro-basilar infarction by FDG- and O-15-H2O-PET using standardized image analysis and image registration to 3-D MR. Nuklearmedizin 1999;38:341–4.

Juengling FD, Kassubek J, Otte A. Standardization of cerebral PET imaging in clinical neurological diagnostics. European Journal of Nuclear Medicine 2000;27:98.

Kim JJ, Fanselow MS. Modality-specific retrograde amnesia of fear. Science 1992;256:675–7.

Linehan MM. Cognitive behavioral treatment of borderline personality disorder. New York: Guilford Press; 1993.

Links PS, Steiner M, Offord DR, Eppel A. Characteristics of borderline personality disorder: a Canadian study. Canadian Journal of Psychiatry 1988;33:336–40.

McEwen BS, Magarinos AM. Stress and hippocampal plasticity: implications for the pathophysiology of affective disorders. Human Psychopharmacology 2001;16:S7–0S19.

Ogata SN, Silk KR, Goodrich S, Lohr NE, Westen D, Hill EM. Childhood sexual and physical abuse in adult patients with borderline personality disorder. American Journal of Psychiatry 1990;147:1008–13.

Phillips RG, LeDoux JE. Differential contribution of amygdala and hippocampus to cued and contextual fear conditioning. Behavioral Neuroscience 1992;106:274–85.

Room P, Groenewegen HJ. Connections of the parahippocampal cortex. I. Cortical afferents. Journal of Comparative Neurology 1986;251(4):415–50.

Sapolsky RM, Uno H, Rebert CS, Finch CE. Hippocampal damage associated with prolonged glucocorticoid exposure in primates. Journal of Neuroscience 1990;10:2897–902.

Schmahl C, Greffrath W, Baumgärtner U, Schlereth T, Magerl W, Philipsen A, Lieb K, Bohus M, Treede R-D. Laser-evoked potentials, spatial discrimination of noxious stimuli, and pain ratings in patients with borderline personality disorder (submitted for publication).

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini—International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry 1998;59(Suppl 20):22–3.

Signorini M, Paulesu E, Friston K, Perani D, Colleluori A, Lucignani G, Grassi F, Bettinardi V, Frackowiak RS, Fazio F. Rapid assessment of regional cerebral metabolic abnormalities in single subjects with quantitative and nonquantitative [18F]FDG PET: a clinical validation of statistical parametric mapping. Neuroimage 1999;9:63–80.

Silk KR. Borderline personality disorder. Overview of biological factors. Psychiatric Clinics of North America 2000;23:61–75.

Soloff PH, Meltzer CC, Greer PJ, Constantine D, Kelly TM. A fenfluramine-activated FDG-PET study of borderline personality disorder. Biological Psychiatry 2000;47:540–7.

Spitzer RL, Williams JBW, Gibbon M. Structured clinical interview for DSM-IV (SCID). New York: New York State Psychiatric Institute, Biometrics Research; 1995.

Stein MB, Koverola C, Hanna C, Torchia MG, McClarty B. Hippocampal volume in women victimized by childhood sexual abuse. Psychological Medicine 1997;27:951–9.

Stiglmayr CE, Shapiro DA, Stieglitz RD, Limberger MF, Bohus M. Experience of aversive tension and dissociation in female patients with borderline personality disorder—a controlled study. Journal of Psychiatric Research 2001;35:111–8.

Swanson LW. Normal hippocampal circuitry. Neuroscience Research Progress Bulletin 1983;20:624–37.

Swedo SE, Schapiro MB, Grady CL, Leonard HL, Kumar A, et al. Cerebal glucose metabloism in chilhood-onset obsessive-compulsive disorder. Archives of General Psychiatry 1989;46:518–23.

Talairach J, Tournoux P. Co-planar sterotaxic atlas of the human brain: 3-dimensional proportional system: an approach to cerebral imaging. Stuttgart-New York: Thieme; 1988.

Treede R-D, Kenshalo DR, Gracely RH, Jones AKP. The cortical representation of pain. Pain 1999;79:105–11.

Westen D, Ludolph P, Misle B, Ruffins S, Block J. Physical and sexual abuse in adolescent girls with borderline personality disorder. American Journal of Orthopsychiatry 1990;60:55–66.

Zanarini MC, Gunderson JG, Frankenburg FR, Chauncey DL. The revised diagnostic interview for borderlines: discriminating BPD from other Axis II disorders. Journal of Personality Disorders 1989a;3:10–18.

Zanarini MC, Gunderson JG, Marino MF, Schwartz EO, Frankenburg FR. Childhood experiences of borderline patients. Comprehensive Psychiatry 1989b;30:18–25.