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Psychiatry Research 121 (2004) 239–252

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## Neurobiological correlates of diagnosis and underlying traits in patients with borderline personality disorder compared with normal controls

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Received 5 November 2002; received in revised form 28 August 2003; accepted 1 September 2003

### Abstract

The purpose of the study was to test the hypothesis that borderline personality disorder (BPD) and its underlying traits are associated with abnormalities in neurotransmitter systems. Subjects were 30 women with BPD and 22 normal controls, assessed using the Diagnostic Interview for Borderlines, revised, the Hamilton Depression Scale (HAM-A) and the Hamilton Anxiety Scale (HAM-A), the Diagnostic Assessment of Personality Pathology, the Buss–Durkee Guilt-Hostility Inventory, the Barratt Impulsivity Scale (BIS), and challenge tests to measure serotonergic, cholinergic and noradrenergic activity. Borderline subjects with high HAM-A and HAM-D scores showed a faster time to peak in prolactin response to meta-chlorophenylpiperazine (m-CPP) challenge. Borderline subjects with high BIS scores showed prolactin blunting. There were no differences in cortisol response to m-CPP, or on the cholinergic and noradrenergic challenges. The results suggest that impulsive traits in borderline patients are associated with abnormalities in serotonergic systems.

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**Keywords:** Borderline personality disorder; Impulsivity; Affective instability; Challenge tests; Serotonin; Neurobiology

### 1. Introduction

In an influential theoretical article, Siever and Davis (1991) proposed that borderline personality

disorder (BPD) is associated with abnormalities on two trait dimensions: impulsivity and affective instability, each linked to abnormalities of central neurotransmitter function. The present study was designed to test this model.

The most consistent empirical data supporting the Siever–Davis model derives from relationships between impulsivity and deficits in central seroto-

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nergic functioning (Siever et al., 1998). Reductions in indices of central 5-hydroxytryptophan (5-HT) function are seen in patients with impulsive aggression, either directed towards the self or towards others (Mann, 1998). Previous studies of the neurobiology of BPD have examined central serotonergic activity through metabolites in cerebrospinal fluid (Gardner et al., 1990; DeVegvar et al., 1998), through platelet serotonin levels (Stahl, 1977; Stahl et al., 1982; Mann et al., 1992), through paroxetine binding and monoamine oxidase (MAO) activity in platelets (Coccaro et al., 1996; Verkes et al., 1997, 1998) and through positron emission tomography (PET) scanning following administration of a serotonin agonist (Siever et al., 1999; Soloff et al., 2000; Leyton et al., 2001; New et al., 1997).

Challenge tests have the advantage of measuring receptor-mediated neurohormonal responses in the periphery following administration of an agonist, providing a dynamic measure of the central serotonergic system. Coccaro et al. (1989) found that male patients with traits of impulsive aggression (many of whom also had BPD) had a blunted peak of prolactin response to fenfluramine challenge. Similar findings have been reported in impulsive men (Moss et al., 1990; Soloff et al., 1994) and in mixed gender samples (DeVegvar et al., 1998). Hollander et al. (1994) observed a 'spacy/high behavioral response' to fenfluramine challenge in men with BPD, as opposed to prolactin blunting. In another study from the same group, in which meta-chlorophenylpiperazine (m-CPP) challenge was given (Stein et al., 1996) prolactin levels actually increased, most particularly among subjects who showed a similar response to m-CPP challenge.

However, gender influences the response of the serotonin system and most patients with BPD are female. A recent study reported by Soloff et al. (2002) showed that male, but not female, BPD subjects had diminished prolactin response to fenfluramine challenge. A PET study of fenfluramine challenge in women with BPD (Siever et al., 1999) also did not observe blunting. Our own research group (Martial et al., 1997), in a pilot study using fenfluramine challenge, found that the central serotonin system in borderline women showed a higher

level of sensitivity than in normal controls, in that BPD patients reached peak response sooner. In contrast, Rinne et al. (2000) used m-CPP, a serotonin agonist that acts at post-synaptic sites (particularly the 5HT<sub>2</sub> receptor), and found that female borderline patients had a blunted peak of prolactin response to serotonergic challenge. Similar findings have been reported by Steiger et al. (2001a,b) in bulimic women.

Apart from the influence of gender, borderline patients may be heterogeneous in regard to central serotonin activity (Coccaro et al., 1994). Therefore, one of the goals of this study was to repeat earlier work using a larger sample size. Moreover, to understand impulsivity, one may need to measure more than one neurotransmitter system. Siever and Davis (1991) suggested that catecholamine activity, related to behavioral activation, may also play some role in impulsivity. In a mixed gender population of personality-disordered patients with impulsive aggression, DeVegvar et al. (1998) described preliminary findings showing that impulsive patients have an increased response of growth hormone secretion when challenged with clonidine, an alpha-2 adrenergic receptor agonist. Similarly, Coccaro et al. (1991a) reported that growth hormone response to clonidine challenge correlated with irritability. Southwick et al. (1990) have reported increased platelet alpha-2 adrenergic receptor binding in BPD.

The neurobiology of affective instability is much less understood. The biological correlates of BPD can also be associated with anxious and depressive symptoms (Siever et al., 1998). Siever and Davis (1991) hypothesized an imbalance between activity in central noradrenergic and cholinergic systems. As noted above, there is some evidence for noradrenergic abnormalities in BPD. When Steinberg et al. (1995) carried out a physostigmine challenge to measure cholinergic function, however, the only finding consisted of a dysphoric response.

Clearly, there are many ambiguities and contradictions in this literature. The present study aims to clarify these issues in three ways: by using multiple challenge tests (measuring serotonergic, noradrenergic and cholinergic activity), by recruiting a larger sample of patients and controls, and

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