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Implications of compulsive and impulsive traits for serotonin status in women with bulimia nervosa

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Abstract

Studies of bulimia nervosa (BN) often report decreased brain serotonin (5-hydroxytryptamine: 5-HT) activity. Across populations, impulsivity has been linked to reduced 5-HT activity, but compulsivity has been associated (at least inconsistently) with an increase. We therefore became interested in the association between behavioral-trait variations and 5-HT status in BN. In 56 bulimic and 29 non-bulimic women, we measured eating symptoms, personality traits, platelet paroxetine binding, and neuroendocrine responses following oral meta-chlorophenylpiperazine (m-CPP). Relative to normal eaters, bulimic women showed reduced density (B_{\max}) of platelet paroxetine-binding sites, blunted prolactin (PRL) responses following m-CPP, and (as a trend) lower basal PRL levels. However, after effects of binge–purge frequencies, body mass, and other extraneous factors were controlled, PRL levels at baseline and other moments in the serial sampling varied systematically with presence of impulsive and compulsive traits. PRL was generally low in BN, but ‘high-compulsive’/‘low-impulsive’ traits were associated with higher (normal-range) PRL values. Comparable trait-related variations were not observed on paroxetine-binding indices. Our findings suggest that 5-HT status in BN may correspond to impulsive or compulsive traits, and they encourage multidimensional modeling of the pathophysiological role of 5-HT in BN.

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1. Introduction

Manipulations that reduce central serotonin (5-hydroxytryptamine: 5-HT) activity often precipitate compulsive or ‘binge’ eating (Brewerton,

1995). Such effects have led to the hypothesis, corroborated by various forms of clinical evidence, that bulimia nervosa (BN) involves reduced 5-HT neurotransmission. For example, as a group, BN patients display reduced platelet binding of 5-HT uptake inhibitors (Marazziti et al., 1988; Steiger et al., 2000, 2001a) and blunted neuroendocrine responses to 5-HT precursors and agonists (Brew-

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erton et al., 1992; Levitan et al., 1997; Steiger et al., 2001a,b).

Intriguing as they are, such findings are amenable to various causal interpretations: Dieting, bingeing and purging have all been thought to promote secondary reductions in brain 5-HT activity, and hence to underlie reduced 5-HT tone in BN (Anderson et al., 1990; Brewerton, 1995). However, in non-eating-disordered populations, low brain 5-HT activity has been associated with psychopathological-trait variations on dimensions like impulsivity and aggression (Åsberg et al., 1987; Coccaro et al., 1989). Prominence of impulsivity and aggression in bulimic patients (Grilo, 2002; Steiger et al., 2003) raises the possibility that decreased 5-HT tone in the population could be (in part) a trait correlate. In keeping with this idea, studies in BN have indicated 5-HT activity to be inversely linked to levels of impulsivity or hostility (Carrasco et al., 2000; Steiger et al., 2001a,b; Verkes et al., 1996; Waller et al., 1996).

If the preceding points to a link between impulsivity and reduced 5-HT function, a question arises concerning a substantial subgroup of BN sufferers who display compulsive (rather than impulsive) traits (Grilo, 2002; Steiger et al., 2003). Findings in non-eating-disordered samples have sometimes (Swedo et al., 1992; Fineberg et al., 1998)—but not always (Baumgarten and Grosdanovic, 1998; Stein et al., 1996)—associated compulsivity with increased 5-HT tone, supporting the proposal that ‘impulsive’ and ‘compulsive’ traits may occupy opposite poles of a continuum of 5-HT under- to overactivity (Cloninger et al., 1993). The present study applied this notion to 5-HT findings in BN. If 5-HT status in BN corresponds to impulsive or compulsive traits, then impulsivity should coincide with decreased 5-HT activity, and compulsivity, the converse. In contrast, if 5-HT status in BN is largely a consequence of bulimic behavior, then 5-HT indices in active bulimics should covary more strongly with ‘eating-symptom’ rather than ‘trait’ variations.

We assessed 5-HT function in two ways: (1) Given relatively direct connection between serotonergic stimulation and release of prolactin (PRL), it has become conventional to draw inferences about central 5-HT functioning based on 5-

HT agonist-stimulated changes in peripheral PRL (Yatham and Steiner, 1993). Meta-chlorophenylpiperazine (m-CPP) binds with highest affinity to 5-HT_{2c} receptors, and lesser affinity to 5-HT_{1a} and alpha₂-noradrenergic receptors—and is therefore thought to constitute a fairly specific probe of postsynaptic 5-HT function. PRL responses following administration of m-CPP have been used to study 5-HT neurotransmission in several studies on BN (Brewerton et al., 1992; Steiger et al., 2001a,b,c). (2) Binding in platelet membranes of 5-HT reuptake inhibitors is believed to model aspects of central (presynaptic) 5-HT reuptake (Coccaro et al., 1996). Studies using platelet imipramine binding (Marazziti et al., 1988) or paroxetine binding (Steiger et al., 2000, 2001a) have shown transporter density (B_{\max}), but not affinity (K_d), to be reduced in bulimic vs. non-bulimic women. A similar association has been documented between aggressiveness, in personality-disordered patients, and reduced density (B_{\max}) of platelet paroxetine uptake sites (Coccaro et al., 1996).

2. Methods

2.1. Participants

This study received institutional ethics-board approval, and involved participation by informed consent. An initial group of 67 bulimics was recruited through a specialized Eating Disorders (ED) program on the basis of the following criteria: Female, aged 18–40, actively bingeing, and not pregnant, anorexic, obese (body mass index of 28 or less), or on psychoactive medications (in the last 6 weeks). ED symptoms were confirmed using the Eating Disorders Examination (Fairburn and Cooper, 1993). We excluded six individuals due to EKG abnormalities or other medical conditions that would contraindicate endocrine challenge, and one more case with an EMIT urine screen revealing amphetamine abuse. In four more cases, a vein could not be obtained for blood draws. We thus completed full assays in 56 women, 45 (80.4%) of whom met DSM-IV (American Psychiatric Association, 1994) criteria for BN-purging subtype, 6 (10.7%) for BN-nonpurging

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