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Reduced platelet [^{3}H]paroxetine binding in anorexia nervosa: Relationship to eating symptoms and personality pathology

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Abstract

Alterations in serotonin function have been implicated in both anorexia and bulimia nervosa, and previous studies suggest associations between serotonin function and variations in pathological personality traits. Women meeting DSM-IV criteria for anorexia nervosa (AN, 16 with the restricting subtype and 14 with the binge–purge subtype) and 49 healthy control women (CW) provided blood samples for analyses of platelet [^{3}H]paroxetine binding. Participants also filled out questionnaires tapping eating disorder symptoms, depression, and personality pathology. Compared with CW, women with restricting and binge–purge AN had significantly lower levels of paroxetine binding (respectively: 1012+487 vs. 560+253 vs. 618+217 fmol/mg protein). Simple correlation analyses showed that, within AN but not within controls, paroxetine binding was inversely related to dieting preoccupations, affective instability, anxiousness, compulsivity, restricted expression and social avoidance but independent of age, body mass index, depression, and other eating symptoms. Findings suggest that reduced peripheral serotonin transporter density in AN relates to increased dieting preoccupations, affective instability and anxiousness–fearfulness.

Keywords: Anorexia nervosa; Paroxetine; Personality

1. Introduction

Various findings associate anorexia nervosa (AN) with alterations in serotonin (5-hydroxytryptamine, 5-HT) functioning. For example, compared with healthy controls, patients with AN show reduced cerebrospinal fluid (CSF) concentrations of 5-hydroxyindoleacetic acid (5-HIAA; Kaye et al., 1984, 1988; Demitrack et al., 1995), decreased platelet imipramine binding (Weizman et al., 1986), reduced monoamine oxidase (MAO) activity (Diaz-Marsa et al., 2000), blunted neuroendocrine responses to *meta*-chlorophenylpiperazine (*m*-CPP; Hadigan et al., 1995; Brewer-

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ton and Jimerson, 1996) and *d*-fenfluramine (Monteleone et al., 1998), greater reductions in serotonin synthesis following acute tryptophan depletion (Kaye et al., 2003), reduced central binding of the 5-HT2A agonist ^{123}I-5-I-R91150 (Audenaert et al., 2003), and decreased platelet paroxetine binding (Ramacciotti et al., 2003). Taken together, the preceding findings point to the presence of reduced 5-HT activity in active AN.

Several factors may account for observed functional alterations in 5-HT activity in AN. Alterations in 5-HT have been attributed by some investigators to the disturbed eating behaviours inherent in AN (e.g., Goodwin et al., 1996; Cowen et al., 1996; O'Dwyer et al., 1996; Ward et al., 1998; Favaro et al., 2000), and they have been interpreted by others as potential precursors to AN (e.g., Kaye et al., 1991; Frank et al., 2002; Kaye et al., 2003; Bailer et al., 2004). Further, differences in behavioural traits may account for some of the variation in 5-HT function in AN. For example, Diaz-Marsa et al. (2000) found that reductions in monoamine oxidase (MAO) activity were associated with increased impulsiveness and decreased persistence in currently symptomatic women with restrictive AN, and Bailer et al. (2004) found that reductions in cortical altanserin (a 5HT2A selective ligand) binding were associated with increased novelty seeking and decreased drive for thinness and harm avoidance in women recovered from binge–purge AN. Taken together, these findings indicate that 5-HT alterations in AN may be related to multiple factors: sequelae of AN, neurobiological causes of AN, and as variations in personality traits.

Our group has previously reported associations among indices of reduced 5-HT function and various personality traits in individuals with bulimia nervosa (whether active or recovered). The role of traits in altered 5-HT function in BN appears robust. For example, reduced neuroendocrine responses to *m*-CPP are associated with increased submissiveness, social avoidance, restricted emotional expression, impulsiveness, affective instability and self-harming behaviours (Steiger et al., 2001; Bruce et al., 2004), and reduced paroxetine binding is linked to decreased perfectionism and compulsivity (Steiger et al., 2004) as well as increased affective instability, impulsiveness, and interpersonal insecurity (Steiger et al., 2005). We designed the current study to extend our investigations of platelet paroxetine binding and personality traits to women with AN; the goal was to examine a similar selection of personality traits as previously investigated in bulimic patients and to identify those that are associated with paroxetine binding in AN.

2. Methods

2.1. Participants

This study received institutional ethics-board approval and involved voluntary participation by informed consent. Thirty Canadian women self-referred for outpatient treatment of AN were recruited through a specialized eating disorders (ED) program on the basis of the following criteria: female, aged 18–40 and not pregnant. ED diagnoses were established using the Eating Disorders Examination (Fairburn and Cooper, 1993), and 14 (47%) of the women met DSM-IV (American Psychiatric Association, 1994) criteria for AN restrictive subtype and 16 for (53%) AN binge–purging type. [We did not exclude AN participants who were taking selective serotonin reuptake inhibitors (SSRIs), and four (29%) of the women with restrictive AN and six (38%) of the women with restrictive AN were taking an SSRI at the time of testing; potential effects of medication use on serotonin and psychological indices were controlled using covariance techniques.] Healthy control women (CW; $N=49$), recruited through university classes or newspaper advertisements (to approximate the student/non-student ratio among women with AN), were aged 18–40, matched for ethnicity, and had normal results on physical examination, blood work, and electrocardiographic examination. They denied (past or present) ED, intense weight concerns, periods of marked intentional weight loss, binge eating, purging, medical problems, mental health problems (e.g., depression, anxiety, substance abuse), pregnancy, or use of psychoactive medications. We did not exclude CW or AN participants who were taking contraceptive medications, and three (21%) of the women with restrictive AN, six (38%) of the women with binge–purge AN, and 32 (65%) of CW were taking contraceptives at time of testing ($\chi^2=9.45$, $df=2$, $P<0.009$); potential effects of contraceptive medication use on