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Reduced plasma leptin concentrations in bulimia nervosa

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Abstract

Leptin is a protein produced by the *ob–ob* gene which inhibits food intake. Plasma levels have previously been reported to be altered in obesity and anorexia nervosa (AN) but not bulimia nervosa (BN). We measured fasting plasma leptin levels by radioimmunoassay in 53 subjects carefully studied at NIMH, including 37 women meeting DSM–III–R criteria for BN [10 with concurrent AN (body mass index (BMI)=14.1±1.4), 27 without AN (BMI=20.4±1.6)] and 16 normal control women (NCs) (BMI=21.1±2.0). Patients were medication-free and abstinent from bingeing and purging for three to four weeks prior to study. Plasma leptin levels were significantly correlated to BMI (r=0.41, $P<0.002$), weight (kg, r=0.43, $P<0.001$), and percent average body weight (%ABW, r=0.45, $P<0.001$) in the total group. Plasma leptin levels were lower in the BN subjects (3.4±2.5 ng/ml) compared to the NCs (6.1±2.6 ng/ml, $P<0.001$, ANCOVA) even after controlling for BMI and weight. There was no significant difference between BN subjects with AN (n=10, 2.6±2.6 ng/ml) and those without AN (n=27, 3.8±2.4 ng/ml), despite lower BMI in BN with AN. Furthermore, leptin levels were decreased in BN without AN compared with healthy controls, even though BMI was comparable in these two subgroups. Plasma leptin concentrations were negatively correlated with baseline plasma cortisol levels (n=49, $r=-0.49$, $P<0.001$) and positively correlated with prolactin responses following L–tryptophan (n=49, r=0.37, $P<0.009$) and m–chlorophenylpiperazine (n=52,

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r=0.24, $P<0.09$). This is the first known report of decreased plasma leptin levels in BN. The decrement in leptin concentration is not related to BMI, body weight, or the presence or absence of BN. HPA axis activation as well as serotonin dysregulation may be related to decreased leptin levels, which may in turn contribute to disinhibited eating in BN. Although current leptin levels were not correlated with self-reported previous binge frequency, the role of leptin in the pathophysiology of BN deserves further study.

Keywords: Leptin; Anorexia nervosa; Bulimia nervosa; Eating disorders; Serotonin; Cortisol

1. Introduction

Leptin is a protein produced by the adipocyte–specific *ob–ob* gene which inhibits food intake (Zhang et al., 1994; Halaas et al., 1995; Campfield et al., 1995). Plasma levels have been reported to be altered in obesity (Considine et al., 1996; Kennedy et al., 1997) and anorexia nervosa (AN) (Hebebrand et al., 1995, 1997; Mantzoros et al., 1997; Grinspoon et al., 1996; Casanueva et al., 1997; Ferron et al., 1997) but not in bulimia nervosa (BN) (Ferron et al., 1997). We undertook the current study to precisely address the relationship between plasma leptin and body mass in BN in relationship to AN and other measures of pituitary/hypothalamic dysregulation. Given leptin's role in satiety in humans (Heini et al., 1998), which is known to be altered in BN (Brewerton, 1995), we also wondered if leptin was linked to other neurochemicals involved in eating, such as serotonin and cortisol. Mantzoros et al. (1997) reported significant relationships between levels of CSF leptin and CSF 5–hydroxyindole acetic acid (5–HIAA). We postulated that plasma leptin levels might also be correlated with other serotonergic measures, such as hormonal response to pharmacologic challenge agents, as well as to cortisol, which has been reported previously (Licinio et al., 1997; Korbonits et al., 1997).

2. Methods

We measured plasma leptin levels in 53 women studied at the National Institute of Mental Health (NIMH). Thirty-seven women met DSM–III–R criteria for BN [10 with concurrent AN (body mass index (BMI, mean±SD)=14.1±1.4) and 27 without lifetime or current AN (BMI=20.4±1.6)] and 16 women were identified as normal controls (NCs)(BMI=21.1±2.0) using a structured clinical interview based on DSM–III–R. Patients were medication-free and abstinent from bingeing and purging for three to four weeks prior to blood drawing for studies of serotonin function using a pharmacologic challenge paradigm, the details of which have been previously published (Brewerton et al., 1992; Brewerton, 1995; Brewerton and Jimerson, 1996). Plasma was frozen at −70°C until analyzed for plasma leptin concentrations, which was measured after an overnight fast by radioimmunoassay (RIA) (Linco, Inc.) as previously described (Kennedy et al., 1997).