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Central dopaminergic function in Anorexia and Bulimia Nervosa: a psychoneuroendocrine approach

F. Brambilla *, L. Bellodi, C. Arancio, P. Ronchi, D. Limonta

Dipartimento di Scienze Neuropsichiche, Istituto Scientifico Ospedale S. Raffaele, Via Prinetti 29, Milano 20127, Italy

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Abstract

Data on central dopamine (DA) function in patients with Anorexia Nervosa (AN) and Bulimia Nervosa (BN) are contradictory. To tentatively clarify the brain secretory state of the amine and its relationship with the nutritional impairments and/or the psychopathological aspects of the two disorders, we measured the responses of growth hormone (GH) to acute stimulation with apomorphine (APO), a selective D-1 and D-2 receptor agonist, in 16 AN patients, 8 restricted (AN–R) and 8 bingeing–purging (AN–BP), in 7 BN patients and in 8 healthy controls (CTR). Interference of impairment of the somatotropic axis in the GH response to APO stimulation was excluded by measuring the GH and insulin-like growth factor-1 (IGF-1) basal levels and GH responses to growth hormone-releasing hormone (GHRH) stimulation. Psychological aspects of patients and controls were investigated by the rating scales Eating Disorder Inventory (E.D.I.), Bulimic Investigation Test Edinburgh (B.I.T.E)., and Yale–Brown Cornell Eating Disorder Scale (YBC–ED).

Basal GH levels were significantly higher and those of IGF-1 lower in AN–R than in AN–BP, BN and CTR subjects. GH responses to GHRH stimulation were significantly higher in AN–R than in AN–BP and BN patients and in CTR. GH responses to APO stimulation were significantly lower in AN–R and AN–BP than in BN and CTR subjects, suggesting that at the hypothalamic level there is a subsensitivity of postsynaptic D-2 receptors and possibly a presynaptic DA hypersecretion. The altered GH responses to APO stimulation did not correlate with the Body Mass Index, while they correlated negatively with E.D.I. scores.

* Corresponding author. Tel.: +39-368-301-7420; fax +39-2-701-22889.

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1. Introduction

Central dopaminergic (DA) dysfunctions have been suggested to be involved in the development and course of Anorexia Nervosa (AN). Since DA is a physiological inhibitor of hunger, acting on D-2 receptors in the hypothalamus (Leibowitz and Brown, 1980; Morley and Blundell, 1988; Inoue et al., 1994), an hypersecretion of the amine has been proposed to be responsible for anorexia and weight loss (Barry and Klavans, 1976). Even though changes in hunger sensation has not been always confirmed in AN (Owen et al., 1985; Nakai et al., 1987; Wash et al., 1989; Halmi, 1996), the possibility that impairments in the very complex control of the feeding system, of which DA function is a substantial part, might be involved in the development and modulation of the Disorders of Eating Behavior (ED) has never been definitely excluded. Increased central DA activity has been suggested to be responsible also for the hyperactivity which is often present during the course of AN (Barry and Klavans, 1976).

Central DA stimulates the function of the limbic–hypothalamo–pituitary–adrenal (LHPA) axis, inhibits the secretion of the hypothalamo–pituitary–gonadal (HPG) axis and of the hypothalamo–pituitary–thyroid (HPT) axis, and by acting directly on the pituitary lactotrops it inhibits the secretion of prolactin (PRL). In AN, and also in BN even though less frequently and severely, the function of the LHPA axis is increased (Gold et al., 1986; Kaye et al., 1987; Kaye, 1996; Walsh et al., 1987; Fichter et al., 1990; Vescovi et al., 1996) and that of the HPG and HPT axes and the PRL secretion are decreased (Casper et al., 1977; Judd et al., 1978; Fichter et al., 1990; Tommaselli et al., 1995; Altemus et al., 1996), which indirectly suggests that the hypothalamic DA stimulatory activity might be higher than normal in these disorders.

A central DA hyperactivity has been observed in Obsessive Compulsive Disorder (Brambilla et al., 1997), a pathology which is frequently combined with AN and BN, and has even been suggested to represent the core of a spectrum of which ED could be part (Rothenberg, 1986; Kasvikis et al., 1986; Pigott et al., 1991; Bellodi et al., 1992).

Finally, it is well known that the mesolimbic dopaminergic system is primarily involved with modulation of natural rewards and motivations (Di Chiara and Imperato, 1988; Di Chiara, 1999). Strong motivation in terms of feeding behavior, and feeling of high reward in successful food avoidance and weight loss are central in the pathology of AN and BN.

Studies of central secretion of DA and its metabolites in AN are contradictory. During the active phase of the disease, cerebrospinal fluid (CSF) concentrations of DA and its main metabolite homovanillic acid (HVA), have been found to be normal (Gerner et al., 1984), increased (Bowers et al., 1994), or decreased, with a return to