SEROTONIN, DIETING, AND BULIMIA NERVOSA

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ABSTRACT

Dieting is a common behaviour which may trigger eating disorders such as bulimia nervosa in predisposed subjects. We found that in healthy women moderate dieting for 3 weeks lowered plasma concentrations of the 5-HT precursor, L-tryptophan (TRP) and impaired brain 5-HT neurotransmission as judged by 5-HT neuroendocrine tests. In recovered female subjects with a history of bulimia nervosa we found that TRP depletion produced by an amino acid mixture lacking TRP caused a temporary return of depressive symptoms together with concerns about weight and shape and fear of loss of control of eating. Taken together the data suggest that dieting-induced decreases in TRP availability may trigger the development of bulimia nervosa in susceptible individuals.

1. DIETING AND EATING DISORDER

Cosmetic dieting is a common behaviour, particularly in young women. While dieting is not a particularly effective method of producing weight control, it is usually fairly harmless although food craving, irritability and cognitive impairment may result. Chronic dieters may also develop impaired satiety which can be linked to the development of binge eating.

From the point of clinical psychopathology the main reason for interest in dieting is that it almost invariably precedes eating disorders such as anorexia nervosa and bulimia nervosa (Hsu, 1997). Clearly subjects who develop these disorders have personal, family and social risk factors of which the most obvious is female gender. However, it does appear that in the presence of these risk factors, excessive dieting can be a key neurobiological trigger to eating disorders. Accordingly, the neurobiological effects of dieting are relevant to understanding of the pathophysiology of eating disorders.
2. EFFECTS OF DIETING ON SEROTONIN

While dieting has many biochemical effects, its consequences for brain serotonin (5-HT) function are of particular interest for studies of eating disorders such as bulimia nervosa. This is because 5-HT pathways have a well-established role in the regulation of food intake probably through increasing satiety (Tecott et al., 1995). Thus drugs which increase brain 5-HT function tend to decrease food intake while drugs with 5-HT receptor antagonist properties are associated with significant weight gain during clinical use. In addition there is evidence that bulimia nervosa is associated with impaired serotonin function (see below).

In a series of studies we found that moderate weight loss by dieting (1,000 kcal daily for 3 weeks) in healthy men and women decreased plasma concentrations of the 5-HT precursor, tryptophan (TRP). Interestingly in women but not men this decrease in plasma TRP was associated with altered brain 5-HT function as judged by neuroendocrine tests. Thus in women the prolactin response to intravenous administration of TRP was increased by dieting, as was the prolactin response to the 5-HT releasing agent d-fenfluramine (Walsh et al., 1995).

We hypothesised that these enhanced neuroendocrine responses were due to a compensatory up-regulation of post-synaptic 5-HT receptors. We were able to confirm this proposal by examining in women the prolactin response to the directly acting 5-HT2C receptor agonist, m-chlorophenylpiperazine (mCPP). This response was indeed increased by dieting (Cowen et al., 1996). We believe that the enhanced prolactin response to mCPP is caused by a compensatory increase in post-synaptic 5-HT receptor sensitivity presumably due to decreased pre-synaptic 5-HT release. This in turn is probably a consequence of diminished TRP availability to the brain (Cowen et al., 1996).

The effects of dieting upon the prolactin response to mCPP are of added interest because this neuroendocrine response is mediated via activation of 5-HT2C receptors in the hypothalamus (Cowen et al., 1996). Animal studies suggest that 5-HT2C receptors play a key role in mediating satiety, and animals that genetically lack 5-HT2C receptors become obese through overeating (Tecott et al., 1995). Thus during dieting we speculate that there is decreased 5-HT neurotransmission onto hypothalamic 5-HT2C receptors with consequent increases in hunger and loss of satiety. This might explain why some dieters experience episodes of loss of control of food intake with binge eating, one of the symptoms of bulimia nervosa.

3. BULIMIA NERVOSA AND 5-HT

3.1. Bulimia Nervosa

Bulimia nervosa is a common eating disorder characterised by recurrent episodes of binge-eating accompanied by extreme weight control measures (dieting, vomiting, purging) and overvalued ideas concerning weight and shape. Sufferers commonly experience concomitant major depression. Body weight is usually normal.

3.2. Bulimia Nervosa and 5-HT

A number of studies have examined indices of 5-HT neurochemistry and function in patients with acute bulimia nervosa. Some but not all studies have found lowered