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SEROTONIN AND APPETITE

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1. GENERAL BACKGROUND TO REVIEW

1.1. Introduction

The proposition that serotonin may be involved in the control of intake of food and the expression of appetite is less than 10 years old. Indeed, in a 600 page anthology of serotonin and behaviour published in 1973 (Barchas and Usdin, 1973) neither feeding behaviour nor food intake were included in the subject index. This late development of the link between serotonin and feeding is surprising. First, serotonin systems occupy a strategic anatomical location, projecting to and coursing through hypothalamic zones (Azmitia, 1978), where they could be expected to contribute to the dramatic changes in food consumption and body weight following experimentally-induced hypothalamic damage. Second, serotonergic neurones are widely distributed in the gut (Gershon and Dreyfus, 1977; Ahlman, 1976; Fozard, 1984) where modifications of gastrointestinal functioning would give rise to repercussions in feeding activity. Although the earliest conceptualisations of neurochemical models of feeding control emphasised noradrenaline (Grossman, 1962; Booth, 1967) or dopamine (Ungerstedt, 1971; Marshall, Richardson and Teitelbaum, 1974), more recently two reviews have been specifically devoted to the role of serotonin (Blundell, 1977, 1979), whilst other reviews have given considerable attention to the issue (Hoebel, 1977; Coscina, 1977; Leibowitz, 1980) or have dealt with specialised aspects (e.g. Garattini, 1978). There is now no doubt that certain experimental manipulations of serotonergic metabolism produce marked effects on food consumption and less potent effects on other aspects of feeding behaviour. Do these results mean that some serotonin-containing neurones play a role in the natural regulatory system which serves to match an organism's nutritional intake to its bodily requirements? The present review will draw together recent research findings and suggest an appropriate interpretation of the data. It should be mentioned immediately that research on serotonin and feeding is progressing only gradually and has not yet been embraced by work on the characterisation of receptor subtypes. There appear to be two reasons for this. First, researchers have been preoccupied with establishing the validity and reliability of the basic relationship between serotonin adjustments and food intake. Second, there has been a concern to verify that any relationship involves a rational link between nutritional factors and neurochemical systems and is not dependent upon the mediation of a third factor such as changes in temperature, arousal or sedation. It is appropriate that a settlement of these methodological issues should precede the investigation of any association between feeding and a particular sub-type.

1.2. Summary

Research over the last 10 years has given rise to a particular pattern of findings and is characterised by certain clear trends. It is appropriate to state these clearly as a basis for the present examination of the field. The most striking and consistent effect is the suppression of food intake by experimental treatments which directly or indirectly activate serotonin receptors. There appears to be no exception (published in the literature) to this general rule. Consequently, activation of serotonin pathways or metabolism is a *sufficient*, though of course not a necessary, condition for the inhibition of food intake in experimental test situations. The converse of this effect, an increase in food intake resulting from an inhibition of serotonin metabolism or a blockade of receptors, is a much weaker phenomenon though it can be detected under suitable experimental circumstances. There are both theoretical and methodological reasons why an increase in food intake is a more elusive phenomenon than an anorexic action (see Blundell, 1981a for a discussion of this issue). One parsimonious interpretation of the effects of serotonin-induced manipulations of food intake is that certain serotonin-containing neurones and pathways mediate in the process of satiation (bringing an eating episode to a halt) and maintain the state of satiety (period of inhibition over further eating).

One further research theme in the field of serotonin and appetite concerns the proposal that serotonin-containing neurones may be involved in the selection of particular nutritional commodities, such as protein or carbohydrate, and in the expression of preferences for these macronutrients. The evidence for this hypothesis arises from experiments on nutritional manipulations and changes in dietary self-selection following experimental interventions in serotonin systems. Considerable methodological and technical