

THE NEURAL BASIS OF THE MOTIVATION TO EAT IN PRADER-WILLI SYNDROME

Elanor C. Hinton

Summary

Prader-Willi syndrome (PWS) is a genetically determined neurodevelopmental disorder characterised by excessive eating and a preoccupation with food, leading to life-threatening obesity if left uncontrolled. The evidence to date suggests that this is due to a dysfunctional satiety response of possible hypothalamic origin. The motivation to eat, however, is controlled by a distributed network of brain regions, encompassing the basic homeostatic system, as well as motivational reward circuits in the brain. The aim of this thesis is to investigate the neural correlates of the conscious experience accompanying fasting and food intake in those with PWS, in order to provide further understanding of the abnormal satiety response that results in the overeating in this syndrome.

An initial study was conducted in those without the syndrome, using positron emission tomography. This study examined the neural response to fasting and food intake, in conjunction with incentive motivational factors, in order to provide the specific hypotheses upon which to base the investigations in PWS. The main study of this thesis examined the neural response, and associated conscious experience, in individuals with PWS to an overnight fast and two disguised energy controlled meals, one of 400kcal and another of 1200kcal, in order to test the hypothesis that the neural processes of satiety are abnormal in PWS. This study also investigated the neural basis of incentive motivation in PWS, following an examination of food preferences in those with the syndrome.

These studies provided evidence for a dysfunctional satiety response in the brain in those with PWS: even after the high energy meal, brain regions that normally elicit a feeling of satiety and signal the end of further food seeking, as found in the comparison group, were not activated. This was accompanied by an altered conscious experience following food - only some of the participants were able to detect a substantial shift to fullness following the high energy meal. Furthermore, extrinsic incentive factors appeared not to contribute to the motivation to eat in those with the syndrome. These findings have implications for the management of the eating behaviour in PWS, particularly with regard to the ethics of controlling the food environment of adults with the syndrome.