

negative rumination. Cognitive behavioural treatments may be useful, but reliable drug therapy awaits further pharmacogenomic developments. A healthy, low-energy, widely accepted 'comfort food' remains a theoretical target.

THE USE OF THE REINSTATEMENT MODEL TO STUDY THE NEUROBIOLOGY OF RELAPSE TO FOOD SEEKING DURING DIETING

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Relapse to old unhealthy eating habits is a major problem in human dietary treatments. The mechanisms underlying this relapse are largely unknown. Until recently, this clinical problem has not been systematically studied in animal models. In this lecture, I will first summarize results from studies in which we adapted a rat reinstatement model (commonly used to study relapse to drug use) to study the effects of pharmacological agents on relapse to food seeking induced by either food priming (non-contingent exposure to small amounts of food), cues previously associated with food, or the pharmacological stressor yohimbine. I will then present results from recent studies in which we used immunohistochemistry to quantify the neuronal activity marker Fos (the protein product of the immediate early gene *c-fos*), as well as optogenetic and electrophysiology methods to study the role of medial prefrontal cortex in reinstatement of food seeking in male and female rats. I will conclude by discussing potential implications of our data for medication development and future research.

THE DARK AND THE LIGHT SIDES OF COMPULSIVE EATING

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Dieting to control body weight involves cycles of deprivation from palatable food that can promote compulsive eating. Our studies show that rats withdrawn from intermittent access to palatable food exhibit overeating of palatable food upon renewed access and an affective withdrawal-like state characterized by hypophagia of the less preferred diet, motivational deficits to obtain less palatable food, depressive-like behavior and anxiogenic-like behavior. Withdrawal was accompanied by increased expression of CRF and CRF1 electrophysiologic responsiveness in the central nucleus of the amygdala (CeA). Peripheral administration of the selective corticotropin-releasing factor-1 (CRF1) receptor antagonist R121919 reversed compulsive eating, hypophagia of the less preferred diet and anxiety-like behavior. Moreover, microinfusion of R121919 into the CeA blocked compulsive eating and anxiety-like behavior, without affecting the hypophagia of the under-accepted diet. On the other hand, microinfusion of R121919 into the basolateral amygdala (BLA) reduced the hypophagia of the less preferred diet, without affecting compulsive eating. Interestingly, during withdrawal, hypophagia and anxiogenic-like behavior were precipitated by peripheral and intra-CeA administration of the cannabinoid receptor type 1 (CB1) inverse agonist, SR141716A; finally, increased levels of the endocannabinoid 2-arachidonoyl glycerol (2-AG) as well as the cannabinoid receptor type 1 (CB1) were observed in CeA. These findings suggest that withdrawal from palatable food activates the extrahypothalamic CRF/CRF1 receptor system which promotes a negative emotional state and sustains compulsive eating. We also propose that the amygdaloid 2-AG/CB1 may be recruited as a counter-adaptive response to oppose the withdrawal-induced negative emotional affect.

ROLE OF CRF SYSTEM IN A MODEL OF BINGE EATING IN FEMALE RATS

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Binge eating (BE) may be caused by a unique interaction between dieting and stress. Hence we considered interesting to evaluate the role of corticotropin releasing factor 1 receptor (CRF-1R) mechanisms in BE.

Four groups of female rats were used: NR + NS was normally fed and not stressed on the test day (d25); NR + S was fed as NR + NS and stressed on d25; R + NS was exposed to 3 cycles of yo-yo dieting but not stressed; R + S was fed as R + NS and stressed on d25. All groups were fed with highly palatable food (HPF) for 2 h on day 5–6 and 13–14. Stress was induced by preventing access to HPF for 15 min, while rats were able to see and smell it. After the stressful procedure the rats had free access to HPF and standard chow.

BE was observed only in the R + S group and injections of R121919 (10–20 mg/kg, s.c.) significantly reduced it. Endocrinological analysis revealed marked increase of corticosterone (CORT) levels under R + S conditions. On the other hand, metyrapone (50 and 100 mg/kg), a CORT synthesis inhibitor, did not prevent BE, neither CORT injection (2.5 and 10 mg/kg) induced it.

When CRHR1 gene expression was monitored, an up-regulation in the bed nucleus of the stria terminalis (BNST), central (CeA) and basolateral amygdala (BLA) of R + S rats was found. Of note, bilaterally injection of the non selective CRF receptor antagonist D-Phe-CRF(12–41) (50 ng/rat) into the BNST potently and selectively reduced BE.

Altogether these findings demonstrated that extra-hypothalamic CRF-1R related mechanisms rather than the endocrine function of these receptors are involved in BE.

FREE ORAL COMMUNICATIONS

INTERACTION BETWEEN GENETIC AND ENVIRONMENTAL FACTORS PROMOTES COMPULSIVE EATING AND ALTERS EXPRESSION OF DOPAMINERGIC AND NORADRENERGIC RECEPTORS

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Eating disorders are multifactorial conditions involving genetic, metabolic, environmental, and behavioral factors. Drugs of abuse and palatable food intake show behavioral similarities and common neurobiological adaptations have been proposed to be involved in both drug and food related-disorders. Compulsive drug-intake in the face of adverse consequences has been shown to emerge following an extended history of drug-taking, as well as compulsive eating emerges following extended access to a palatable diet. Finally, stress exposure influences both the propensity to take drugs and food intake. Although mesolimbic dopamine is critically involved in motivational aspects of food and drugs of abuse, recent reviews suggest a critical role of prefrontal catecholamine transmission in eating disorders, and we have previously demonstrated a major role of prefrontal noradrenergic transmission in food-related motivated behavior.

Here we show that interaction between extended access to chocolate and chronic stress is able to transform adaptive food seeking/intake behavior into compulsive eating in DBA/2J mice, previously shown to be