The dark and the light sides of compulsive eating

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Palatability

Subjective evaluation of a tastant’s properties is a major determinant of its acceptability and preferredness as a food.

Promotes consumption of energy-containing foods in scarce environments (e.g. sugary substances sensed as sweet and experienced as pleasant).

In rich Western environments, may contribute to the epidemic overeating and obesity (the latter proposed to be included as a mental disorder in DSM-V).
Progression of drug dependence

- Work hard to get praise from your boss
- Work hard to avoid getting laid off

Positive Reinforcement  
Negative Reinforcement
A history of dieting results in repeated, discrete alternations in food palatability

Hypothesis
To determine whether limiting access to a palatable diet induces compulsive eating through a negatively reinforced mechanism

Positive Reinforcement

Negative Reinforcement
Limited access to a highly palatable diet
Body weight fluctuations make cycled rats heavier and fatter with increased metabolic syndrome-related adipocytokine levels

Cottone et al. Psychoneuroendocrinol, 2009
Cycled rats withdrawn from palatable food show spontaneous anxiety-like and hypohedonic-like behavior.

Cottone et al. *Psychoneuroendocrinol*, 2009
Palatable Food Addiction Cycle

Withdrawal

Intake of regular chow food

↓ Intake of palatable food

↑ Anxiety-like behavior

↔ Hedonic-like behavior

↔ Depressive-like behavior

Compulsive eating
The CRF$_1$ receptors mediate anxiety and drug withdrawal responses

Corticotropin-releasing factor (CRF), is a 41-amino acid peptide secreted by the paraventricular nucleus of the hypothalamus in response to stress.

**Extrahypothalamic** CRF system is activated during withdrawal from cocaine, alcohol, nicotine, opiates, and THC and mediates many of the associated behavioral responses to stress.

Systemic administration of anxiolytic-like doses of small molecule selective CRF$_1$ receptor antagonists are sufficient to reduce increased anxiety-like behavior and excessive intake during drug withdrawal and to attenuate stress-induced reinstatement of heroin, cocaine and ethanol seeking.

Heinrichs et al. 1995; Koob et al. 1994; Richter and Weiss 1999; Rodriguez de Fonseca et al. 1997; Funk et al., 2006; Sabino et al., 2006; Breese et al., 2005; Lu et al., 2000; Shaham et al., 2000.
CRF₁ receptor blockade differentially *increases* the intake of the regular chow diet, and *decreases* compulsive eating

Cottone et al, *PNAS*, 2009
CRF₁ receptor blockade antagonizes anxiety-like and hypohedonic-like behavior in cycled rats

Cottone et al, PNAS, 2009
CRF mRNA and peptide levels increase in the central amygdala in cycled rats during withdrawal from palatable food

Cottone et al, PNAS, 2009
Palatable Food Addiction Cycle

Withdrawal

Intake of palatable food
Anxiety-like behavior
Hedonic-like behavior
Depressive-like behavior

Intake of regular chow food
Anxiety-like behavior
Hedonic-like behavior
Depressive-like behavior

Amygdaloid CRF
Amygdaloid 2-AG/CB₁

Compulsive eating

Laboratory of Addictive Disorders (LAD)