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The interplay between cocaine and the feeding hormone leptin in genetically diverse rats

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Cocaine is used mainly for its stimulant effects by young adults. A substantial fraction of females states weight control as the motivator to initiate and continue cocaine use. Moreover, weight gain during cocaine abstinence hinders recovery and leads to increased relapse. Identifying the effects of cocaine on feeding, metabolism, weight gain, and the reverse, regulated by feeding hormones like leptin, is critical for successful treatment in females.

Over 500 heterogeneous stock (HS) rats were characterized for their addiction-like behaviors using extended access of cocaine self-administration. Weight changes were monitored throughout the paradigm. A subset of 60 rats underwent measurements of fat mass, body mass index (BMI), blood leptin levels, food intake, and the effect of leptin on cocaine-seeking.

A significant weight gain was detected in vulnerable abstinent females compared to resistant abstinent and naïve females, but not in male groups. The weight gain was not the result of increased feeding but could be a consequence of altered metabolism. Baseline plasma levels of the feeding hormone leptin, a regulator of food intake and metabolism, were inversely correlated with the severity of addiction-like behaviors in the genetically diverse population. Moreover, systemically administered leptin reduced cocaine craving.

Our results indicate that leptin may, in addition to its role in regulating food intake, also represent a protective factor in regulating addiction-like behaviors and get dysregulated sex-dependently by drug intake, causing weight gain specifically in high addicted female subjects.