Diet-induced obesity promotes depressive-like behaviour that is associated with neural adaptations in brain reward circuitry.

BACKGROUND: The biological mechanisms that link the development of depression to metabolic disorders such as obesity and diabetes remain obscure. Dopamine- and plasticity-related signalling in mesolimbic reward circuitry is implicated in the pathophysiology and aetiology of depression. OBJECTIVE: To determine the impact of a palatable high-fat diet (HFD) on depressive-like behaviour and biochemical alterations in brain reward circuitry in order to understand the neural processes that may contribute to the development of depression in the context of diet-induced obesity (DIO). METHODS: Adult male C57Bl6 mice were placed on a HFD or ingredient-matched, low-fat diet for 12 weeks. At the end of the diet regimen, we assessed anxiety and depressive-like behaviour, corticosterone levels and biochemical changes in the midbrain and limbic brain regions. Nucleus accumbens (NAc), dorsolateral striatum (DLS) and ventral tegmental area dissections were subjected to SDS-PAGE and immunoblotting using antibodies against D1A receptor, D2 receptor, brain-derived neurotrophic factor (BDNF), phospho-DARPP-32(thr75), phospho-CREB and ΔFosB. RESULTS: HFD mice showed significant decreases in open arm time and centre time activity in elevated plus maze and open field tasks, respectively, and increased immobility (behavioural despair) in the forced swim test. Corticosterone levels following acute restraint stress were substantially elevated in HFD mice. HFD mice had significantly higher D2R, BDNF and ΔFosB, but reduced D1R, protein expression in the NAc. Notably, the expression of BDNF in both the NAc and DLS and phospho-CREB in the DLS was positively correlated with behavioural despair. CONCLUSIONS: Our results demonstrate that chronic consumption of high-fat food and obesity induce plasticity-related changes in reward circuitry that are associated with a depressive-like phenotype. As increases in striatal BDNF and CREB activity are well implicated in depressive behaviour and reward, we suggest these signalling molecules may mediate the effects of high-fat feeding and DIO to promote negative emotional states and depressive-like symptomology.