**Título:** Cafeteria diet temporarily affects brain reward dopaminergic pathway through DNA methylation mechanisms.
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We analysed the short and long-term effects of a highly palatable cafeteria diet(CAF) intake on the expression of key genes of the reward dopaminergic pathway of the brain(RW). Female rats were fed chow or CAF for 4(CAF4) or 11(CAF11) weeks. Ventral Tegmental Area(VTA), Accumbens Nucleus Core(NAC) and Shell(NAS), and Ventral Pallidum(VP) were isolated by micropunching technique. For mRNA analysis, qPCR was performed. Digestion with methylation-sensitive restriction enzymes followed by qPCR was used for epigenetic studies. Serum leptin was assessed by RIA. CAF4 increased energy intake and adiposity. In VTA, CAF4 enhanced dopamine active transporter(DAT) and decreased both isoforms of glutamate decarboxylase(GAD), without altering Tyrosine Hydroxylase levels. CAF4 decreased dopamine receptor 2 mRNA in NAS and increased GAD2 levels in VP. The changes in DAT mRNA were related to a decrease in the methylation status of its promoter region. CAF11 further increased energy intake and adiposity, leading to hyperleptinemia, and increased mRNA of leptin receptor in VTA, without affecting the expression of any gene of the RW studied. Our results indicate that, in the short-term, CAF deregulates the RW, at least in part via epigenetic changes, possibly reflecting a state of RW hyposensitivity, which might promote the excessive intake of palatable foods to compensate this status. This is reverted in the long-term, when the hypercaloric intake could respond to an altered homeostatic control.