High fat diet-induced obesity causes a reduction in brain tyrosine hydroxylase levels and non-motor features in rats through metabolic dysfunction, neuroinflammation and oxidative stress

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Abstract

Obesity is a health problem that has been associated with neuroinflammation, decreased cognitive functions and development of neurodegenerative diseases. Parkinson's disease (PD) is a chronic neurodegenerative condition characterized by motor and non-motor abnormalities, increased brain inflammation, *α*-synuclein protein aggregation and dopaminergic neuron loss that is associated with decreased levels of tyrosine hydroxylase (TH) in the brain. Diet-induced obesity is a global epidemic and its role as a risk factor for PD is not clear. Herein, we showed that 25 weeks on a high-fat diet (HFD) promotes significant alterations in the nigrostriatal axis of Wistar rats. Obesity induced by HFD exposure caused a reduction in TH levels and increased TH phosphorylation at serine 40 in the ventral tegmental area. These effects were associated with insulin resistance, increased tumor necrosis factor-*α* levels, oxidative stress, astrogliosis and microglia activation. No difference was detected in the levels of *α*-synuclein. Obesity also induced impairment of locomotor activity, total mobility and anxiety-related behaviors that were identified in the open-field and light/dark tasks. There were no changes in motor coordination or memory. Together, these data suggest that the reduction of TH levels in the nigrostriatal axis occurs through an *α*-synuclein-independent pathway and can be attributed to brain inflammation, oxidative/nitrosative stress and metabolic disorders induced by obesity.

Palabras clave

Obesity,Parkinson's disease,Tyrosine hydroxylase, Inflammation, Locomotion, Anxiety, Neuroinflammation, High-fat diet