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NEUROPSYCHIATRIC DISORDERS

Side effects of olanzapine worsened by metabolic dysfunction

Olanzapine, which is a second-generation antipsychotic drug, can cause metabolic side effects, including hyperphagia, weight gain and acute hyperglycaemia. Previously, researchers used lean, healthy rodents to investigate the mechanisms behind olanzapine-associated acute hyperglycaemia; however, individuals with schizophrenia are often obese and display perturbations in glucose metabolism prior to taking medication. Now, new research shows that high-fat diet (HFD)-induced obesity exacerbates olanzapine-associated acute metabolic side effects.

To investigate the acute metabolic response to olanzapine in lean and obese mice, David Wright and Logan Townsend fed mice either a standard chow or a HFD for 4 weeks before treating the mice with olanzapine. To examine the effect olanzapine had on the development of hyperglycaemia and insulin resistance in the mice, the authors measured markers of glucose homeostasis, insulin resistance and liver glucose production.

Mice fed a HFD were obese, hyperglycaemic and insulin resistant before treatment with olanzapine. The authors found that both hyperglycaemia and insulin resistance were exacerbated following treatment with olanzapine in mice fed a HFD compared to chow fed mice. In addition, the greater development of hyperglycaemia in HFD mice was associated with increases in liver glucose output and a marked attenuation of insulin signalling in muscle and liver.

The present study suggests that research examining the metabolic effects of antipsychotic drugs in lean, healthy mice potentially underestimates the severity of the side effects. Wright and colleagues are now working towards identifying new methods to counteract the metabolic side effects of antipsychotics.

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