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Recovery from sucrose-induced metabolic and cognitive impairments in male rats



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While many rat studies have examined the metabolic and behavioral impairments produced by excessive consumption of sugar solutions, few have focused on factors such as exercise that could influence recovery when access to such solutions is withdrawn. This issue is important, since excessive consumption of sugar-sweetened beverages makes a major contribution to the current obesity epidemic. In the first stage of four experiments rats were given unrestricted access to 10% sucrose solution for six weeks and in the second stage various factors including voluntary wheel running were manipulated to assess their impact on metabolic and behavioral measures. In Experiment 1 the second stage compared the effects of sugar withdrawal, sugar withdrawal plus food restriction, and sugar withdrawal combined with both food restriction and exercise. In Experiments 2 and 3 the second stage consisted of removing sucrose and restricting food access for all rats, while access to exercise varied across groups. In Experiment 4 the amount of exercise was manipulated during Stage 2. In all four experiments food restriction reduced body weight gain and fat pads relative to groups maintained on sucrose and in Experiments 3 and 4 improvements in performance on a spatial memory task were found. However, no additional benefits from wheel running were detected in any of the experiments. Paradoxically, in Experiment 2 the group given low exercise exhibited larger visceral fat pads than non-exercised rats. These experiments suggest that the most effective factor promoting recovery from the deleterious effects of excessive sugar consumption is restriction of energy intake and that voluntary wheel running has little or no additional impact.

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Metformin administration in pregnant high-fat fed rats improves metabolic function and adiposity



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Background: Obesity is a global health epidemic, where 28% of pregnant Australian women are obese. Maternal obesity increases the risk of a complicated pregnancy, including gestational diabetes mellitus (GDM) and cardiovascular dysfunction, highlighting the need for pregnancy interventions to improve maternal and fetal health. The anti-diabetic drug metformin is considered safe to be administered during pregnancy as a therapeutic for GDM. However, there is limited evidence of the effect metformin has in obese pregnancies.

Methods: Five week old female Wistar-Kyoto rats were allocated to a Control or High-fat (HF) diet. Prior to and during pregnancy rats underwent physiological measurements to determine metabolic and cardiovascular health, with 24 h food intake

measured. Rats allocated to HFD were allocated to receive metformin (300 mg/kg/day) or vehicle via oral gavage from gestation day 7 (E7–E18). At *post-mortem* (E20), fetal and placental weights were recorded and maternal tissues collected. Data were analysed by a one-way ANOVA.

Results: Not surprisingly, HFD increased pre-pregnant weight gain (+9%) indicative of increased adiposity, which is likely attributed to increased energy consumption (+44%), with no changes in cardiometabolic health. Although Metformin reduced energy consumption (–30%) and improved adiposity to Control values, pregnancy weight gain was not different across groups. Metformin improved glucose tolerance to Control values with HFD-vehicle being intermediate and no changes in blood pressure. Metformin reduced fetal (female) and placental (male and female) weights compared to Control, however placental efficiency was not affected.

Conclusion: We demonstrated that HFD consumption in rats resulted in glucose intolerance during pregnancy, which was resolved to chow rats with Metformin. These data highlight that Metformin has beneficial actions on maternal metabolic health and adiposity during pregnancy in overweight rats. Future studies are required to determine the impact this has on placental nutrient transportation and fetal development, which may impact long-term offspring health.

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N-acetylcysteine reduces ‘addiction-like’ behaviour towards high-fat high-sugar food in diet-induced obese rats



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Pathological overeating displayed by obese individuals shares similarities with compulsive drug taking behaviour observed in drug-addicted subjects. This raises the possibility that drug addiction treatments may show utility in the treatment of compulsive overeating. N-Acetylcysteine (NAC) is a cysteine pro-drug which has experienced some success in clinical trials to reduce the use of cocaine, marijuana and cigarettes, as well compulsive behaviours such as gambling and trichotillomania. We assessed the impact of NAC on addiction-like behaviour towards highly palatable food in a rat model of diet-induced obesity. Diet-induced obesity-prone (OP) and resistant (OR) rats were subjected to an operant conditioning paradigm where they were given the opportunity to lever press for high-fat high-sugar food pellets (S+). This alternated with periods of signalled reward unavailability (S–). Responding during S– periods is reflective of compulsive-like food-seeking behaviour (modelling the loss of control over behaviour observed in people suffering from addiction). OP rats had greater difficulty regulating reward-seeking behaviour during S– periods compared to OR rats. This persistent S– responding in OP rats was ameliorated by daily injections of NAC (100 mg/kg, i.p.) administered 2 h prior to the operant session for 10 days. By the end of the treatment period, there was no significant difference in S– responding between NAC treated OP rats and OR rats whereas vehicle treated OP rats remained significantly higher ($p < 0.05$). These findings show that NAC can attenuate palatable food-seeking behaviour in OP rats and supports the potential use of this compound as an ‘anti-craving’ compound to reduce compulsive overeating in obesity.

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