High-fat diet

- Electroacupuncture at ST36 ameliorates gastric dysmotility in rats with diabetic gastroparesis via the nucleus tractus solitarius-vagal axis
- FCGR2B knockdown alleviates diabetes-induced cognitive dysfunction by altering neuronal excitability
- Role of gut microbiota in bempedoic acid against hyperlipidemia: a new candidate target for bempedoic acid on the therapeutic regulation
- MiR221/222 in the conditioned medium of adipose-derived stem cells attenuates particulate matter and high-fat diet-induced cardiac apoptosis
- Non-alcoholic fatty liver disease enhances the beneficial effect of renal denervation on gut microbiota aberrations in rats with heart failure
- Neuroprotective Effect of beta-1,3-Glucans-Rich Euglena gracilis Against Ischemic Stroke in Middle-Aged Mice Fed With a High-Fat-High-Fructose Diet
- Unveiling the Important Role of Gut Microbiota and Diet in Multiple Sclerosis
- Metabolic stress and age drive inflammation and cognitive decline in mice and humans

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The ketogenic diet is a very low-carb, high-fat diet that shares many similarities with the Atkins and low-carb diets. It involves drastically reducing carbohydrate intake and replacing it with fat. This reduction in carbs puts your body into a metabolic state called ketosis.

Dearden et al. identified programmed overexpression of hypothalamic miR-505-5p that is established in the fetus, lasts to adulthood and is maintained in hypothalamic neural progenitor cells cultured in vitro. Metabolic hormones and long-chain fatty acids associated with obesity increase miR-505-5p expression in hypothalamic neurons in vitro. They demonstrated that targets of miR-505-5p are enriched in fatty acid metabolism pathways and overexpression of miR-505-5p decreased neuronal fatty acid metabolism in vitro. miR-505-5p targets are associated with increased BMI in human genetic studies. Intra-cerebroventricular injection of miR-505-5p in wild-type mice increased HFD intake, mimicking the phenotype observed in offspring exposed to maternal obesity. Conversely, maternal exercise intervention in an obese mouse pregnancy rescued the programmed increase of hypothalamic miR-505-5p in offspring of obese dams and reduced high-fat diet (HFD) intake to control offspring levels. This study identifies a novel mechanism by which maternal obesity programs obesity in offspring via increased intake of high-fat foods [1)].

It was observed that HFD (50% of diet) on chronic administration aggravates metabolic problems by causing reduced imbalanced oxidative stress, ATP production, and altered selective GLUT protein expression. Long-term HFD administration reduced ($p < 0.001$) the SOD, and CAT levels significantly along with elevated liver function marker AST and ALT. MLHEF administration diminishes this oxidative stress. HFD administration also causes decreased ATP/ADP ratio owing to suppressed mitochondrial function and elevated LDH levels. This oxidative imbalance further leads to dysregulated GLUT expression in hepatocytes, skeletal muscles, and white adipose tissue. HFD leads to significant ($p < 0.001$) upregulation in GLUT 1 and 3 expressions while significant ($p < 0.001$)

downregulation in GLUT 2 and 4 expressions in WAT, liver, and skeletal muscles. Administration of MLHEF significantly ($p < 0.001$) reduced the LDH level and also reduced the mitochondrial dysfunction.

Imbalances in GLUT levels were significantly reversed to maintain GLUT expression in tissues on the administration of MLHEF [2)]

High-fat diet (HFD) consumption is known to be associated with ovulatory disorder among women in reproductive age. Previous studies in animal models suggest that HFD-induced microglia activation contributes to hypothalamic inflammation. This causes the dysfunction of hypothalamic-pituitary-ovarian (HPO) axis, leading to subfertility. Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a novel class of lipid-soluble antidiabetic drugs that target primarily the early proximal tubules in kidney. Recent evidence revealed additional expression site of SGLT2 in the central nervous system (CNS), indicating a promising role of SGLT2 inhibitors in the CNS. In type 2 diabetes (T2D) patients and rodent models, SGLT2 inhibitors exerted the neuroprotective properties through antioxidative stress, alleviation of cerebral atherosclerosis, and the suppression of microglia-induced neuroinflammation. Furthermore, clinical observations in patients with polycystic ovary syndrome (PCOS) demonstrated that SGLT-2 inhibitors ameliorated the patient anthropometric parameters, body composition, and insulin resistance. Therefore, it is of importance to explore the central mechanism of SGLT-2 inhibitors in the recovery of reproductive function in patients with PCOS and obesity. Here, we review the hypothalamic inflammatory mechanisms of high-fat diet-induced microglial activation, with a focus on the clinical utility and possible mechanism of SGLT2 inhibitors in promoting reproductive fitness. Abstract figure legend Abstract figure legend: Summary of HFD feeding-induced anovulation and SGLT2 inhibitors ameliorate this dysfunction. This diagram illustrates that hypothalamic inflammation caused by HFD impairs GnRH surge release and ovulatory dysfunction, a progression mediated by proinflammatory factors secreted by activated microglia. In addition, the improvement of ovulatory dysfunction by SGLT2 inhibitors may be mediated by repair of GnRH surge release and neuroprotective properties. The pathways for how SGLT2 inhibitors have neuroprotective properties is that A. Inhibition of microglial activation results in decreasing proinflammatory factors release and neuroinflammation; B. Alleviation of cerebral atherosclerosis; C. Reduction of oxidative stress in neuron; D. Inhibition of ROS-dependent neuronal apoptosis [3)].

Injury severity is correlated with poor prognosis after traumatic brain injury (TBI). It is not known whether triglycerides (TGs) or total cholesterol (TC) is a good biomarker of increased injury of neuroinflammation and apoptosis in a high-fat diet (HFD)-treated rat after TBI episodes. Five-week-old male Sprague-Dawley (SD) rats were fed a HFD for 8 weeks. The anesthetized male SD rats were divided into three sub-groups: sham-operated and TBI with 1.6 atm or with 2.4 atm fluid percussion injury (FPI). Cell infarction volume (triphenyltetrazolium chloride stain), tumor necrosis factor-alpha (TNF-α) expression in the microglia (OX42 marker) and astrocytes (Glial fibrillary acidic protein marker), TNF-α receptor expression in the neurons (TNFR1 and TNFR2 markers), and the extent of neuronal apoptosis (TUNEL marker) were evaluated by immunofluorescence, and the functional outcome was assessed by an inclined plane test. These tests were performed 72 h after TBI. Serum triglyceride and cholesterol levels were measured at 24, 48 and 72 h after TBI. The FPI with 2.4 atm significantly increased body weight loss, infarction volume, neuronal apoptosis and TNF-α expression in the microglia and astrocytes, and it decreased the maximum grasp degree and TNFR1 and TNFR2 expression in neurons at the 3rd day following TBI. The serum TG level was positively correlated with FPI force, infarction volume, Neu-N-TUNEL, GFAP-TNFα, and OX42-TNFα Simultaneously; the serum TG

level was negatively correlated with Neu-N-TNFR1 and Neu-N-TNFR2. TG is a good biomarker of increased injury for neuroinflammation and apoptosis at the 3rd day after TBI in HFD rats [4].

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