Glutaredoxin 2

Type 2 diabetes mellitus (T2D) appears to be a significant risk factor for brain injury. Glutaredoxin 2 (GRX2) belongs to the oxidoreductase family and plays an essential role in regulating various cellular processes. However, the pathogenic role of GRX2 in high-fat diet (HFD)-induced brain injury is poorly understood. In the study, the loss-of-function approach was used to explore the effects of GRX2 on brain injury in HFD-challenged mice. The results indicated that HFD treatment resulted in significant increases in the change of body weight, insulin resistance and serum lipid deposition, which were markedly exaggerated by the loss of GRX2. Moreover, HFD-caused cognitive dysfunction was further promoted in GRX2 knockout mice. Histological analysis suggested that HFD administration led to the hippocampus damage, which was potentiated by GRX2 deficiency. In addition, GRX deletion enhanced HFD-induced inflammatory response in hippocampus of mice. Furthermore, GRX2 knockout markedly enhanced HFD-triggered insulin resistance in hippocampus of mice through down-regulating the protein levels of p-insulin receptor substrate 1 (IRS1) (Y632) and p-AKT (S473). The phosphorylation of glycogen synthase kinase-3β (GSK-3β) suppressed by HFD administration was further reduced by GRX2 ablation. Moreover, HFD-induced oxidative stress and mitochondrial dysfunction were significantly aggravated in hippocampus of GRX2-knockout mice, which were largely dependent on the modulation of GSK-3β signaling. These results above demonstrated that GRX2 was responsible for HFD-induced brain injury by enhancing insulin resistance, inflammation, oxidative stress and mitochondrial impairment via the meditation of GSK-3β [1)].

1)
Wohua Z, Weiming X. Glutaredoxin 2 (GRX2) deficiency exacerbates high fat diet (HFD)-induced insulin resistance, inflammation and mitochondrial dysfunction in brain injury: A mechanism involving GSK-3β. Biomed Pharmacother. 2019 Aug 2;118:108940. doi: 10.1016/j.biopha.2019.108940. [Epub ahead of print] PubMed PMID: 31382130.