Diabetes mellitus complications

see Diabetic neuropathy.

see Diabetic stroke.

Chronic diabetic wounds.

Spinal epidural abscess

Urinary retention from detrusor muscle areflexia or hypotonia (autonomic neuropathy).

Myelitis

Visual impairment in diabetes is a growing public health concern. Apart from the well-defined diabetic retinopathy, disturbed optic nerve function, which is dependent on the myelin sheath, has recently been recognized as an early feature of visual impairment in diabetes. However, the underlying cellular mechanisms remain unclear. Using a streptozotocin-induced diabetic mouse model, Wu et al. observed a myelin deficiency along with a disturbed composition of oligodendroglial lineage cells in the diabetic optic nerve. They found that new myelin deposition, a continuous process that lasts throughout adulthood, was diminished during pathogenesis. Genetically dampening newly generated myelin by conditionally deleting olig2 in oligodendrocyte precursor cells within this short time window extensively delayed the signal transmission of the adult optic nerve. In addition, clemastine, an antimuscarinic compound that enhances myelination, significantly restored oligodendroglia and promoted the functional recovery of the optic nerve in diabetic mice. The results point to the role of new myelin deposition in optic neuropathy under diabetic insult and provide a promising therapeutic target for restoring visual function [1)]

Macrovascular complications develop in over a half of the diabetic individuals, resulting in high morbidity and mortality. This poses a severe threat to public health and a heavy burden to social economy. It is therefore important to develop effective approaches to prevent or slow down the pathogenesis and progression of macrovascular complications of diabetes (MCD). Oxidative stress is a major contributor to MCD. Nuclear factor (erythroid-derived 2)-like 2 (NRF2) governs cellular antioxidant defence system by activating the transcription of various antioxidant genes, combating diabetes-induced oxidative stress. Accumulating experimental evidence has demonstrated that NRF2 activation protects against MCD. Structural inhibition of Kelch-like ECH-associated protein 1 (KEAP1) is a canonical way to activate NRF2. More recently, novel approaches, such as activation of the Nfe2l2 gene transcription, decreasing KEAP1 protein level by microRNA-induced degradation of Keap1 mRNA, prevention of proteasomal degradation of NRF2 protein and modulation of other upstream regulators of NRF2, have emerged in prevention of MCD. This review provides a brief introduction of the pathophysiology of MCD and the role of oxidative stress in the pathogenesis of MCD. By reviewing previous work on the activation of NRF2 in MCD, we summarize strategies to activate NRF2, providing clues for future intervention of MCD. Controversies over NRF2 activation and future perspectives are also provided in this review [2)].

Data suggest that diabetes in Chinese patients with intracerebral hemorrhage (ICH) is not associated with increased mortality or functional outcome. Future studies are needed to clarify possible confounders affecting prognosis after ICH [3].

Diabetes-associated cognitive decline

Targeting the PPARγ might be a potential therapeutic strategy for diabetes-associated cognitive decline (DACD). In this study, Gypenoside LXXV (GP-75), a dammarane-type triterpene compound isolated from Gynostemma pentaphyllum, was found to be a novel PPARγ agonist using a dual-luciferase reporter assay system. However, whether GP-75 has protective effects against DACD remains unknown. Interestingly, intragastric administration of GP-75 (40 mg/kg/day) for 12 weeks significantly attenuated the cognitive deficit in db/db mice. GP-75 treatment significantly improved the glucose tolerance and lipid metabolism, and suppressed neuroinflammation. Notably, GP-75 treatment dramatically increased the uptake of glucose by the brain, as detected by 18 F-FDG PET. Incubation of primary cortical neurons with GP-75 significantly increased 2-deoxyglucose uptake. In addition, GP-75 treatment markedly increased the p-Akt (Ser 473)/total Akt levels and the expression levels of PPARγ and GLUT4, while decreasing the levels of p-IRS-1 (Ser 616)/total IRS-1. Importantly, all of these protective effects mediated by GP-75 were abolished by cotreatment with the PPARγ antagonist, GW9662. However, GP-75-mediated PPARγ upregulation was not affected by coincubation with the phosphatidylinositol 3-kinase inhibitor, LY294002. Collectively, GP-75 might be a novel PPARγ agonist that ameliorates cognitive deficit by enhancing brain glucose uptake via the activation of Akt/GLUT4 signaling in db/db mice [4].

The prevalence of both Alzheimer disease (AD) and vascular dementia (VaD) is increasing with the aging of the population. Studies from the last several years have shown that people with diabetes have an increased risk for dementia and cognitive impairment. Therefore, the authors of this consensus review tried to elaborate on the role of diabetes, especially type 2 diabetes mellitus (T2DM) in both AD and VaD. Based on the clinical and experimental work of scientists from 18 countries participating in the International Congress on Vascular Disorders and on literature search using PUBMED, it can be concluded that T2DM is a risk factor for both, AD and VaD, based on a pathology of glucose utilization. This pathology is the consequence of a disturbance of insulin-related mechanisms leading to brain insulin resistance. Although the underlying pathological mechanisms for AD and VaD are different in many aspects, the contribution of T2DM and insulin resistant brain state (IRBS) to cerebrovascular disturbances in both disorders cannot be neglected. Therefore, early diagnosis of metabolic parameters including those relevant for T2DM is required. Moreover, it is possible that therapeutic options utilized today for diabetes treatment may also have an effect on the risk for dementia. T2DM/IRBS contribute to pathological processes in AD and VaD [5].

1)
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