Role of hippocampal lipocalin-2 in experimental diabetic encephalopathy

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Diabetic encephalopathy is a severe diabetes-related complication in the central nervous system that is characterized by degenerative neurochemical and structural changes leading to impaired cognitive function. While the exact pathophysiology of diabetic encephalopathy is not well understood, it is likely that neuroinflammation is one of the key pathogenic mechanisms that cause this complication. Lipocalin-2 (LCN2) is an acute phase protein known to promote neuroinflammation via the recruitment and activation of immune cells and glia, particularly microglia and astrocytes, thereby inducing proinflammatory mediators in a range of neurological disorders. In this study, we investigated the role of LCN2 in multiple aspects of diabetic encephalopathy in mouse models of diabetes. Here, we show that induction of diabetes increased the expression of both Lcn2 mRNA and protein in the hippocampus. Genetic deficiency of Lcn2 significantly reduced gliosis, recruitment of macrophages, and production of inflammatory cytokines in the diabetic mice. Further, diabetes-induced hippocampal toxicity and cognitive decline were both lower in Lcn2 knockout mice than in the wild-type animals. Taken together, our findings highlight the critical role of LCN2 in the pathogenesis of diabetic encephalopathy.