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Dysfunction of microglia in hyperglycemia

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Microglia play important roles in maintaining brain homeostasis. Dysfunction of microglia is implicated in various neurological disorders. Recent studies have shown that microglia are also involved in the metabolic diseases. In hyperlipidemia, long chain fatty acids induced microglial activation, resulting in exacerbation of the disease. However, the involvement of hyperglycemia in microglial functions has not been clarified.

First, we investigated the effect of high glucose on primary mouse microglia. Chronic high glucose treatment (2-3 weeks) increased inflammatory cytokine levels such as IL-1β and TNFα, and decreased microglial phagocytosis and migration, indicating that chronic exposure of high glucose led to dysregulation of microglial function. Then, we examined the impact of chronic hyperglycemia on microglia using streptozotocin-induced diabetic model mice. IL-1β and TNFα expressions in microglia from diabetic mice were increased compared with control mice. Minocycline, a microglial inhibitor, decreased the expressions of these cytokines. Minocycline intervened in diabetic mice also decreased food intake and blood glucose level with the enhanced expression of proopiomelanocortin which inhibited appetite.

Our study might demonstrate that chronic hyperglycemia activated microglia and induced hypothalamic inflammation, leading to the stimulation of appetite and the exacerbation of hyperglycemia. Abnormally activated microglia in diabetic conditions might be one of the therapeutic targets for hyperglycemia.

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