Potential role of immediate early expression of G protein-coupled receptor 3 in mast cells after cerebral brain ischemia

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G protein-coupled receptor 3 (GPR3) is highly expressed in the central nervous system (CNS) and can constitutively activate the Gαs protein in the absence of ligands. However, the physiological roles of GPR3 in the CNS have not been fully elucidated. Here, we investigated whether GPR3 expression is modulated following brain ischemia. GPR3 mRNA expression was transiently upregulated in the ischemic hemisphere as early as 4 h after transient middle cerebral artery occlusion in Wistar rats and C57BL/6 mice. Analyses of brain homogenates indicated that brain mast cells (BMCs) were the source of upregulated GPR3 in ischemic brains. Several reports have shown that the degranulation of BMCs alters the permeability of the blood–brain barrier, thereby influencing the pathophysiology of stroke. Thus, utilizing bone marrow-derived mast cells (BMMCs), we asked whether GPR3 expression could modulate degranulation of mast cells. When BMMCs were stimulated by IgE-mediated dinitrophenyl conjugated human serum albumin (DNP-HSA) or adenosine triphosphate (ATP), GPR3 mRNA was found to be highly upregulated as early as 1–2 h, and declined thereafter. In addition, the degranulation of BMMCs by DNP-HSA or ATP was significantly inhibited by the elevation of intracellular cAMP. Moreover, BMMCs from GPR3 knockout mice showed significantly increased degranulation in response to various degranulation stimuli. These results suggest that GPR3 could play a role in inhibiting the degranulation of mast cells, and could modulate immediate early responses after brain ischemia.