Roles for microglial N-type Ca^{2+} channel in aging-related enhanced neuroinflammation

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Voltage-dependent calcium channel (VDCC) is generally known to be functional only in excitable cells. However, we have reported recently that N-type VDCC (Cav2.2) could become functional in non-excitable cells under pathological conditions. In the present study, we have demonstrated that Cav2.2 channels are also functional in physiological microglial activation process. MG6 cells, a mouse microglial cell line, showed an enhanced neuroprotective M2 transition in the presence of a Cav2.2 blocker but no changes in the efficacy of the neuroinflammatory M1 transition. Treatment with a specific blocker of hypoxia inducible factor 2 (HIF-2) completely abolished this enhancement, suggesting an involvement of HIF-2 in this process. It is known that enhanced neuroinflammation occurs in aging brains. And we found that the efficacy of microglial M1 transition was enhanced but that M2 transition was reduced by aging in primary culture experiments. Interestingly, blockade of microglial Cav2.2 expression restored this aging-dependent reduction of microglial M2 transition and reduced the aging-induced exaggerated cytokine response, as revealed by a fast recovery from depressive-like behaviors in microglia-specific Cav2.2 deficient mice. These results suggest a critical role for microglial Cav2.2 channel in the aging-related neuroinflammation.

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