Pathophysiological role of reactive astrocytes in a mouse chronic cerebral hypoperfusion model

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Chronic cerebral hypoperfusion (CCH) is manifested in various CNS diseases accompanied by cognitive impairment. We have previously reported that microglial activation induced excessive inflammatory responses, white matter injury, and resultant aggravation of cognitive impairment in a mouse CCH model with bilateral common carotid artery stenosis (BCAS). Prior to the onset of cognitive impairment, we also observed the increase in the number of GFAP-immunopositive astrocytes at day 14 after BCAS operation. Although the increase remained until day 28, the pathophysiological role of astrocytes in CCH remains to be elucidated. Here, we focused on the pathophysiological significance of the increased number of astrocytes and their regulating mechanisms in CCH. To clarify the involvement of reactive astrocytes in CCH, we checked the subtype of reactive astrocytes, a pro-inflammatory A1-like phenotype or an anti-inflammatory A2-like phenotype, and observed the increase in the expression of A2-like gene in BCAS-operated mice at day 14, whereas no significant difference was seen in the expression of A1-like gene between BCAS- and sham-operated mice. These results imply that anti-inflammatory astrocytes play important roles in the early stage of development in CCH prior to the white matter injury and cognitive impairment.