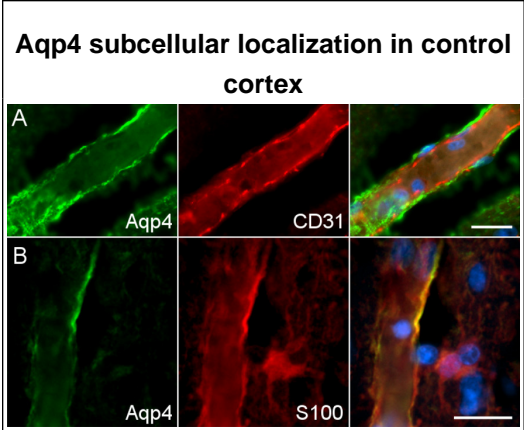


Introduction

Ischemic stroke, a major cause of mortality, is frequently accompanied by life-threatening cerebral edema. Aquaporin-4 (Aqp4), an astrocytic transmembrane water channel, is an important molecular contributor to cerebral edema formation. Past studies of Aqp4 expression and localization after ischemia examined grey matter exclusively. However, as white matter astrocytes differ developmentally, physiologically, and molecularly from grey matter astrocytes, we hypothesized that functionally important regional heterogeneity exists in Aqp4 expression and subcellular localization following cerebral ischemia.

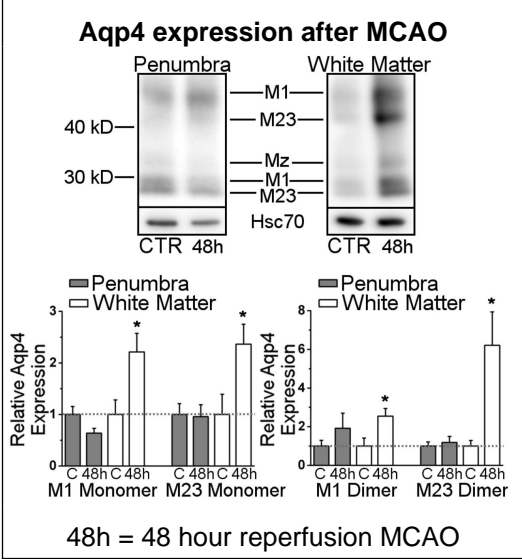
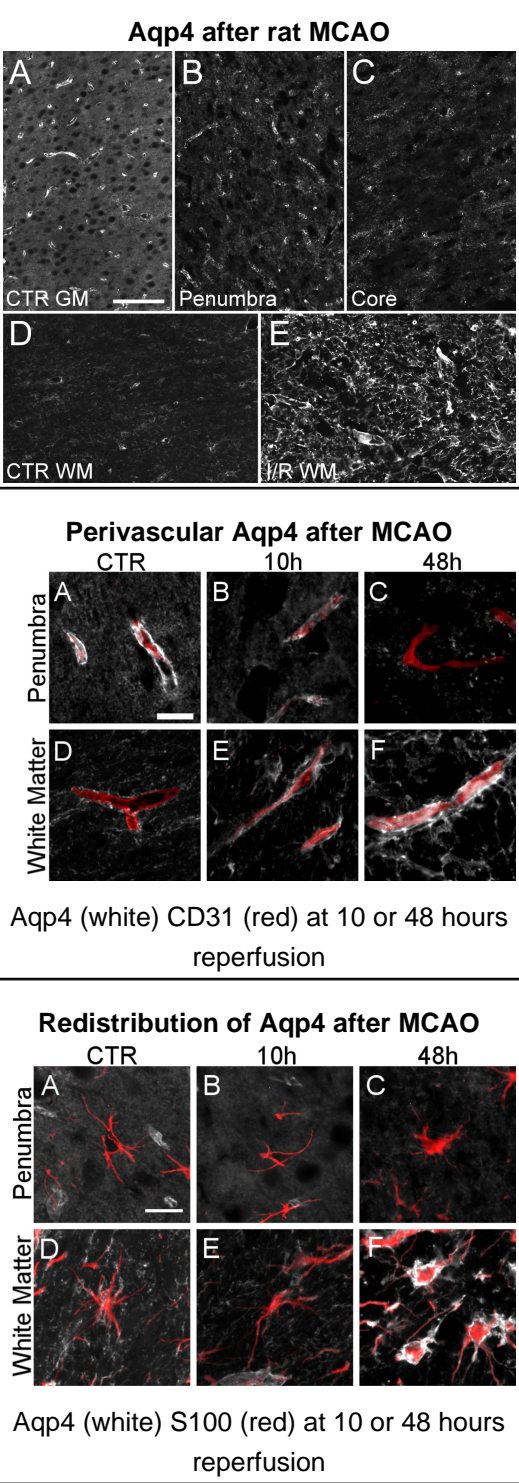
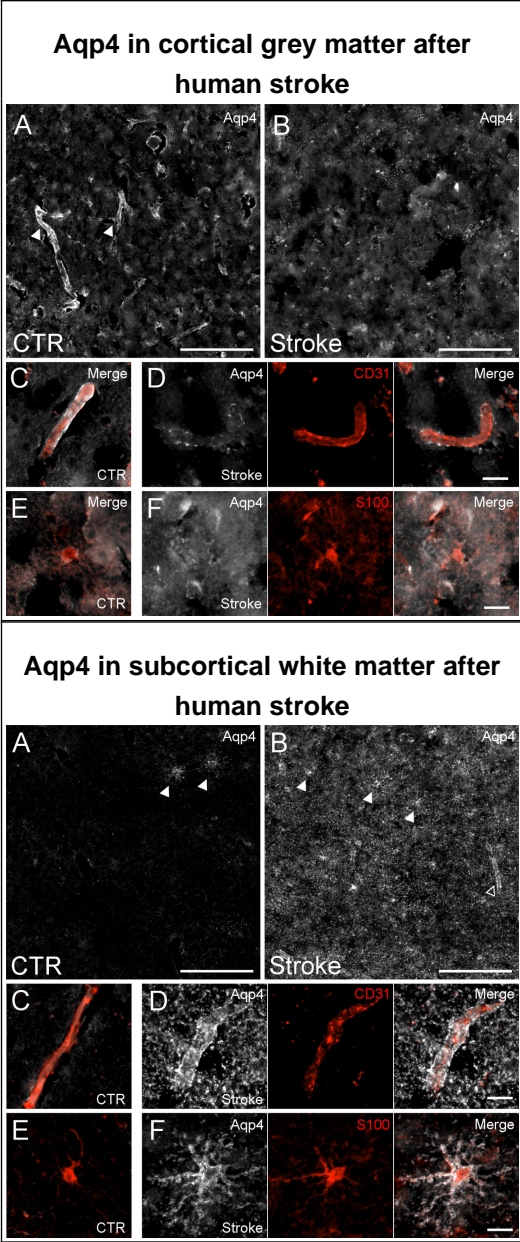


Methods

Localization of Aqp4 was compared between cortical and white matter astrocytes in postmortem specimens of patients with focal ischemic stroke versus controls. Subcellular localization and expression of Aqp4 was examined in rats subjected to MCAO (2 hour ischemia and varying reperfusion). Volumetric analysis was performed on the cortex and white matter of rats subjected to MCAO.

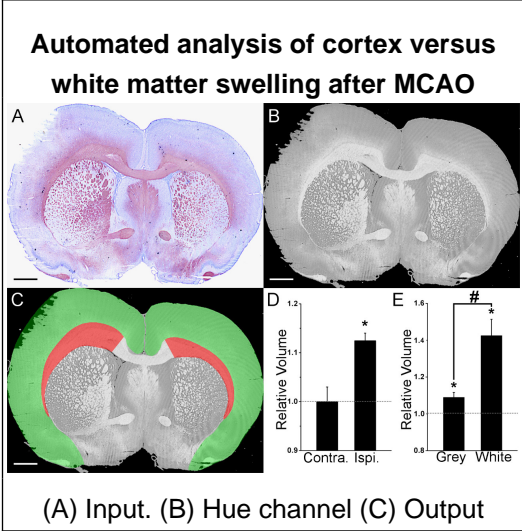
Results

Cortical astrocytes exhibited reduced perivascular Aqp4 and unchanged Aqp4 protein abundance. In contrast, white matter astrocytes exhibited increased perivascular and plasmalemmal Aqp4.



Results

Ischemic white matter swelled by approximately 40%, while cortex swelled by approximately 9%.



Conclusions

These results raise the possibility that cerebral white matter may play a heretofore underappreciated active role in the formation of cerebral edema following ischemia.