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Aquaporin-4 facilitates paravascular space closure and neuronal activity reduction after water intoxication

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Rapid intraperitoneal water injection induces acute hyponatremia that creates an osmotic gradient driving for water entry into the brain, leading to subsequent cerebral edema. Paravascular spaces, which are covered by astrocyte end-feet, have been suggested to participate in the fluid circulation in cerebral cortex, however, it has not been clarified whether they morphologically change during the edema formation. Here we have established an *in vivo* imaging method with a closed cranial window under isoflurane anesthesia to observe paravascular spaces and astrocytes using CAG-GFP transgenic mice. We simultaneously monitored electro-corticogram (ECoG) and other physiological parameters, such as cerebral blood flow (CBF), heart rate, and arterial blood pressure, to examine their responses up to 40 min after the bolus injection of distilled water equal to 10% of body weight. We first confirmed that water injection indeed increased brain tissue water content, which was alleviated in aquaporin-4 (AQP4) knockout mice. While control and AQP4 knockout mice did not differ in the cell swelling of astrocyte, even AQP4 are expressed in the astrocyte end-feet, paravascular space closure was prevented in AQP4 knockout mice. Furthermore, the ECoG power reduction in AQP4 knockout mice was less than that in control mice. These results implicate that the regulation of paravascular spaces may play roles in modulating brain water circulation and brain edema formation, which might be controlled by AQP4.