

O-20(기초) Effect of Estrogen on the Expression of Aquaporin 1 in Ovariectomized Mouse Brain

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Background & Objectives: Brain aquaporins (AQP) play important roles in the dynamic regulation of brain water homeostasis and the production of cerebrospinal fluid (CSF) under normal, as well as pathological, conditions. To elucidate the role estrogen in the maintenance of brain water homeostasis, changes in the expression of AQP1, an important structural element of choroid plexus following ovariectomy (OVX), as well as the effect of estrogen (17 β estradiol) on the expression of AQP1 in OVX brain, was examined in mice.

Method: Cyclic adult female mice were prescreened by vaginal smearing and selected animals were subjected to ovariectomy. After recovery, to allow clearance of circulating estrogen following OVX or sham, mice were rested for two weeks, and then subjected to estrogen treatment. Additionally, some OVX mice received intraperitoneal injections of 17 β estradiol (E2) at 20 μ g/head (single injection) or 1 μ g/head (for 7 days) dissolved in sesame oil (n=4 for each treatment). As a control, sesame oil was injected as a vehicle (n=4). Normal cyclic mice (n=4) were sacrificed at the estrous stage. OVX mice were sacrificed 24 h after final dosing of E2.

Results: Throughout brain development, the immunoreactivity of AQP1 was found in the choroid plexus. Ependyma, pia, and veins were also positive for AQP1 immunoreactivity. AQP1 mRNA level showed gradual decrease until postnatal day 8 but reincreased at adulthood. Two forms of AQP1 polypeptides with Mr. 35 and 28 kDa in brain. Both forms were much higher in the fetal brain but only 35 kDa form was detected in adult brain. AQP1 was significantly down regulated in OVX brain compared with the sham control at the estrous stage. In OVX mice, estrogen significantly up-regulated AQP1 mRNA levels together with transthyretin, a marker for estrogen response in choroids plexus, compared with OVX-vehicle control.

Conclusions: Together, these results suggest that expression of AQP1 in female brain tissue is tightly regulated by estrogen. To our knowledge, this is the first report on the estrogen dependent regulation of brain AQPs.