Effects of Female Gonadal Hormones on Neuromedin S and its Receptor Following Experimental Traumatic Brain Injury

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Abstract
Brain edema plays an important role in secondary tissue damage following traumatic brain injury (TBI) but the underlying mechanisms are not entirely elucidated. The G protein coupled receptor FM-4 and its ligands, neuromedin S (NMS) and neuromedin U (NMU), are expressed in diverse brain areas, and have a variety of roles in nociception, inflammation, and stress but their probable changes after brain trauma has not yet been investigated. In the current study, we investigated the effect of low and high physiological levels of progesterone (P4) and 17 β-estradiol (E2) replacements on brain NMS and NMU and expression of FM-4 as well as cerebral edema following TBI. Female Albino N-Mari rats were given female sex steroid hormones by capsule implantation for one week before brain injury or were not given hormone replacement therapy. The animal groups were included: Ovariectomized (OVX)+low estradiol (LE), OVX+high estradiol (HE), OVX+low progesterone (LP), OVX+high progesterone (HP), OVX+TBI, blank, vehicle (Veh). At 24 hrs after trauma, brain edema was estimated by measuring the brain water content. expression of prepro-NMS and FM-4, and the NMU protein content were evaluated. The results demonstrated that following TBI, the cerebral water content in (OVX+HP) and (OVX+HE) groups was less than in TBI untreated groups ($P<0.01$). Quantitative real time PCR indicated the higher expression of FM-4 gene and western blot analyses revealed an increase in prepro-NMS protein expression in progesterone-replaced rats compared to the both traumatic-unreplaced and estradiol-replaced groups. Our findings suggest that progesterone-replacement attenuates brain edema and induces an enhance in prepro-NMS and FM-4 mRNA expression which may mediate the anti-edematous effects of this hormone following TBI.

Keywords: Trauma Brain Injury, Estradiol, Progesterone, Neuromedin U, Neuromedin S.

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