Extended Abstract

Intranasally-applied oxytocin alleviates aberrant maternal behaviors evoked by cesarean section in rats: Involvement of supraoptic neurons

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Milk shortage and aberrant maternal behaviors in women with cesarean section (CS) have become an increasing concern for the health of mothers and the babies recently; however, the underlying mechanisms and optimal therapeutic approaches remain to be explored. In this study, we found that CS significantly reduced' retrieving, anogenital licking and suckling behaviors of rat dams while increasing the rate of self-grooming. Moreover, early dam-pup contact evoked more self-grooming while delayed maternal contacts resulted in severe hypogalactia. Intranasal application of oxytocin (OXT), a hypothalamic neuropeptide largely restored normal pattern of maternal behaviors in the CS dams. In whole-cell patch-clamp recordings putative OXT neurons in the supra optic nucleus (SON) in brain slices from the CS dams had lower firing rate and more depolarized resting membrane potential. Western blot and immunohistochemical analyses revealed that CS increased the expression of phosphorylated extracellular signal regulated protein kinase (pERK) 1/2, particularly at non-OXT neuronal components and glial fibrillary acidic protein (GFAP) of astrocytes in the somatic section of the SON. In the CS dams, intranasal application of OXT increased c-Fos protein in the area rich in OXT neurons but reduced GFAP in the somatic section of the SON while decreasing pERK 1/2 expression. These results indicate that CS can lead to postpartum depression and anxiety in association with the time of postpartum mother-baby contact, which is largely due to the suppression of hypothalamic OXTsecreting system; intranasal OXT can partially reverse these aberrant behaviors, thereby highlighting a novel therapeutic target. Oxytocin (OT) is a key factor for maternal behavior. However, neurochemical regulation of OT neurons, the major source of OT, remains incompletely understood. Here we report the effect of intranasally-applied OT (IAO) on OT neuronal activity in the supraoptic nucleus (SON) and on maternal behavior in a rat model of cesarean delivery (CD) at day 4-5 (stage I) and day 8-9 (stage II) following delivery. We found that at stage I, CD dams exhibited significantly longer latency of pup retrieval, lower number of anogenital licks and smaller acinar area of the mammary glands. In the SON, the number of OT neurons expressing phosphorylated extracellular signal-regulated protein kinase 1/2 (pERK 1/2) decreased significantly. IAO reversed the depressive-like maternal behavior and involution-like change in the mammary glands, and restored the number of pERK1/2-positive OT neurons in CD dams. At stage II, CD did not significantly influence the latency of retrieval and pERK1/2 expression in the SON. However, CD still reduced the number of anogenital licks during suckling, which was reversed by IAO. Notably, IAO but not hypodermic OT application in CD dams significantly increased litter's body weight gains. In brain slices, CD but not CD plus IAO significantly depolarized membrane potential and increased spike duration in OT neurons. In vasopressin neurons, CD, but not CD plus IAO, significantly depolarized membrane potential and increased the firing rate. Thus, decreased OT neuronal activity and increased vasopressin neuronal activity impair maternal behavior in CD dams, which can be prevented by IAO.