Neuroprotective effects of oxytocin on hypoxic-ischemic brain injury in neonatal rats

Chang-ning Xie¹, Jian Wu¹, Si-cong Peng¹, Jing Wu¹, Ling-hui Xiao¹, Tao Liu¹,²*

¹ Department of Pediatrics, the First Affiliated Hospital of Nanchang University, Nanchang 330006, China;
² Center for Experimental Medicine, The First Affiliated Hospital of Nanchang University, Nanchang 330006, China;

*Corresponding author
E-mail: liutaommm@hotmail.com

Abstract: Objective Neonatal hypoxic-ischemic encephalopathy (NHIE) is one of the most prevalent causes of death or lifelong disability in children. Thus, it is urgent to seek for new and more effective neuroprotective therapy to minimize the consequences of HIE. Previous studies have shown that oxytocin can improve learning and memory ability after ischemic stroke of adult rats. Here, we ask whether oxytocin has neuroprotective effects on neonatal rats with hypoxic-ischemic brain injury. Methods Brain slices of 350 μm-thick from 7-10 days old Sprague-Dawely rats were used. Visualized whole-cell patch-clamp recordings were obtained from hippocampal CA1 pyramidal neurons. In-vitro model of hypoxic-ischemic cell injury was used by exposing the brain slices to the oxygen-glucose deprivation (OGD) solution for 10 min or longer. Results In 12 out of 16 neonatal CA1 pyramidal neurons, bath application of oxytocin (0.1 μM) induced an inward current (16.11 ± 1.98 pA) at a holding potential of -70 mV under voltage-clamp recording, which suggest a probable effect of exogenous oxytocin on CA1 pyramidal neurons. Therefore, when switched to current-clamp (I=0), we observed that oxytocin significantly prolonged the onset time of anoxic depolarization from 13.44 ± 1.84 min to 23.19 ± 2.04 min after the superfusion of OGD solution. Interestingly, both oxytocin receptor antagonist dVOT and GABA receptor antagonist bicuculline
blocked this effect. Moreover, oxytocin increased both the amplitude and frequency of spontaneous inhibitory postsynaptic currents (sIPSCs) in a concentration-dependent manner but had no significant influence on spontaneous excitatory postsynaptic currents (sEPSCs) in CA1 pyramidal neurons. In addition, the facilitation effect of oxytocin on IPSCs was blocked by either tetrodotoxin or dVOT. **Conclusion** Oxytocin exerts a neuroprotective effect by enhancing the inhibitory synaptic transmission through oxytocin receptors in neonatal CA1 pyramidal neurons. Therefore, oxytocin could be used as a candidate for neuroprotective treatment after NHIE.

**Keywords:** Hypoxic-ischemic brain damage; neonate; oxytocin; hippocampal neuron; GABA receptor