Involvement of supraspinal orexin-A/orexin receptors in the regulation of central post-stroke pain

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Central post-stroke pain (CPSP) is one of the secondary diseases of cerebral stroke. However, the detailed mechanism remains unclear. Recently, it is reported that the ablation of supraspinal orexin neurons induced mechanical allodynia in mice. In this study, we tested the involvement of supraspinal orexin system in the regulation of CPSP. Male ddY mice (5 weeks old) were subjected to 30 min of bilateral carotid artery occlusion (BCAO). Colocalization of fluorogold (a retrogradely transported tracer) with orexin-A were determined by double-immunofluorescence. Mechanical allodynia was measured by von Frey filament test. Intrathecal (i.t.) injection of fluorogold was colocalized with orexin-A positive cells in the hypothalamus. On day 3 after BCAO, the withdrawal responses to mechanical stimuli were significantly increased and prepro-orexin was decreased as compared with sham. The BCAO-induced mechanical allodynia suppressed by the intracerebroventricular injection of orexin-A. This effect of orexin-A was significantly inhibited by the i.t. injection of an orexin 1 or 2 receptor antagonist. These results suggest that the supraspinal orexin-A system mediated by the OX1R and OX2R play an important role in the regulation of CPSP.