

**P222-D.07.a Pain: Peripheral receptors****Abstract: 2969****D042 - The role of NMDA receptors in peripheral trigeminal nociception**

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The peripheral trigeminovascular system (TVS) in meninges has been proposed to participate in migraine pain. Central terminals of trigeminal neurons release glutamate to transmit pain signals to the higher brain centres. However, the peripheral glutamatergic signalling is poorly understood. In the present study, we investigated the role of the ionotropic glutamate NMDA receptors (GluN) in peripheral migraine pathophysiology. The localization of GluN subunits (GluN2A and GluN2B) in rat trigeminal ganglia cells was determined by immunohistochemistry. The functional responses of rat trigeminal neurons exposed to NMDA were explored by calcium imaging in control and after the exposure to the migraine mediator calcitonin gene-related peptide (CGRP). The excitability of cranial meningeal trigeminal nerve terminals was studied by electrical recording of spikes with a suction electrode. We observed that the GluN2A receptor subunits were expressed in both trigeminal neurons and satellite glial cells, whereas GluN2B subunits were expressed only in neurons. NMDA (co-applied with glycine) evoked intracellular calcium responses in a small fraction of neurons; and this fraction was increased after exposure to CGRP, the effect most notable in young rats. NMDA also increased the nociceptive firing in peripheral trigeminal nerve terminals. In conclusion, our data suggest that NMDA receptors in TVS contribute to migraine-related nociception at the level of somas of trigeminal neurons and in peripheral trigeminal nerve terminals in meninges.