Involvement of spinal cholecystokinin-8 and histamine in diabetic neuropathic pain in mice

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Diabetes mellitus is one of the major causes of peripheral neuropathy, which can reveal the spontaneous allodynia. Our study was designed to determine a potential involvement of spinal cholecystokinin-8 (CCK-8) and histamine in mediating streptozotocin (STZ)-induced diabetic allodynia in mice. STZ (200 mg/kg)-induced mechanical allodynia was evoked significantly 7 day after intravenous (i.v.) injection. The mechanical allodynia elicited by STZ was concentration-dependently inhibited by intrathecal (i.t.) administration of antisera against CCK-8 (1:100 – 1:25) and histamine (1:200 – 1:50). No significant of mechanical allodynia induced by i.v. administration of STZ was shown in histidine decarboxylase deficient mice. The mechanical allodynia elicited by STZ were suppressed by i.t. administration of agmatine (40 – 160 pmol), antagonists for the NMDA receptor polyamine-binding site. The inhibitor of the activation and proliferation of microglia, minocycline (0.25 – 2 nmol, i.t.), inhibited the mechanical allodynia elicited by STZ in a dose-dependent manner. The present results suggest that the STZ-induced mechanical allodynia are mediated through the spinal CCK-8 and histamine and are elicited via activation of NMDA receptors in glial cell.