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Inhibitory effects of anti-high mobility group box-1 neutralizing antibody on nociceptive hypersensitivity in Parkinson's disease

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Parkinson's disease (PD) patients have complained of pain, but mechanisms mediating nociceptive hypersensitivity have been poorly understood. High mobility group box-1 (HMGB1) plays an important role in maintenance of nociceptive hypersensitivity under neuropathic pain state. Moreover, HMGB1 is increased in cerebrospinal fluid in PD patients. However, little is known about the relationship between HMGB1 and nociceptive hypersensitivity in PD. Then, the current study investigated that the effect of anti-HMGB1 neutralizing antibody (nAb) on mechanical allodynia with mouse PD model. To generate PD model, male ddY mice were injected with 6-hydroxydopamine (6OHDA) into right striatum. Anti-HMGB1 antibody (10 µg) was administrated by intranasal (i.n.) route. The mechanical allodynia was evaluated by von Frey filaments. In PD mice, dopamine neurons were decreased in ipsilateral substantia nigra. Moreover, the PD mice exhibited mechanical allodynia of hind paws and microglial activation in bilateral spinal dorsal horn. The i.n. administration of anti-HMGB1 nAb inhibited mechanical allodynia and microglial activation in PD mice. These findings suggested that HMGB1 is involved in mechanical allodynia in PD models. Therefore, i.n. treatment with anti-HMGB1 nAb might be a new strategy for nociceptive hypersensitivity in PD.