Abstract

High mobility group box-1 (HMGB1) is a ubiquitous non-histone nuclear protein that plays a key role as a transcriptional activator, with its extracellular release provoking inflammation. Inflammatory responses are essential in methamphetamine (METH)-induced acute dopaminergic neurotoxicity. In the present study, we examined the effects of neutralizing anti-HMGB1 monoclonal antibody (mAb) on METH-induced dopaminergic neurotoxicity in mice. BALB/c mice received a single intravenous administration of anti-HMGB1 mAb prior to intraperitoneal injections of METH (4 mg/kg×2, at 2-h intervals). METH injections induced hyperthermia, an increase in plasma HMGB1 concentration, degeneration of dopaminergic nerve terminals, accumulation of microglia and extracellular release of neuronal HMGB1 in the striatum. These METH-induced changes were significantly inhibited by intravenous administration of anti-HMGB1 mAb. In contrast, blood-brain barrier disruption occurred by METH injetions was not suppressed. Our findings demonstrated the neuroprotective effects of anti-HMGB1 mAb against METH-induced dopaminergic neurotoxicity, suggesting that HMGB1 could play an initially important role in METH toxicity.