Stimulation of LXA_4 receptor alleviates motor dysfunction in intracerebral hemorrhage model mice

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Intracerebral hemorrhage (ICH), a bleeding into the brain parenchyma, is a devastating neurologic disease with the highest mortality among all stroke subtypes. In ICH brain, thrombin induces activation of microglia/macrophages followed by neuroinflammation. Furthermore, ICH leads to infiltration of numerous leukocytes. Recent report shows the arachidonic acid metabolite, leukotriene B_4 (LTB_4), participates pathological progression of ICH (Hijioka *et al.*, 2017). In this study, we focused on lipoxin A_4 (LXA_4), synthesized from arachidonic acid as same as LTB_4. Treatment of murine microglial cell line BV-2 cells with thrombin (30 U/mL) increased mRNA expression level of inducible NO synthase (iNOS) and interleukin-6 (IL-6). Pretreatment with LXA_4 (100 μM) suppressed thrombin-induced increases in iNOS and IL-6 mRNA expression. Moreover, immunocytochemical analysis revealed the translocation of nuclear factor-κB (NF-κB) into the nucleus induced by thrombin, and thrombin-induced nuclear translocation of NF-κB was suppressed by LXA_4. Finally, daily intravenous administration of LXA_4 receptor agonist, BML-111 (1 mg/kg) attenuated the motor dysfunction of mouse model of ICH. These data suggest that LXA_4 may be the novel therapeutic agent for ICH.