Induction of microsomal prostaglandin E synthase-1 contributes to neuroinflammation and neurological dysfunctions in a mouse intracerebral hemorrhage model.

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We have demonstrated that microsomal prostaglandin E synthase-1 (mPGES-1), an inducible terminal enzyme for PGE_2 synthesis, is a critical factor of stroke-reperfusion injury. In this study, we investigated the role of mPGES-1 in neuroinflammation and neurological dysfunctions observed after intracerebral hemorrhage (ICH). Collagenase was injected into the left striatum of adult mPGES-1 knockout (KO) and wild-type (WT) mice. In WT mice, mRNA and protein of mPGES-1 were significantly up-regulated in striatum and cerebral cortex after ICH. In mPGES-1 KO mice, although the hemorrhage and edema size were almost the same as WT mice, survival rate was significantly higher than WT mice. The PGE_2 production, TNF-α induction and glial activation after ICH in mPGES-1 KO brain were significantly less than those in WT brain. DAPI and TUNEL staining showed ICH-induced nuclear condensation and DNA fragmentation in mPGES-1 KO striatum were less than those in WT striatum. Furthermore, mPGES-1 KO mice showed better performance in stepping error test, rotarod test and neurological dysfunction scoring compared with the WT mice. These results suggest that mPGES-1 contributes to ICH-induced neuroinflammation, neuronal apoptosis, neurological dysfunctions and mortality through PGE_2 production. Thus, mPGES-1 may be a new therapeutic target for ICH.