<Sample: KAA Abstract>

**Alarmin HMGB1 induces brain and systemic inflammatory exacerbation in the post-stroke infection rat models (Times New Roman, Bold, 18 pt)**

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Post-stroke infection (PSI) is known to worsen functional outcomes of stroke patients and accounts to one-third of stroke-related deaths in hospital. In our previous reports, we demonstrated that massive release of high-mobility group box protein 1 (HMGB1), an endogenous danger signal molecule, is promoted by N-methyl-D-aspartic acid-induced acute damage in the postischemic brain, exacerbating neuronal damage by triggering delayed inflammatory processes. Moreover, augmentation of proinflammatory function of lipopolysaccharides (LPS) by HMGB1 via direct interaction has been reported. The aim of this study was to investigate the role of HMGB1 in aggravating inflammation in the PSI by exacerbating the function of LPS. PSI animal model was produced by administrating a low-dose LPS at 24 h after post-middle cerebral artery occlusion (MCAO). Profound aggravations of inflammation, deterioration of behavioral outcomes, and infarct expansion were observed in LPS-injected MCAO animals, in which serum HMGB1 surge, especially disulfide type, occurred immediately after LPS administration and aggravated brain and systemic inflammations probably by acting in synergy with LPS. Importantly, blockage of HMGB1 function by delayed administrations of therapeutic peptides known to inhibit HMGB1 (HMGB1 A box, HPep1) or by treatment with LPS after preincubation with HMGB1 A box significantly ameliorated damages observed in the rat PSI model, demonstrating that HMGB1 plays a crucial role. Furthermore, administration of Rhodobacter sphaeroides LPS, a selective toll-like receptor 4 antagonist not only failed to exert these effects but also blocked the effects of LPS, indicating its TLR4 dependence. Together, these results indicated that alarmin HMGB1 mediates potentiation of LPS function, exacerbating TLR4-dependent systemic and brain inflammation in a rat PSI model and there is a positive-feedback loop between augmentation of LPS function by HMGB1 and subsequent HMGB1 release/serum. Therefore, HMGB1 might be a valuable therapeutic target for preventing post-stroke infection. (Times New Roman, Plain, 12 pt)

**Key Words (5-6 word)**

HMGB1, Post-stroke infection, Inflammation, TLR4

**Coresspondence**

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