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Serum amyloid a-dependent inflammasome activation, BBB leakage and acute injury in experimental stroke

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Serum amyloid A (SAA) proteins increase dramatically in the blood following ischemic injury. The impact of SAAs in the pathogenesis of stroke was addressed in this study. Wildtype and SAA deficient mice were exposed to transient intraluminal middle cerebral artery occlusion (MCAo), examined for infarct volumes, behavioral changes, inflammatory markers, TUNEL staining, and BBB changes. In addition, over expression of SAA via transgene or viral vectors were examined in the SAA deficient mice. SAA levels were significantly increase following ischemia and reperfusion injury (IRI) and mice deficient in SAAs showed reduced infarct volumes and improved behavioral outcomes. SAA deficient mice showed a reduction in TUNEL staining, inflammation and decreased glial activation. Mice lacking both acute phase SAAs demonstrated a reduction in expression of the NLRP3 inflammasome protein and SAA/NLRP3 KO mice showed a slight improvement. Restoration of SAA expression via SAA tg mice or adenoviral expression reestablished the detrimental effects of SAA on infarct volume. A reduction in BBB permeability was seen in the SAA KO mice and anti-SAA antibody treatment reduced the effects on ischemic injury.The data suggest that acute phase SAAs play an injurious role in stroke outcomes. Therefore, therapeutics that target elevated SAA levels following stroke might help to reduce the harmful effects and improve long-term consequences.