

RNS60 Provides Acute and Chronic Protection of Brain Cells and Function in a Mouse Stroke Model

RNS60 is an experimental treatment containing oxygen nanobubbles that has been shown to reduce neuroinflammation and increase neuronal survival in a variety of pathophysiological conditions that activate neurodegeneration. We evaluated whether RNS60 can reduce brain injury and rescue cognitive functions in a mouse model of ischemic stroke. Male C57BL/6J mice (4 months old) were subjected to either transient (60 minutes) occlusion of the middle cerebral artery (tMCAo) followed by reperfusion, or sham surgery. We investigated the effects of post-stroke RNS60 treatment for 3 or 13 days (beginning 1 hour after reperfusion, 0.2 mL administered I.P, 1/day). Two control treatments (normal saline or oxygenated saline without nanobubbles) were used for comparison. Experimenters were blinded to the treatment groups throughout the study. To assess the post-stroke effects of RNS60 treatments, we performed multiple neurobehavioral tests that included modified neurological severity score (mNSS), novel object recognition (NOR), active place avoidance (APA), and the conflict variant of APA. Brains were collected for assessment of infarct volumes and for immunofluorescence measurements of amyloid beta, neurons, microglia, and axons. Three days of treatment with RNS60 reduced brain infarction, edema, sensory-motor, and cognitive deficits. Thirteen days of treatment reduced brain infarction, amyloid pathology, neuronal cell death, microglial activation, and white matter damage. Noteworthy behavioral effects included recovery of memory during NOR, APA and cognitive flexibility in the APA conflict variant. RNS60 treated mice exhibit acute and chronic protection of brain cells and neurobehavior after experimental stroke. This strongly suggests further investigations be made into RNS60s mechanism of action, the optimization of experimental dosing and treatment durations, and longer post-stroke recovery.