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**“Effect of Novel Docosanoids on Behavior, Physiological Parameters and Survival After Experimental Stroke in Female Rats”**

Stroke is the fifth leading cause of death and long-term health complications. Tissue plasminogen activator, most commonly known as tPA, is a potent blood thinner used for emergency stroke treatment and only an approved drug that should be administered within 4.5h of stroke onset, but still only 5-8% of patients qualify for this therapy. Sex and gonadal hormone exposure have a considerable independent impact on stroke outcomes.

This study focuses on the neuroprotective bioactivity of docosanoid mediators: Neuroprotectin D1 (NPD1), Resolvin D1 (RvD1), and their combination in experimental stroke. Recently, we have shown that NPD1 and RvD1 are neuroprotective in male rats, but whether a similar effect occurs in female rats is unknown.

*Methods:* Female Sprague-Dawley rats (280-300g) were anesthetized with 1-3% isoflurane, 70% nitrous oxide, and 30% oxygen, mechanically ventilated, and subjected to 2h of middle cerebral artery occlusion (MCAo) by poly-L-Lysine-coated intraluminal suture. Rectal and temporal muscle temperatures, blood gases (pH, pCO<sub>2</sub>, pO<sub>2</sub>), hematocrit, and plasma glucose were monitored before, during, and after MCAo. NPD1 (IV, 222 µg/kg), RvD1 (IV, 222 µg/kg), both, or vehicle (IV, 0.9% 1mL/kg, ethanol saline mixture) were administered at 3 hours after stroke onset. A gap of 15 minutes was given between the administration of NPD1 and RvD1. The composite neuroscore comprises two different neurological tests, the postural reflex test and the forelimb placing test, to measure visual, tactile, and proprioceptive stimuli, which were evaluated on days 1, 2, 3, 7, 14, 21, and 28 (normal score=0; maximal deficit score=12). Rats were perfused on day 28, and their brains were sent to UCI for MRI imaging.

*Results:* Physiological variables were stable and showed no significant differences between groups. In the NPD1 treatment group, the neuroscore improved on days 1, 2, 3, 7, 14, 21, and 28 by 29, 30, 32, 37, 41, 39, and 33%, respectively, compared to the vehicle. In the RvD1 treatment group, the neuroscore improved on days 1, 2, 3, 7, and 14 by 30, 34, 33, 28, and 26%, respectively, compared to the vehicle. Combinatory treatment with NPD1 +RvD1 improved neuroscore on days 1, 2, 3, 7, 14, 21, and 28 by 36, 41, 47, 52, 58, 55, and 52%, respectively, compared to the vehicle.

*In conclusion,* treatments with NPD1 and RVD1 alone significantly improved neurological scores during 28 days survival period. Combinatorial treatment by NPD1 plus RvD1 affords synergistic neuroprotection in the post-ischemic brain when treatment is administered at 3 h after stroke onset. We are currently exploring the cell-specific and molecular mechanisms involved. These findings open avenues for ischemic stroke therapeutics.