

# MicroRNA363-3p treatment after ischemic stroke protects the cortex in reproductively senescent female rats.

## INTRODUCTION

- Stroke is one of the leading causes of death in the United States.
- Ischemic strokes are about 87% of all strokes and a major cause of long-term disability, reduces mobility in more than half of stroke survivors over 65 (Virani SS et al. 2020), and dementia including Alzheimer's disease.
- MCAo stroke induces cognitive dysfunction (cortical function), affects input to spatial memory/learning (hippocampal-dependent) (Panta et al., 2020), and leads to malfunctions in retrograde connections from the thalamus altering the hippocampal-thalamic network activity (Baumgartner, P et al. 2018).
- Our previous work has shown that the use of microRNA mir 363-3p in the acute phase after an ischemic stroke reduces infarct volume (Selvamani et al., 2017) and alleviates cognitive impairment (Panta et al., 2020).

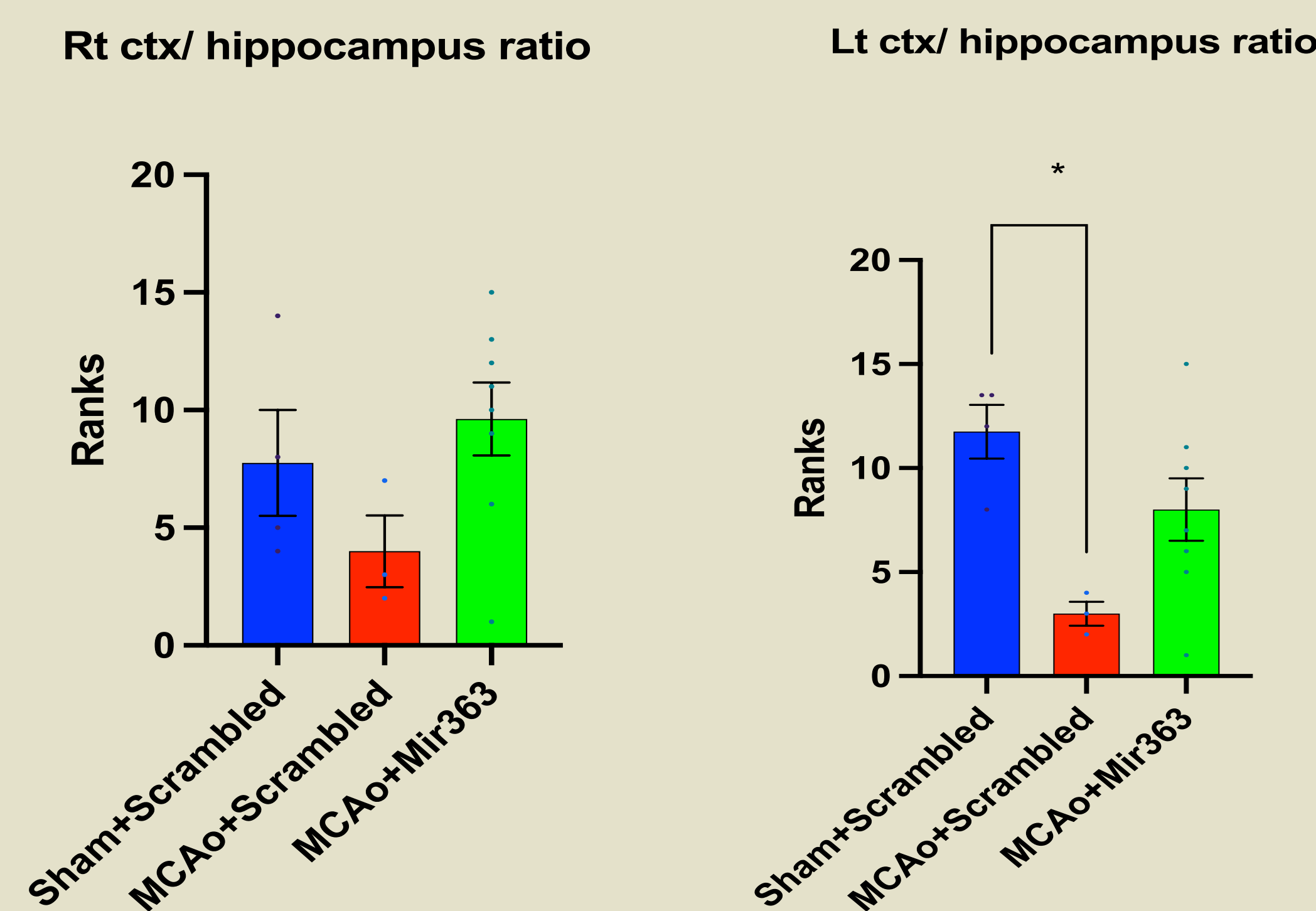
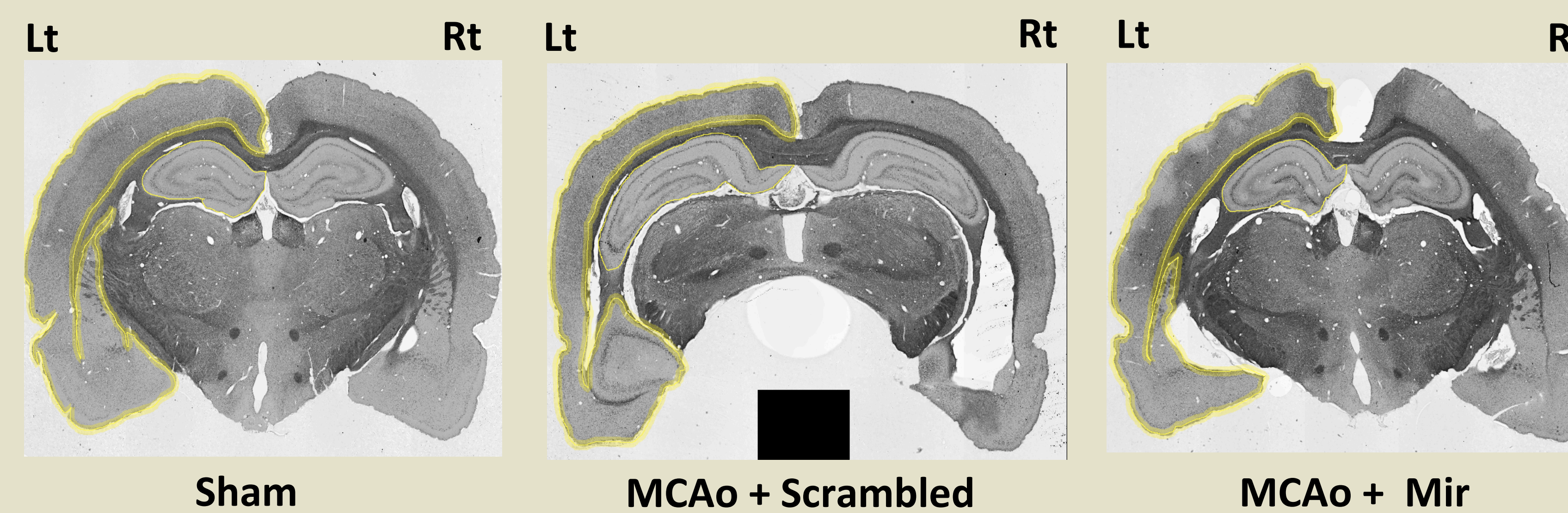
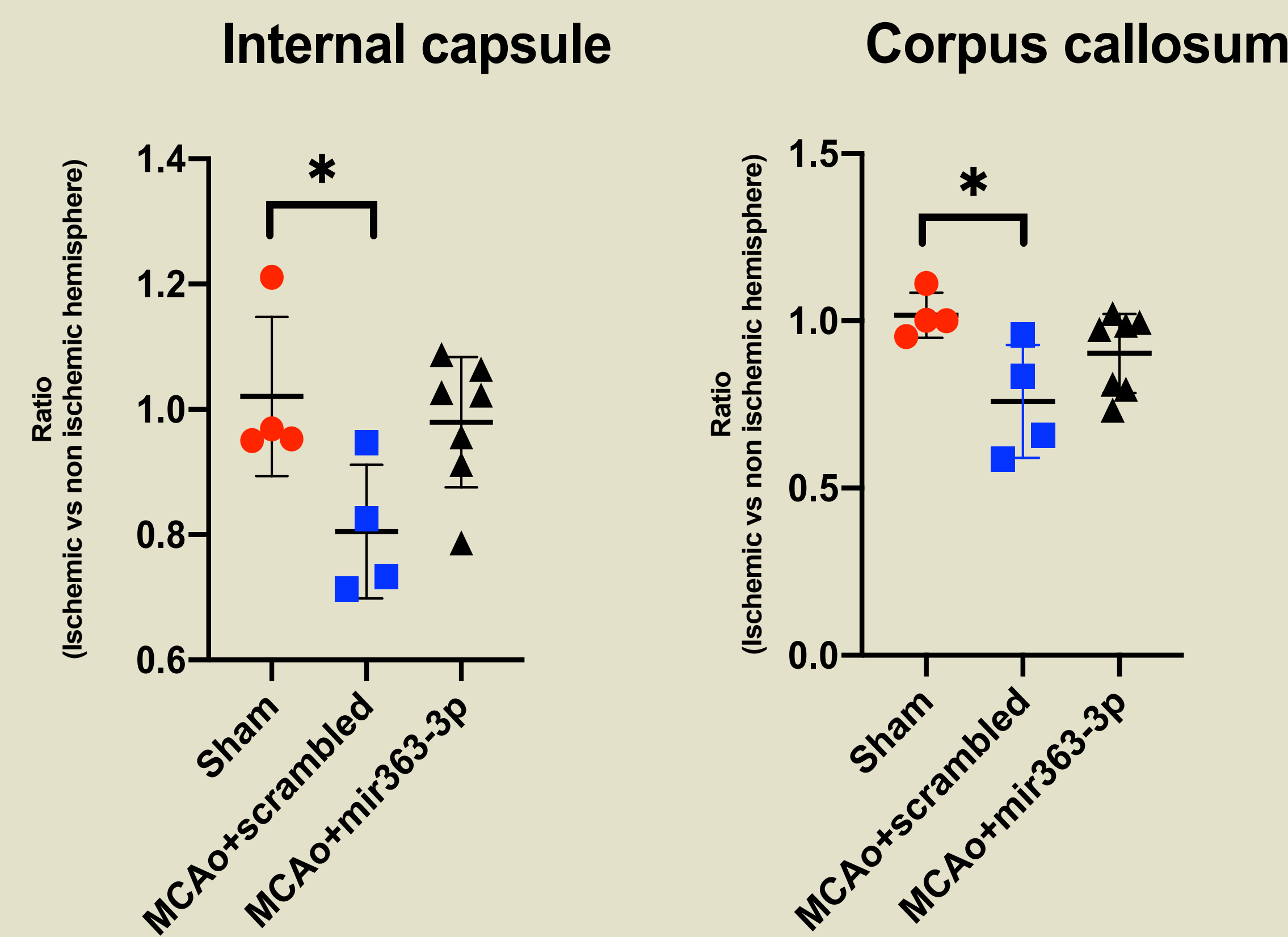
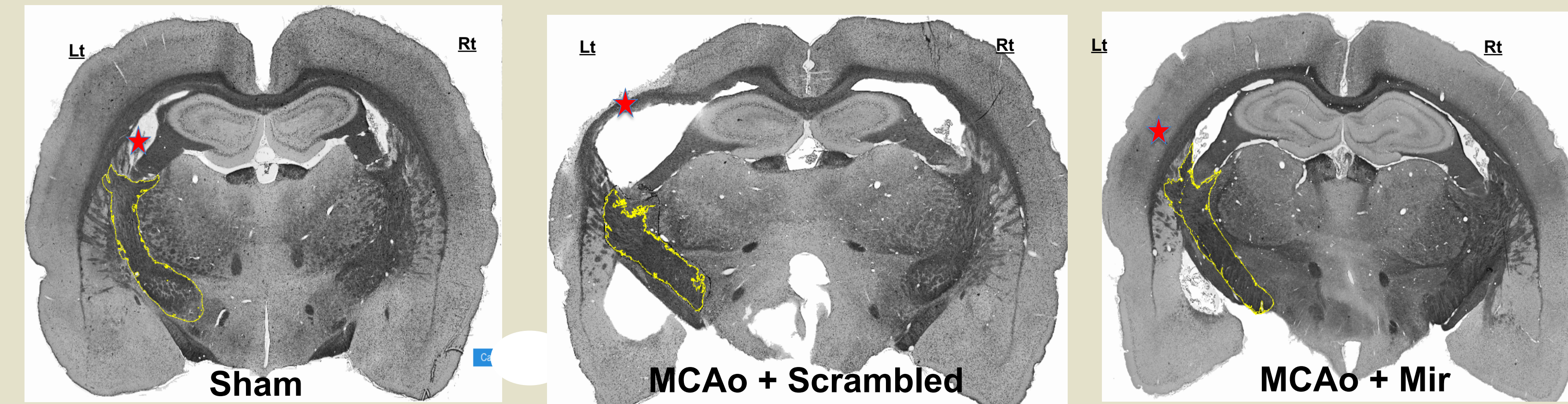
## HYPOTHESIS

- To determine if cognitive impairment on the Barnes maze task, a spatial memory task, is associated with volumetric changes in the hippocampus and cortex.

## EXPERIMENTAL DESIGN AND METHODOLOGY

- Female rats, aged 10-12 months, were subjected to an ischemic stroke on the left hemisphere through an injection of a vasoconstrictor endothelin-1, in the territory of Middle Cerebral Artery (MCAo).
- Rats were injected intravenously with mir 363-3p or scrambled oligos (7ug / Kg BWT).
- Rats were tested on cognitive tasks 3-6 months after stroke.
- Brains were processed for analysis of the Weil myelin stain.
- Volume quantification was performed with FIJI (For Image J2-NIH) software and the ratio of the cortical and hippocampal volume was derived.
- Kruskal-Wallis test was done to compare the three groups (sham, MCAo + Scrambled, & MCAo + Mir), followed by Dunn's post hoc test to correct for multiple comparisons.

## WEIL MYELIN STAIN SECTIONS



## RESULTS

- No significant group differences were observed in hippocampal and cortical volume ( $p>0.05$ ).
- Further analysis showed a significant reduction in the ratio of the cortex/ hippocampal volume in the ischemic hemisphere in the scrambled-treated stroke group, as compared to the sham group.
- The ratio of the cortex/ hippocampus in the ischemic hemisphere of the mir363-3p treated stroke group was no different from the sham group.
- No group differences were seen in the ratio of cortex/ hippocampus in the non-ischemic hemisphere, indicating this was a consequence of ischemia.

## CONCLUSIONS & FUTURE DIRECTIONS

Mir363-3p is neuroprotective in the acute phase after stroke and the current data suggests that mir363-3p may also prevent secondary neurodegeneration in the hippocampus and cortex. This is consistent with our findings that mir363-3p treatment preserves the volume of the white matter tracts. Expansion of this project will conduct a volumetric analysis of the habenula, as the striatal-habenula connection is significant in decision making.

## REFERENCES

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## ACKNOWLEDGEMENT