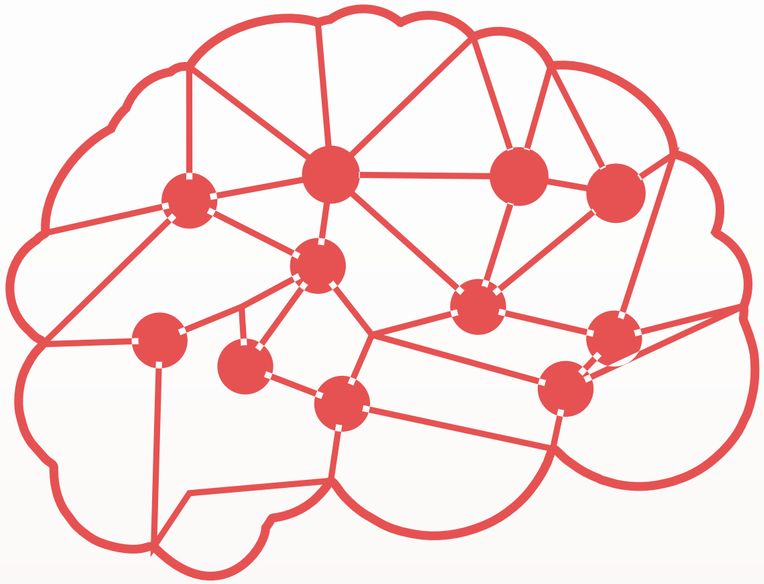
Bezafibrate Exerts Neuroprotective Effects in a Rat Model of Sporadic Alzheimer's Disease



INTRODUCTION

Alzheimer’s disease (AD)

The most common cause of dementia

Progressive and irreversible neurodegenerative processes

The hallmarks of AD are

- **deposition of beta-amyloid (Aβ) plaques**
- **accumulation of hyperphosphorylated tau protein (p-tau) as neurofibrillary tangles**

Alzheimer’s disease (AD)

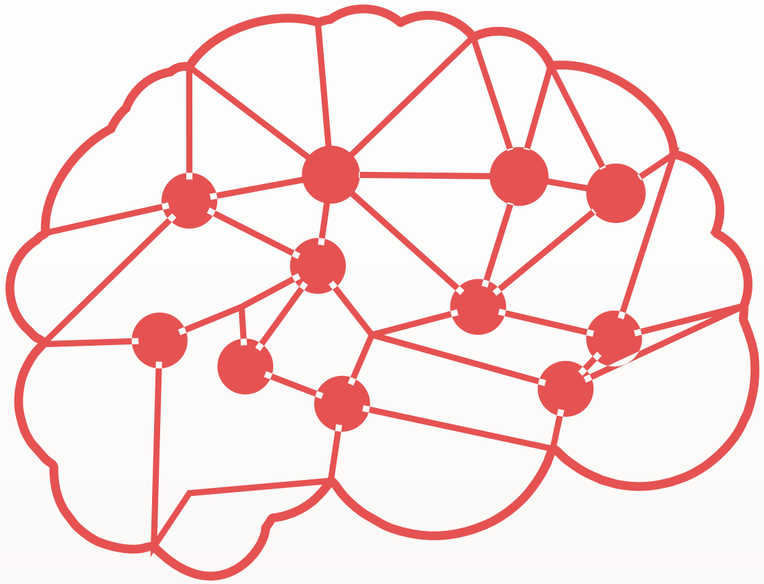
- **The precise pathogenesis of AD is unclear**

- **A recent research suggests that AD might be a metabolic disease in which the brain is unable to efficiently utilize glucose required for energy production due to brain insulin resistance .**

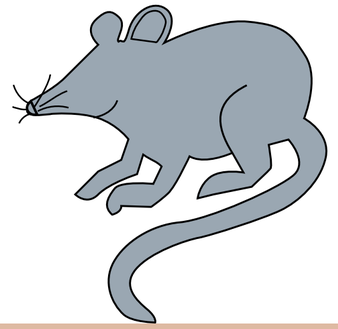
Bezafibrate

- **It is a pan-peroxisome proliferator-activated receptor (PPAR) agonist**
- **treats dyslipidemia for over 25 years patients**
- **decrease the severity of tau pathology in a transgenic mouse model of primary tauopathy by:**

improving energy metabolism
suppressing oxidative stress
inhibiting neuroinflammation



METHOD



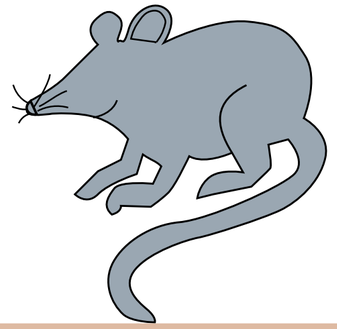
A sporadic AD rat model

Induced by

intracerebroventricular (ICV) injection of streptozotocin(STZ)

Result in

evaluating the effects of bezafibrate



Expresses

progressive Aβ and p-tau overaccumulation

STZ-ICV-induced sporadic AD model

Accompanied by neuroin flammation

Decreased brain glucose utilization

Neuronal loss

STZ injected intracerebroven-tricularly

+

Followed by

bezafibrate (50 mg/kg/day) intraperitoneal (IP) injection for 4 weeks.

1

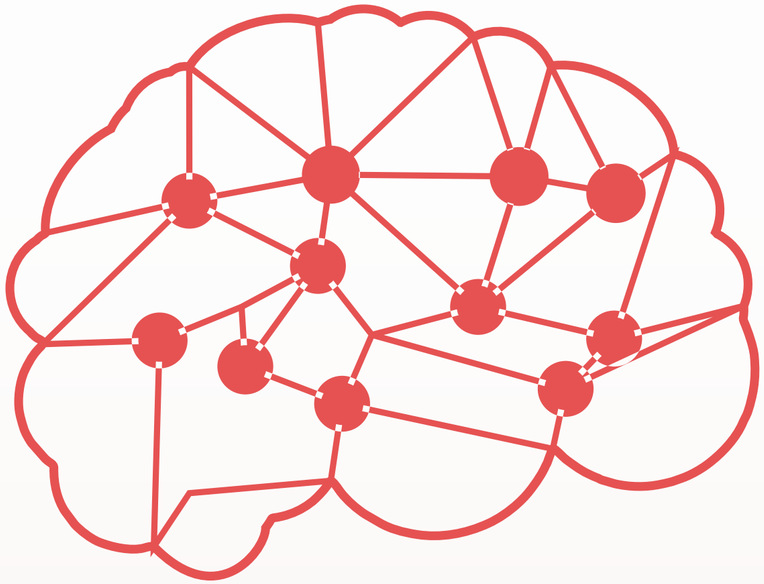
Results assessed using longitudinal animal behavior tests and positron emission tomography

2

assessed on the 4th, 8th, and 12th week after STZ-ICV administration.

3

Immunofluorescence staining performed at the third month to confirm the long-term protective effects

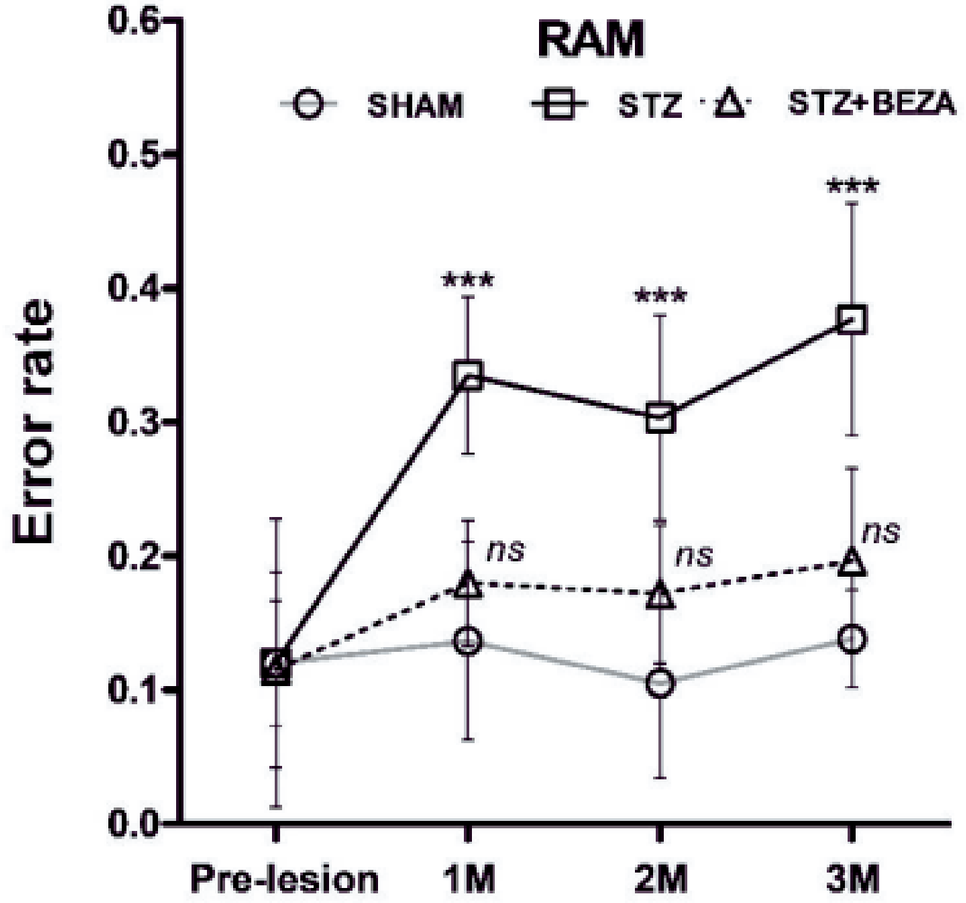


RESULT

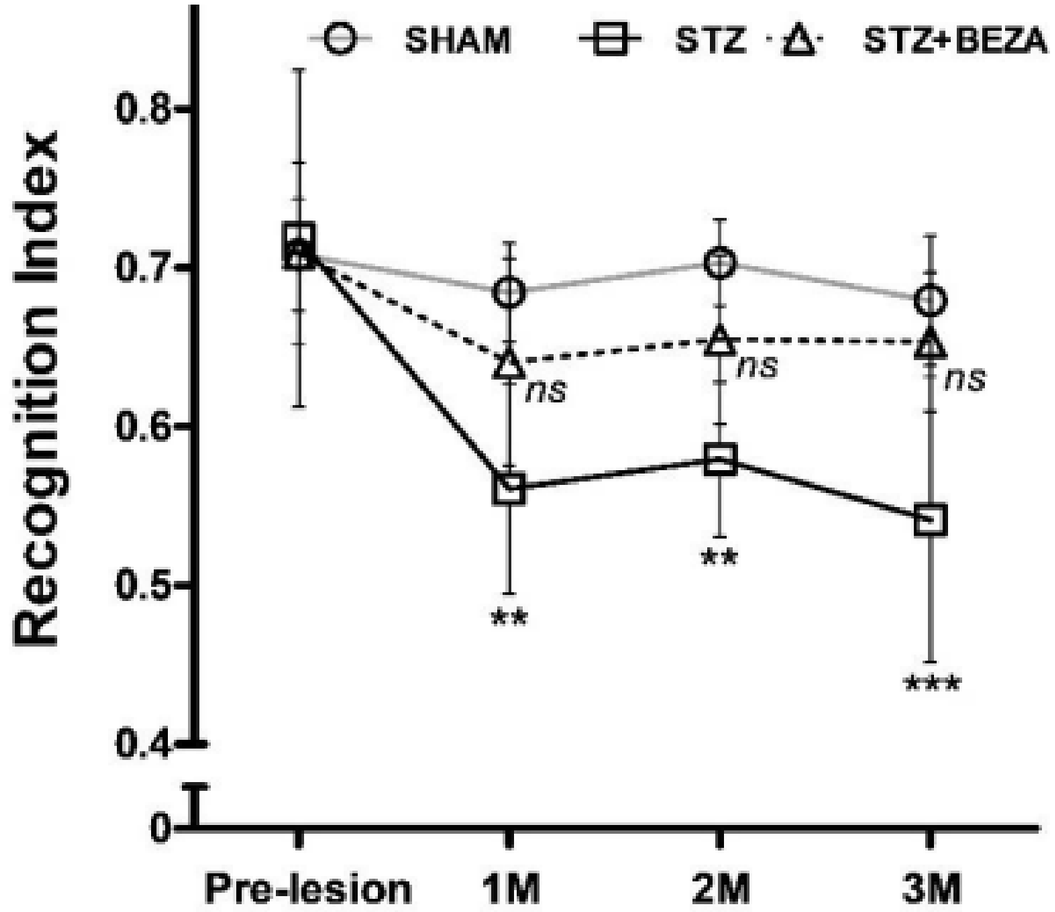
Bezafibrate Rescued the STZ-ICV-Induced Behavioral Deficits

- **Radial arm maze (RAM) tests were performed at one-month intervals.**

	After the ICV injection	After STZ-ICV administration
SHAM group	The error rates did not show any significant differences until the third month ($p > 0.05$, post- vs. pre-lesion)	error rate were Lower than STZ group
STZ group	———	error rates were significantly higher ($p < 0.001$, STZ vs. SHAM)



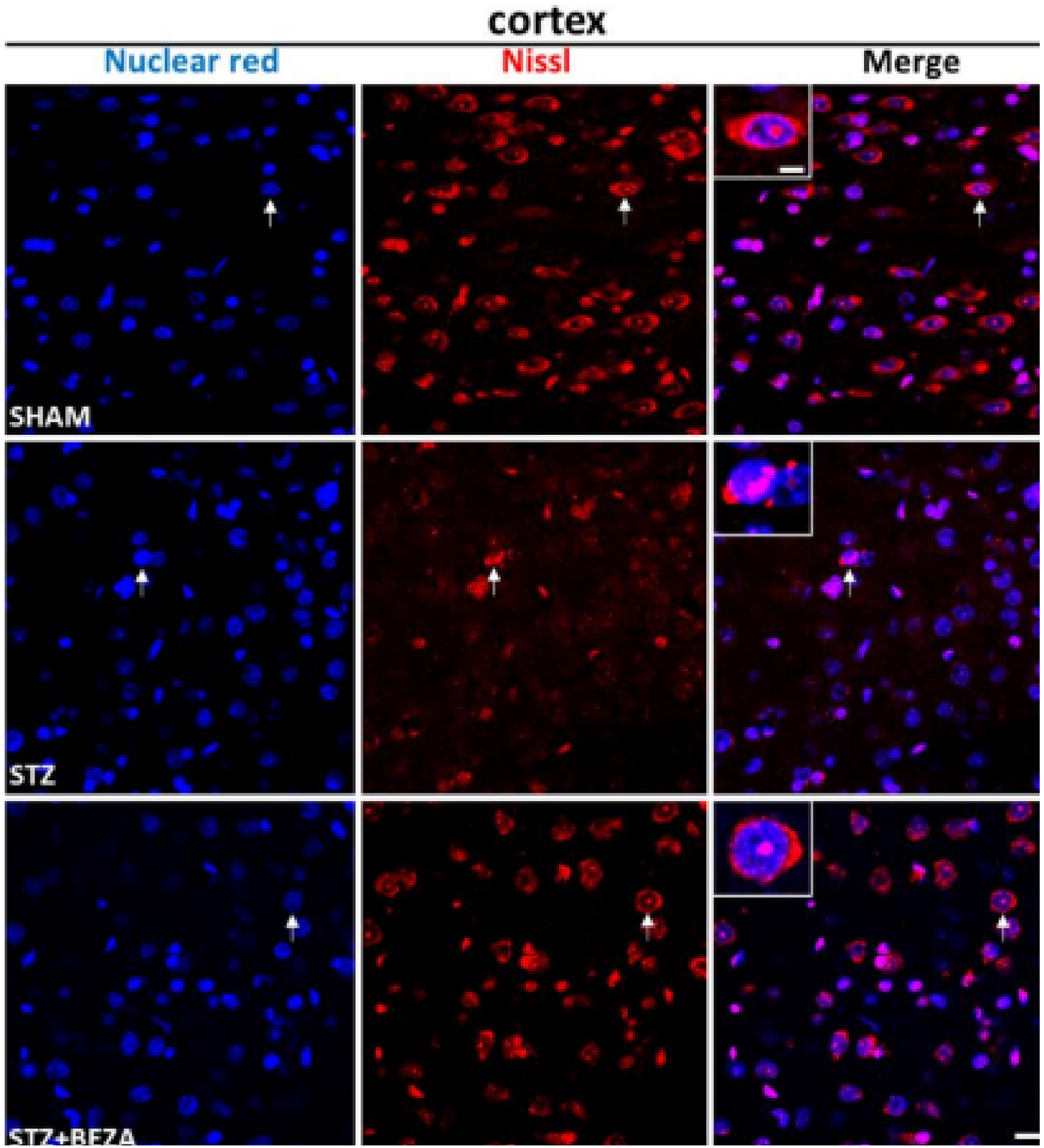
RAM tests demonstrated that the error rates of the STZ group were significantly higher compared to those of the SHAM group after STZ-ICV administration



The novel object recognition (NOR) tests used to evaluate the object recognition memory of animals

Bezafibrate Mitigated the STZ-ICV-Induced Brain Neuronal Loss

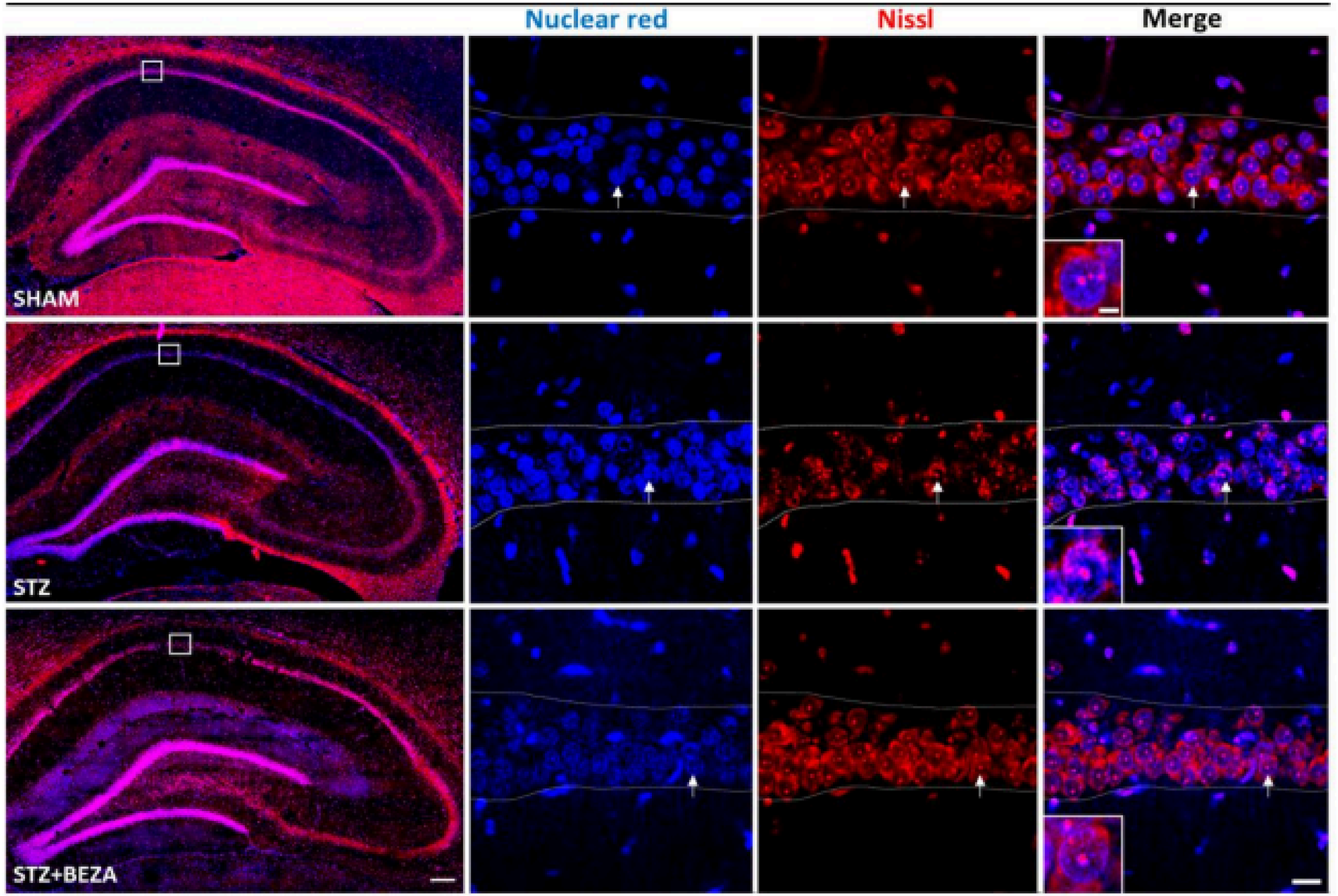
- Neuronal survival in the cortex and hippocampus was assessed by Nissl staining in the third month after STZ-ICV administration.



Changes of cortex in different groups

- A significant loss of Nissl staining positive cells was observed in the cortex of the STZ group as compared to those in the SHAM.

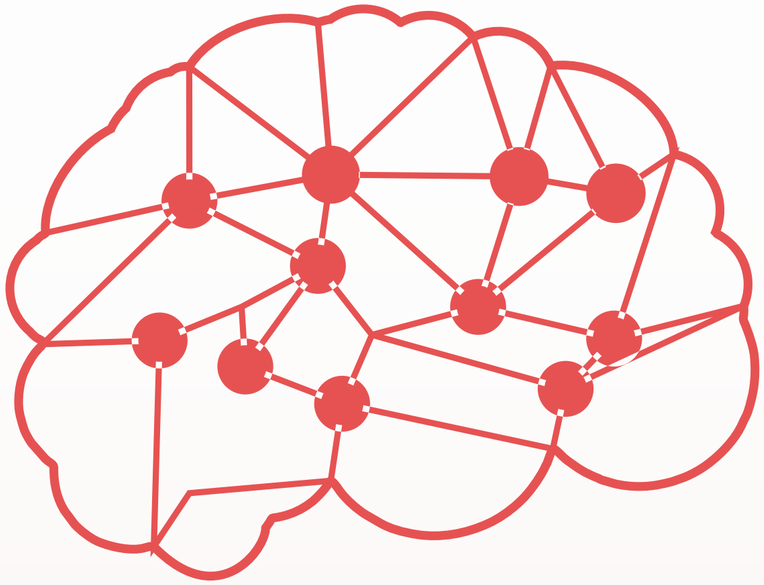
Changes of in hippocampus of different groups



- **Bezafibrate mitigated the STZ-ICV-induced brain neuronal loss. Neuronal survival was evaluated by immunofluorescence staining with Nissl stain (red, for neurons) and nuclear red (blue, as nuclear counterstain).**

- **The Nissl staining-positive cells in the cortex and hippocampus of the STZ group were significantly fewer than those in the SHAM group.**

- **The STZ+BEZA group showed Nissl-positive cells in both the cortex and hippocampus.**



Disscusion

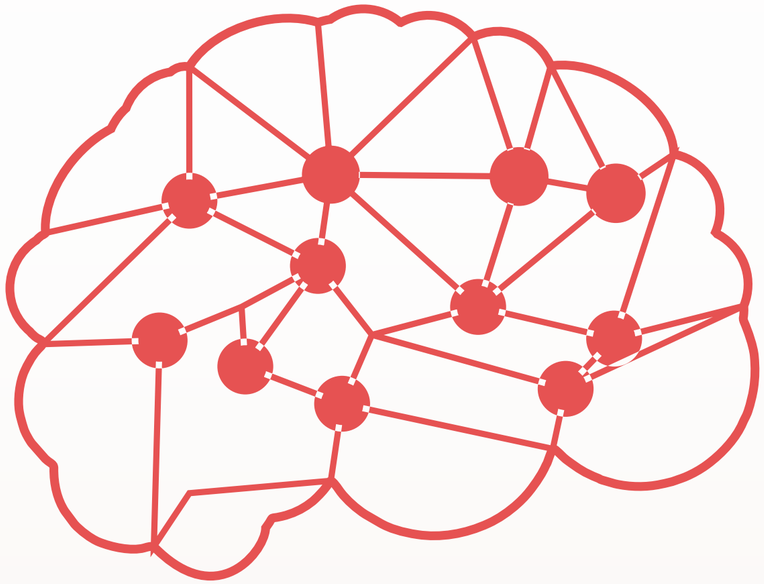
STZ-ICV administration induced sporadic AD-like changes :

- **significant cognitive impairment**
- **substantial neuronal loss**
- **tau pathology**
- **glucose hypometabolism**
- **microgliosis in the cortex and hippocampus of rats.**

- **This study is the first to show that bezafibrate treatment could prevent cognitive impairment in a rat model of sporadic AD.**

- **bezafibrate has a neuroprotective effect in a sporadic AD model.**

- **PET is an in-vivo imaging tool that allows noninvasive monitoring of biological and pathological processes at the molecular level.**



Materials and Methods

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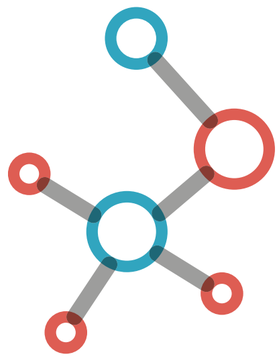
Animals

Animal Groups and Drugs Treatments

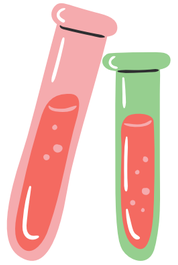


Animal PET and Radiopharmaceuticals

Immunofluorescence Staining

Statistical Analysis

Animal Behavior Tests



Conclusion

Bezafibrate has a considerable and long-lasting protective effects on:

- **cognitive impairment**
- **neuronal loss**
- **tau pathology**
- **cerebral glucose hypometabolism**
- **neuroinflammation induced by STZ-ICV**

This is the first in-vivo study to evaluate the neuroprotective benefits of bezafibrate.

Reference

Bezafibrate effects in a Rat Model of Sporadic Alzheimer’s Disease

Thank You