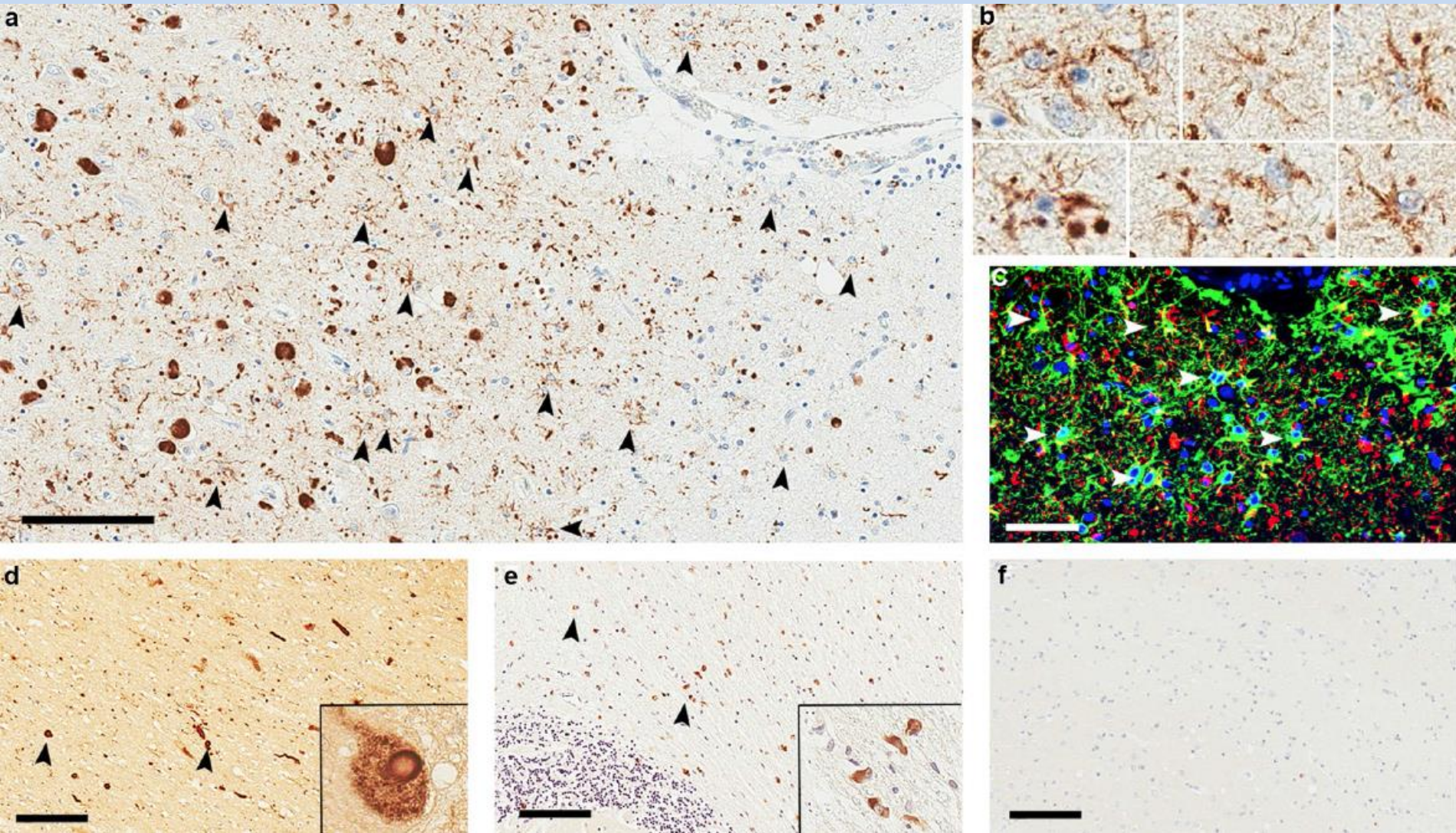


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Bologna 23-25 maggio 2019

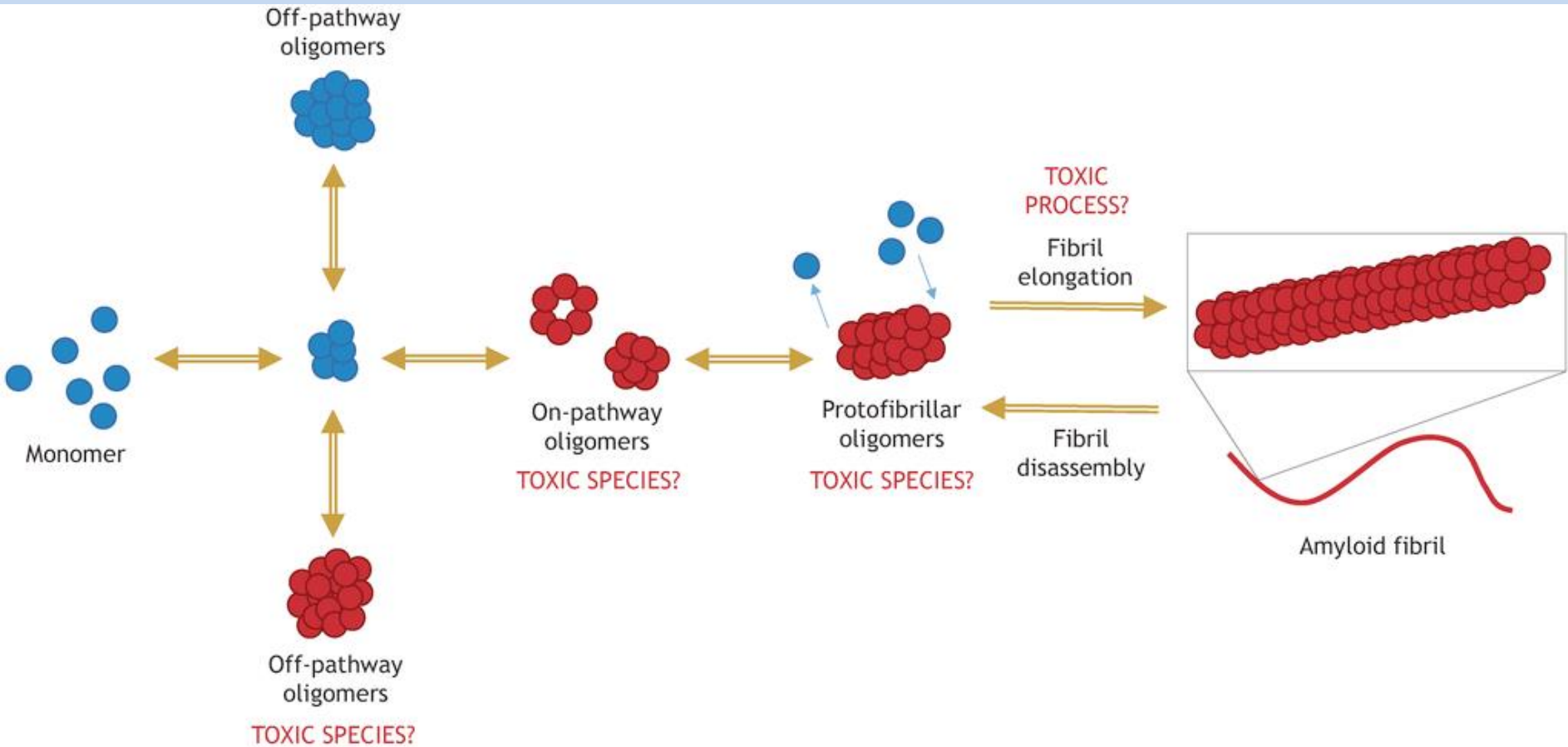
**Neuroinflammation is crucial in mediating deleterious effects of alpha-synuclein oligomers**

Gianluigi Forloni  
Dipartimento di Neuroscienze  
Istituto di Ricerche Farmacologiche “Mario Negri” IRCCS

# $\alpha$ synuclein deposition in DLB



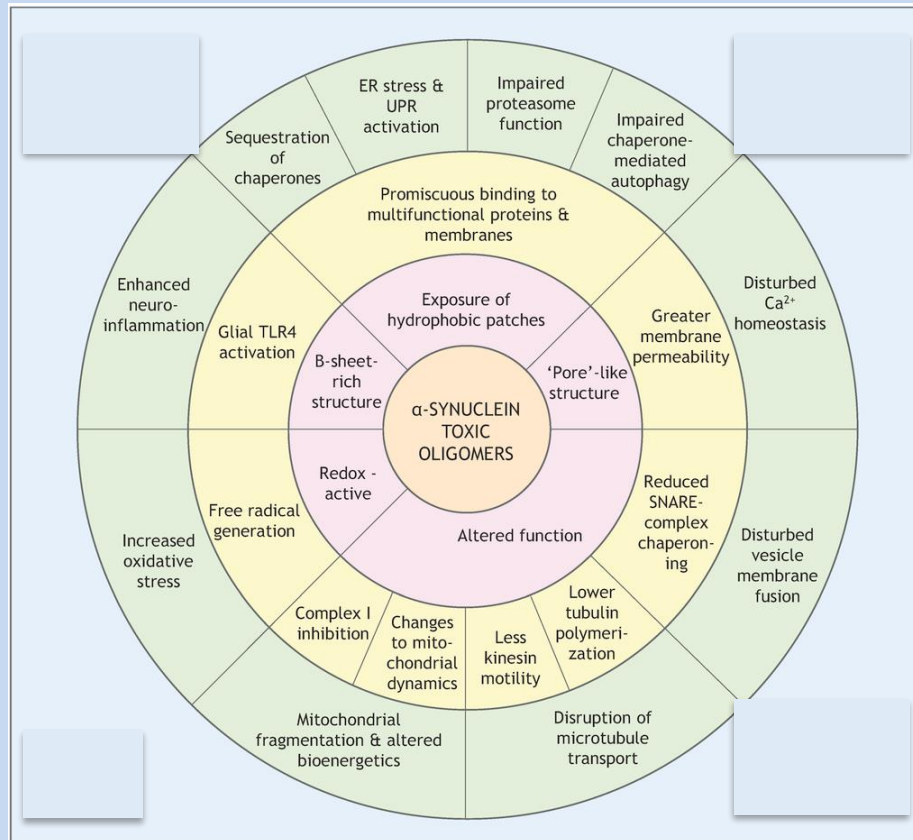
# Oligomers pathways



# Oligomeropathies: mechanisms $\alpha$ -synuclein oligomers toxicity

Deposition of insoluble  
Protein aggregates

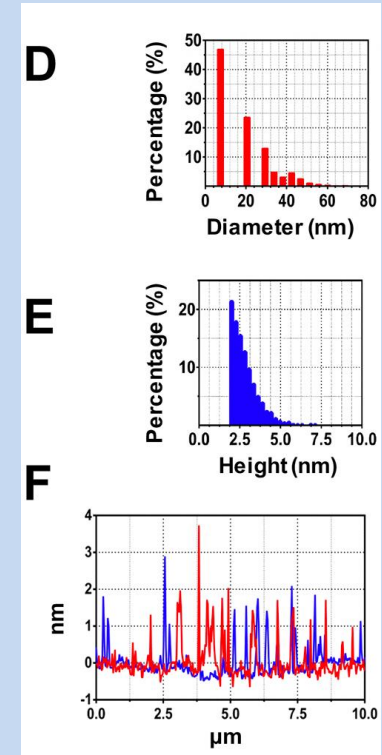
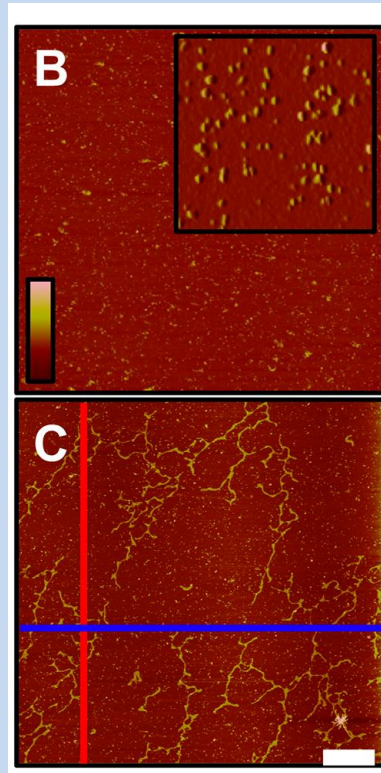
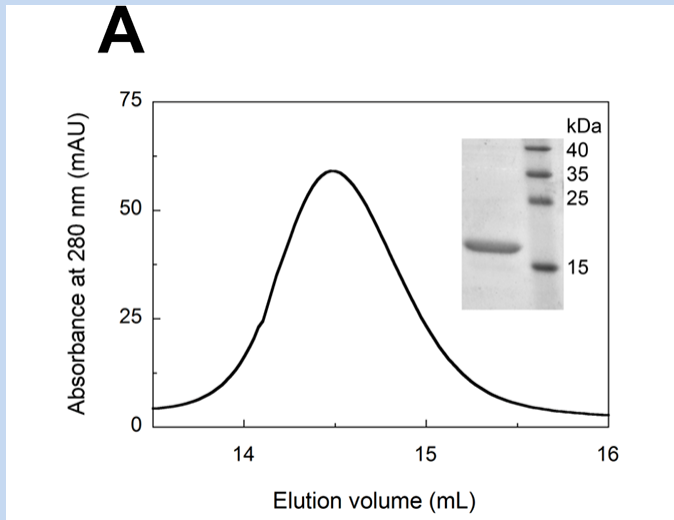
Reduced synaptic  
transmission



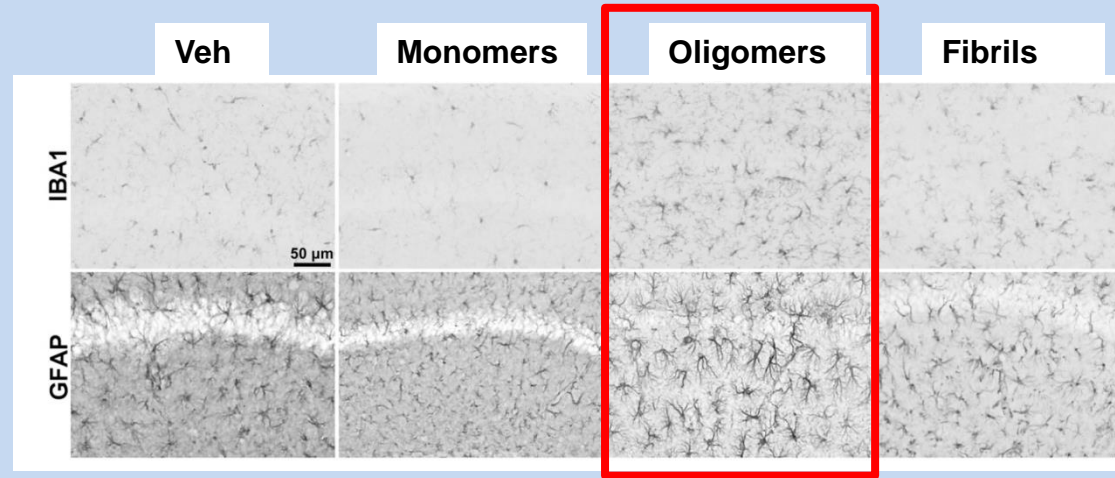
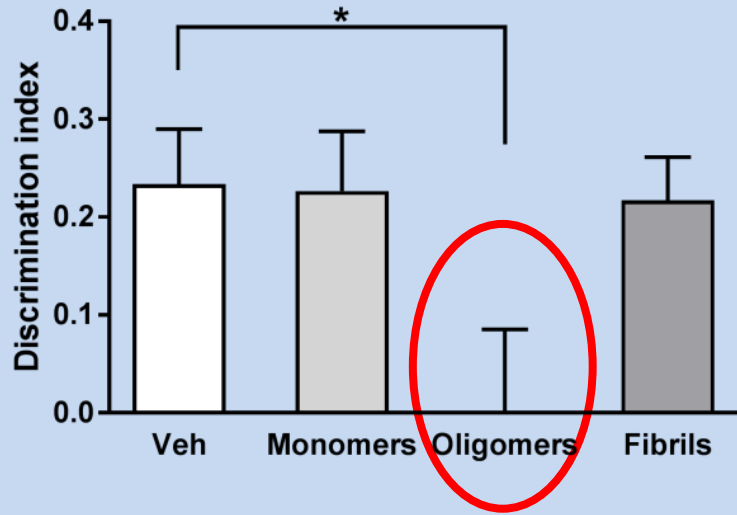
Cell Death

Retraction of neurites

# Purification alpha synuclein oligomers

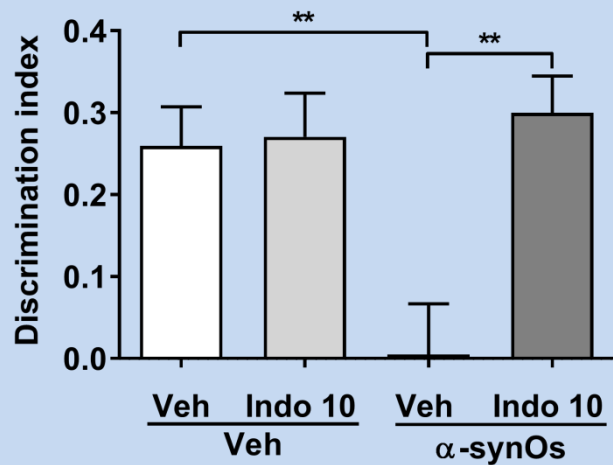


# Alpha-synuclein oligomer trigger memory impairment in association to neuroinflammation

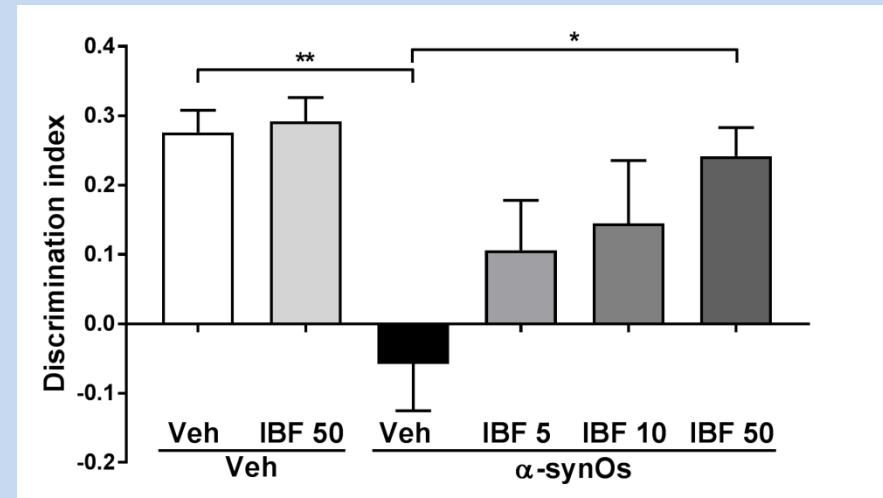


## Neuroinflammation mediates the memory damage induced by alpha-synuclein oligomers

### *Indomethacin*

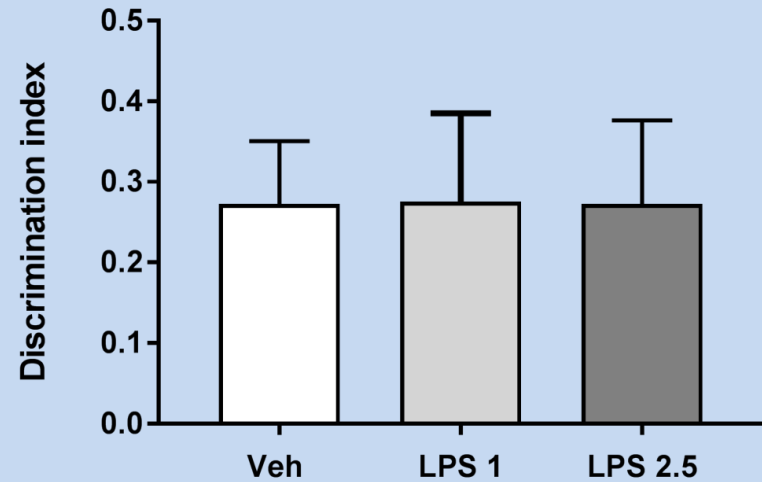
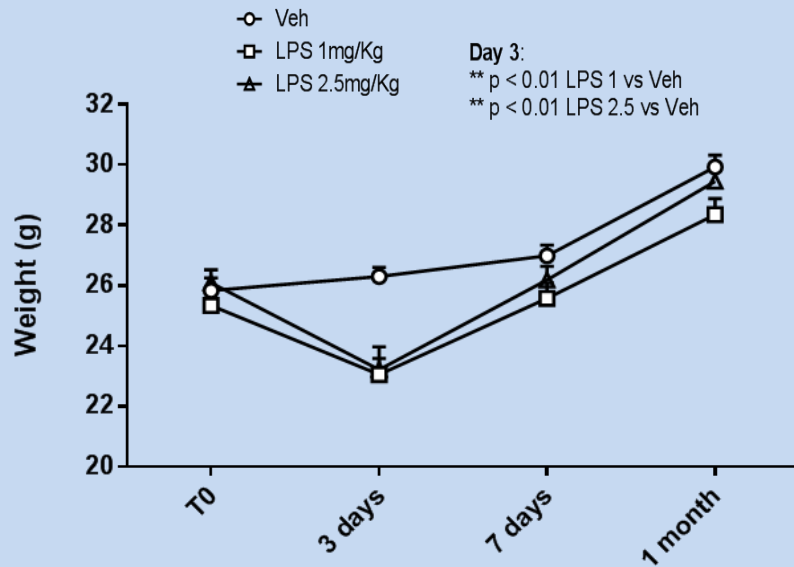
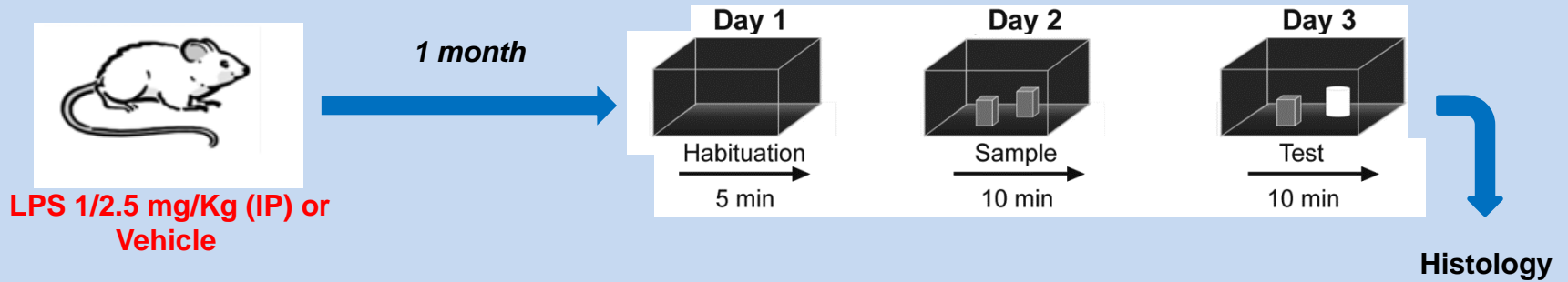


### *Ibuprofen*



Neuroinflammation exacerbates alpha-synuclein oligomers toxicity in vivo

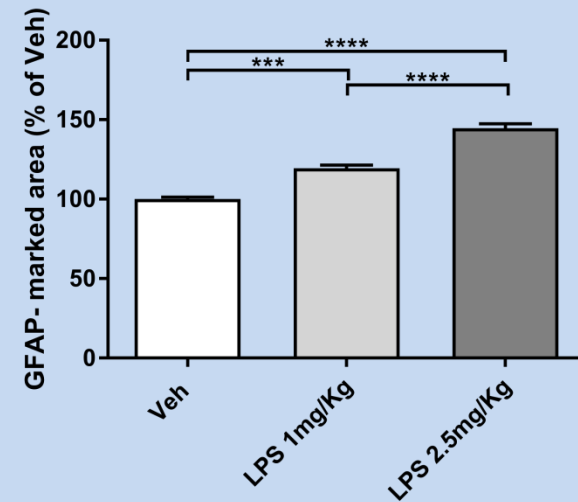
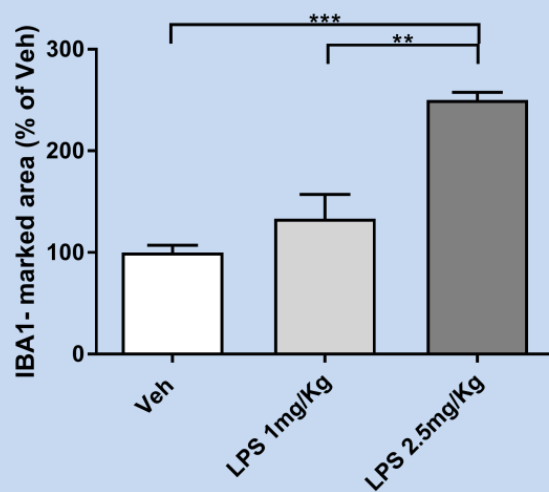
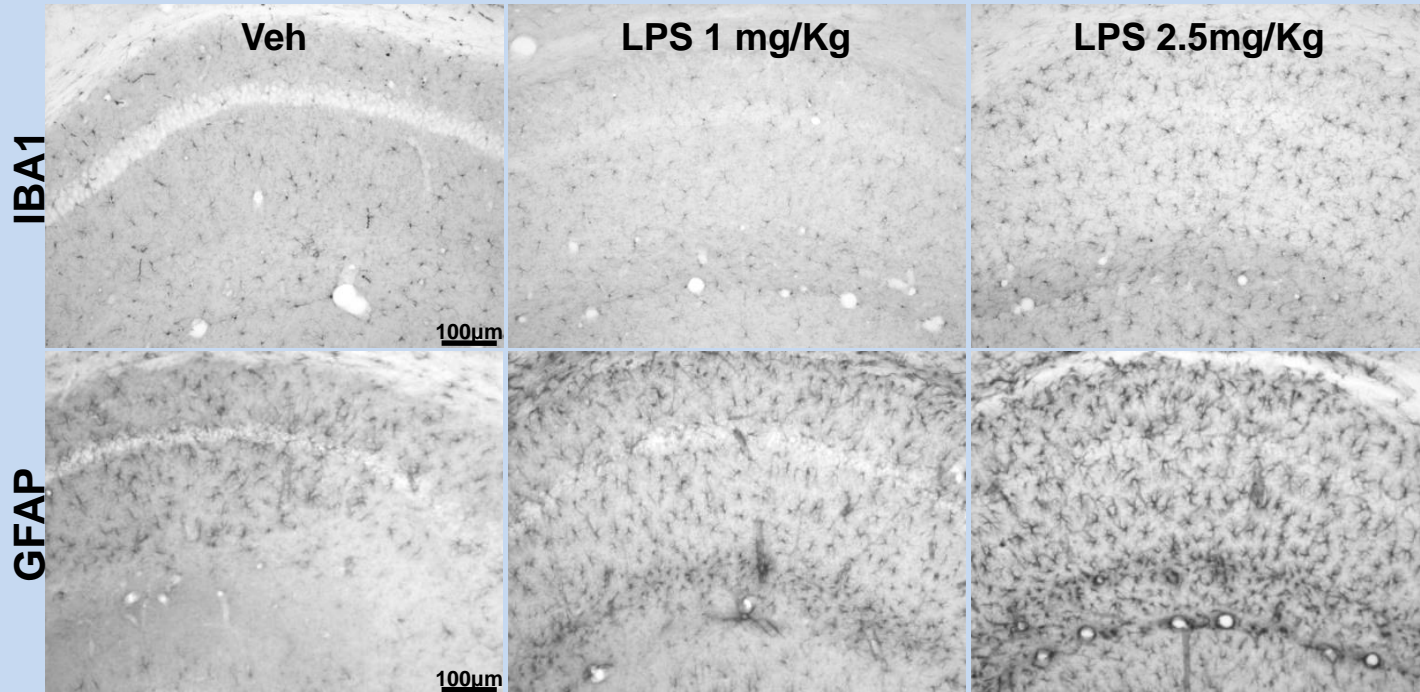
# Characterization of the LPS-induced neuroinflammatory model





# Characterization of the LPS-induced neuroinflammatory model

## Hippocampal neuroinflammation



# “Double-hits” acute mouse model

## LPS 2.5 mg/Kg and $\alpha$ -synuclein oligomers (0.5 $\mu$ M)



1 month

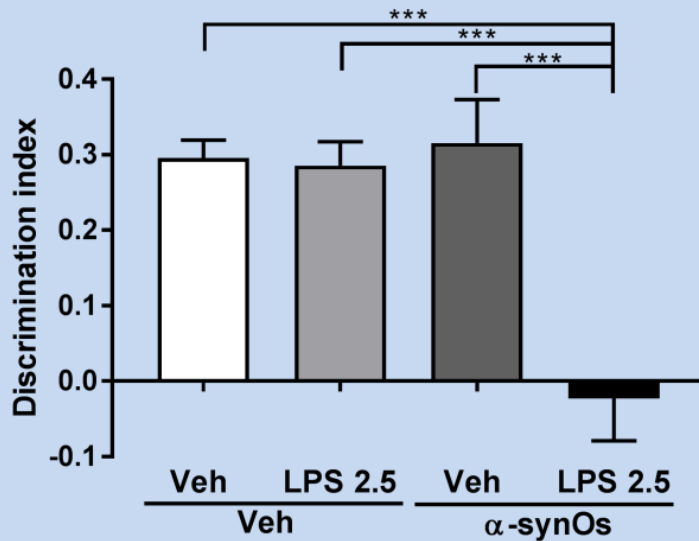
Alpha-synuclein oligomer injection  
NORT and Y-MAZE



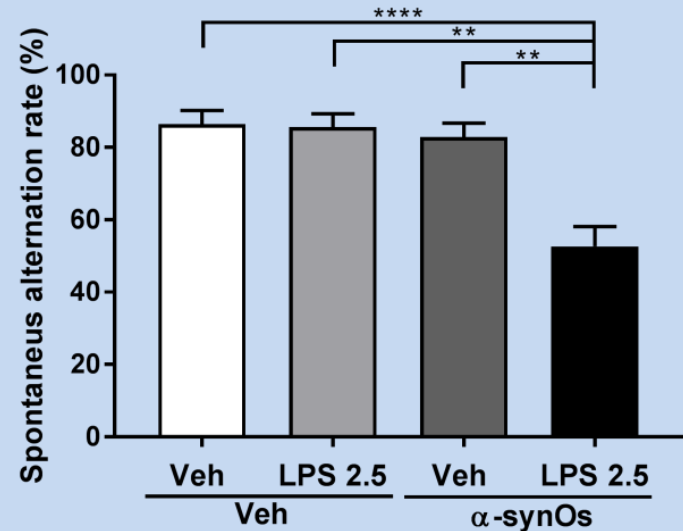
Histology

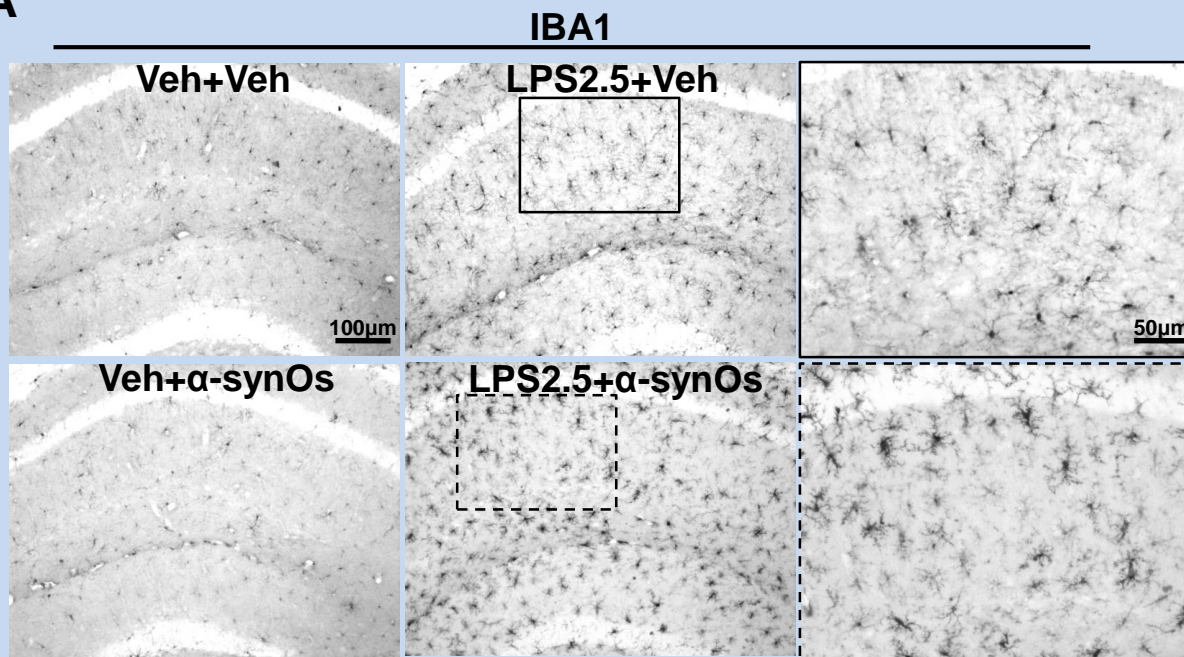
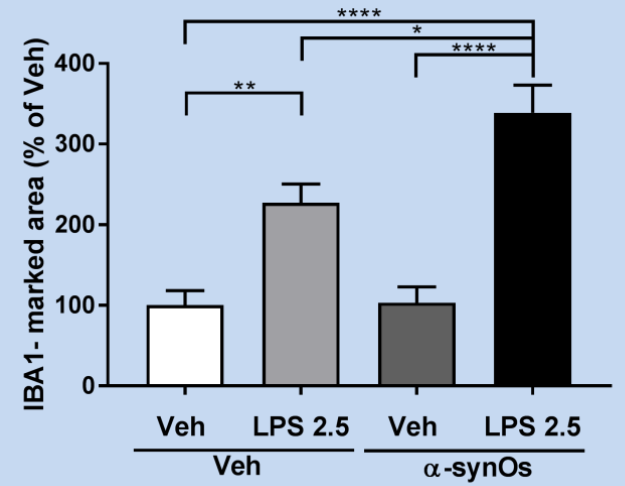
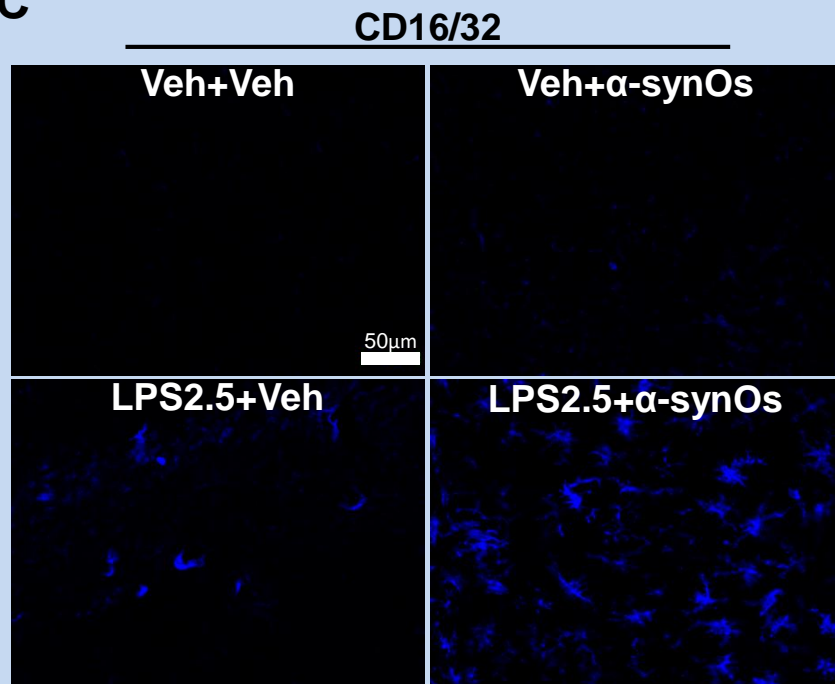
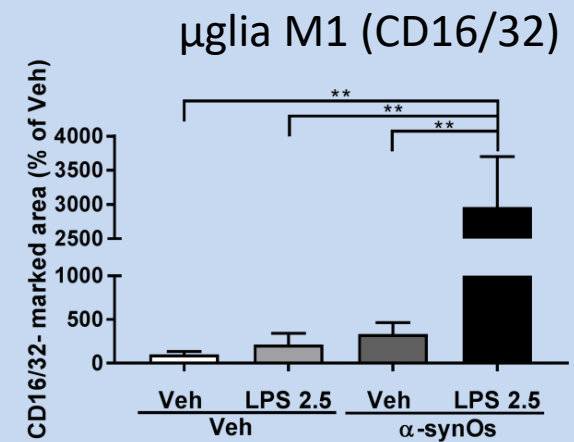
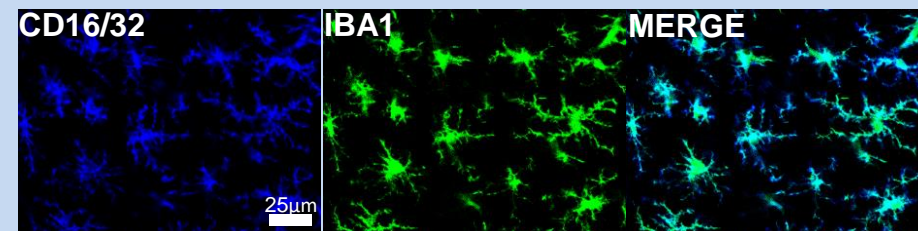
LPS 2.5 mg/Kg (IP) or  
Vehicle

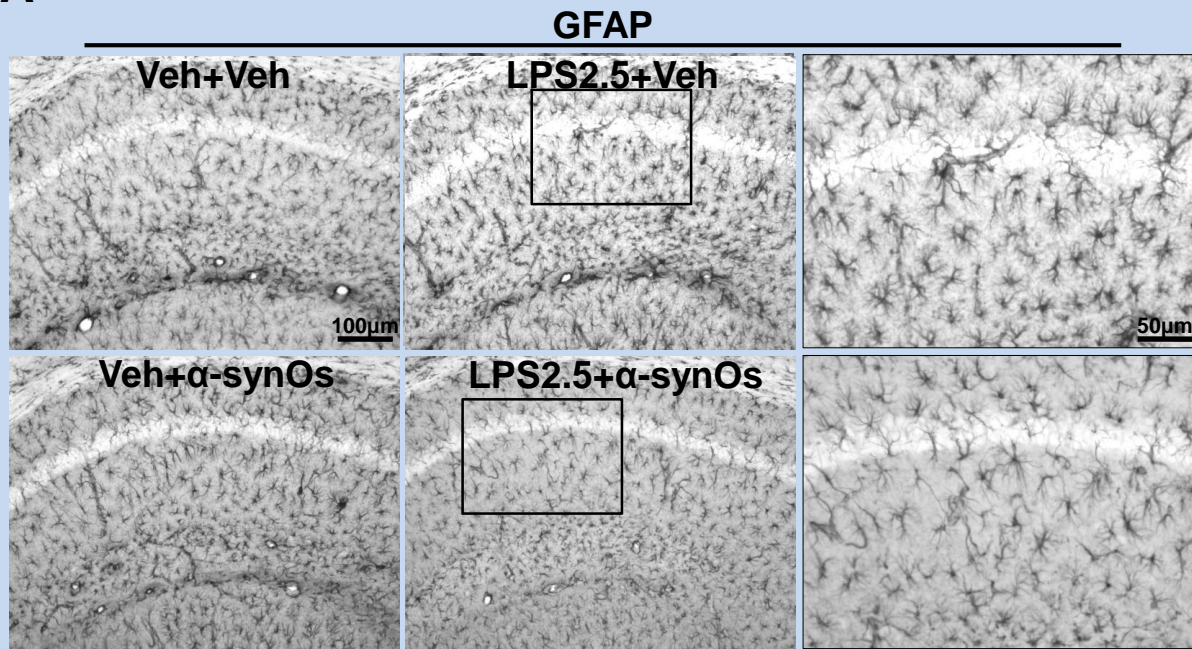
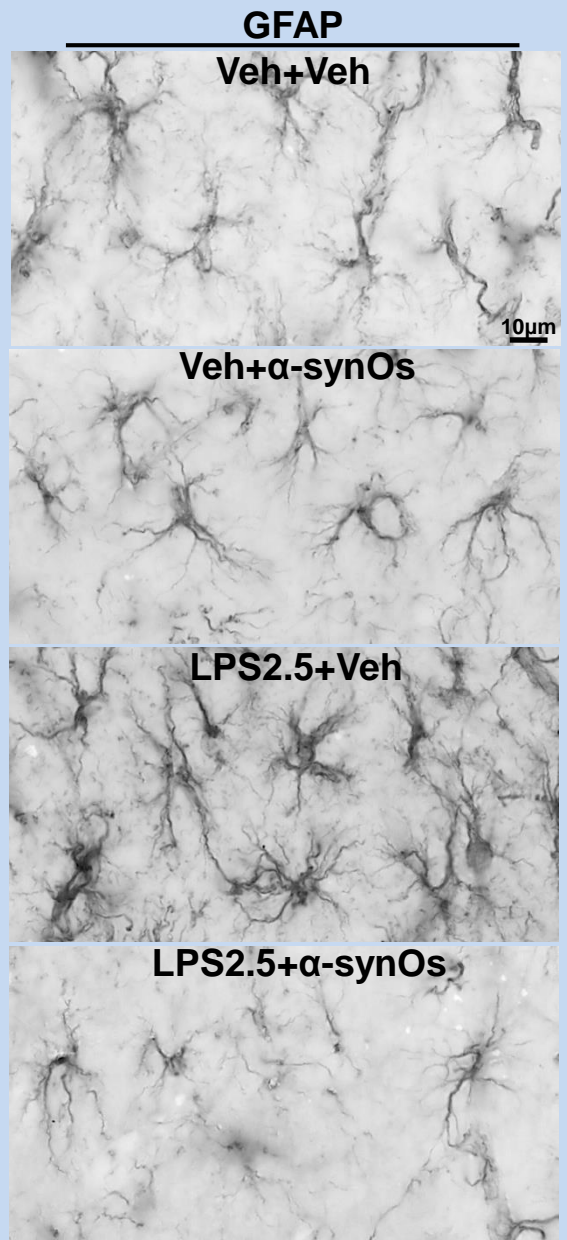
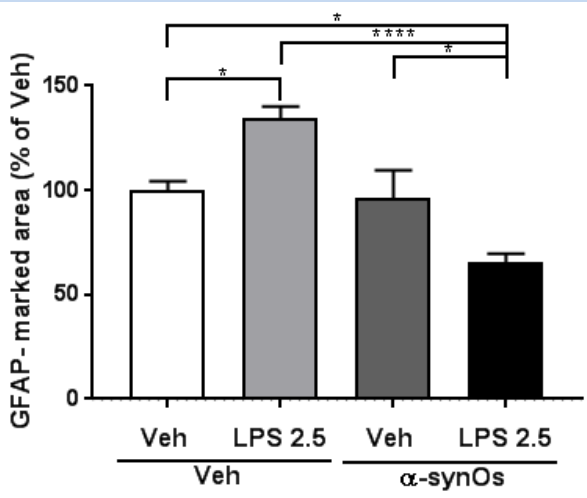
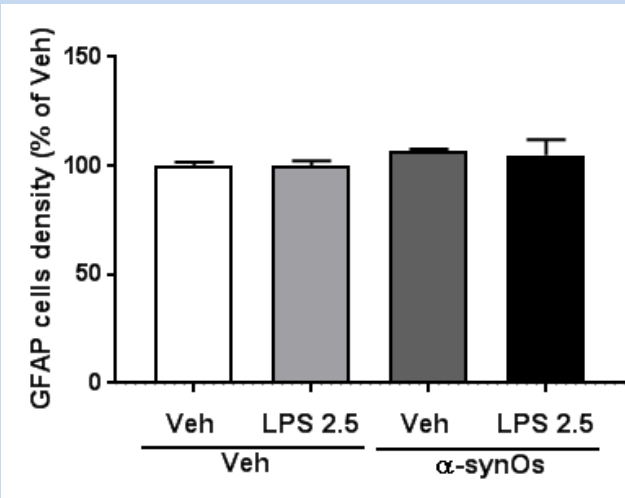
### NORT



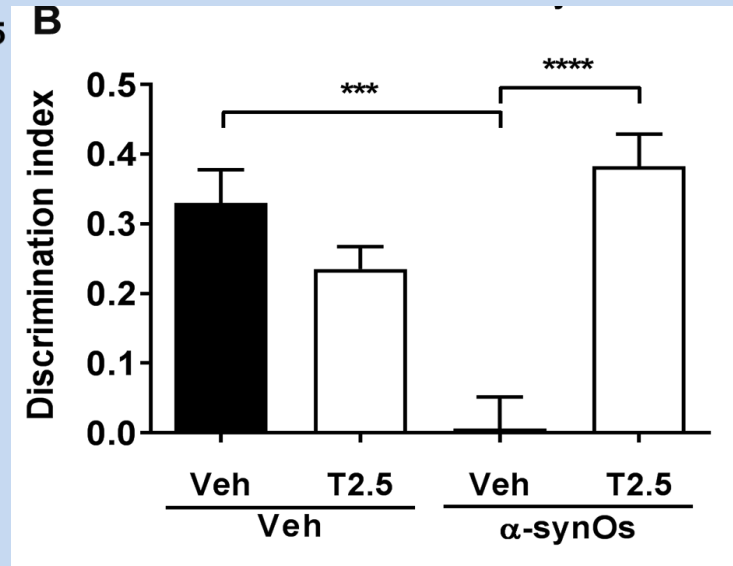
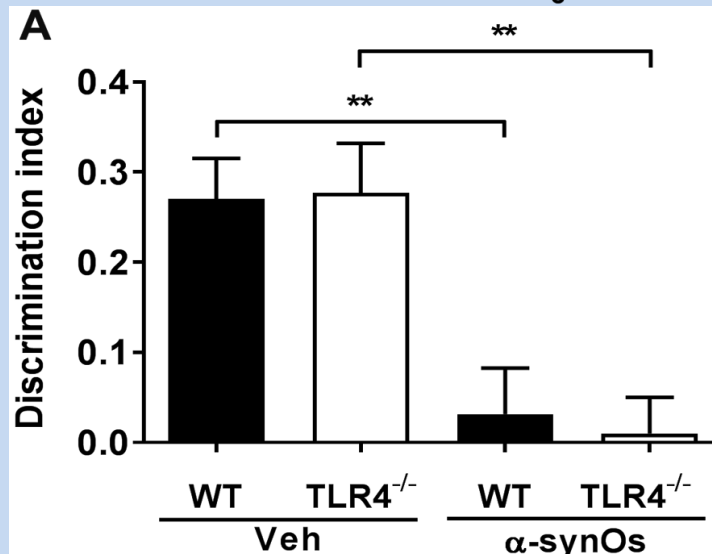
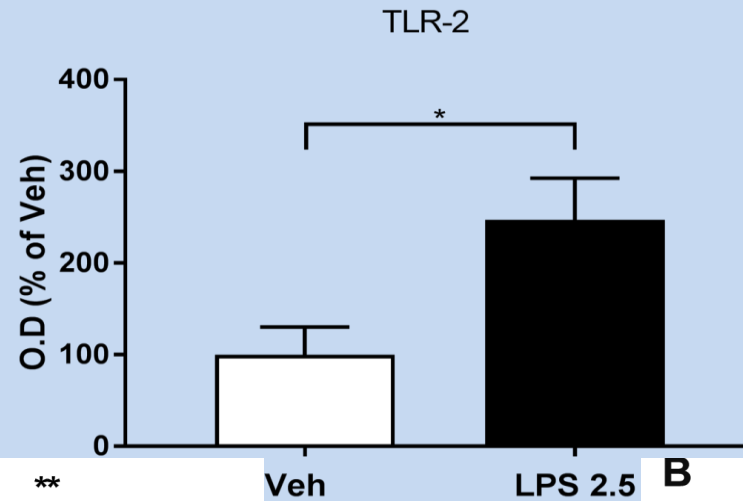
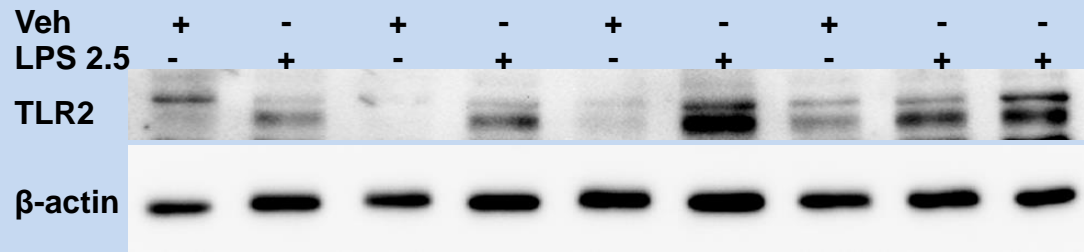
### Y-MAZE



**A****B****C****D****E**

**A****B****C****D**

## A potential role for the TLR-2

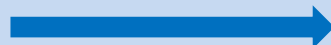


Neuroinflammation worsens non-  
motor deficits in A53T mice

# Characterization of the LPS-induced neuroinflammatory model in A53T mice



1 month



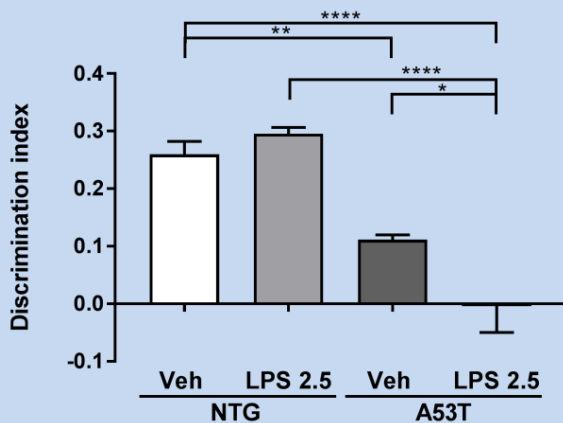
Behavioral characterization



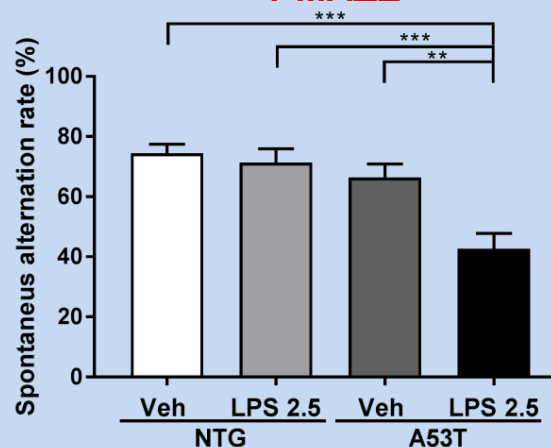
Histology

LPS 2.5 mg/Kg (IP) or Vehicle

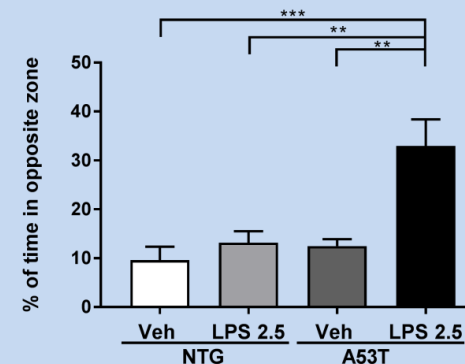
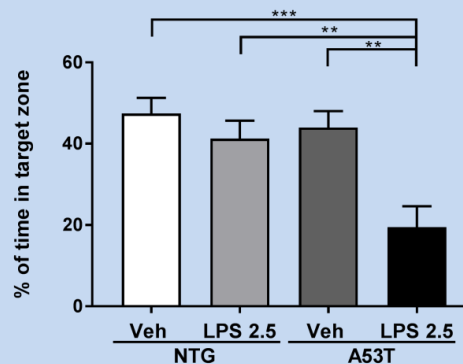
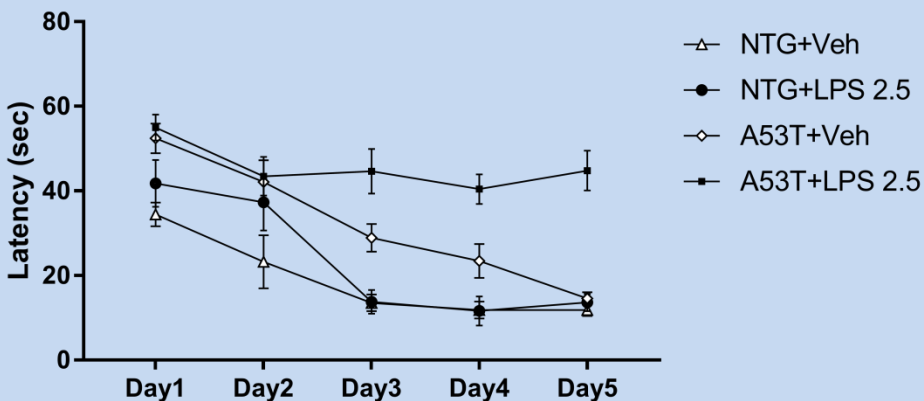
## NORT



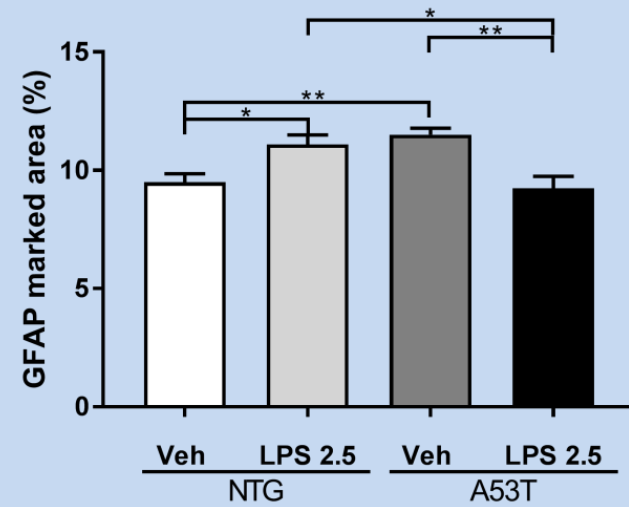
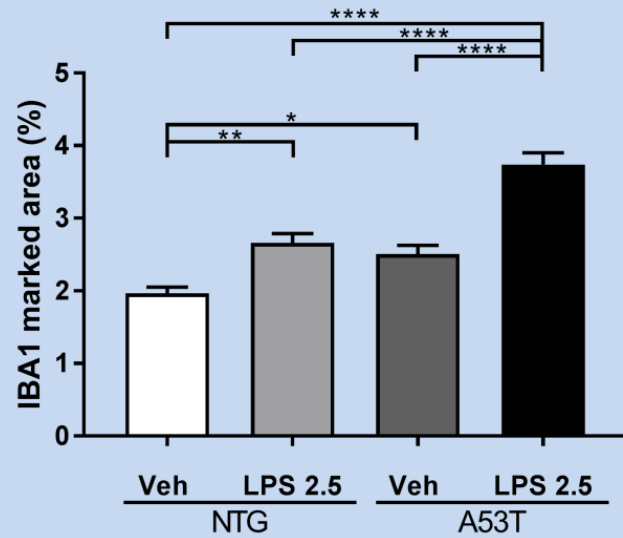
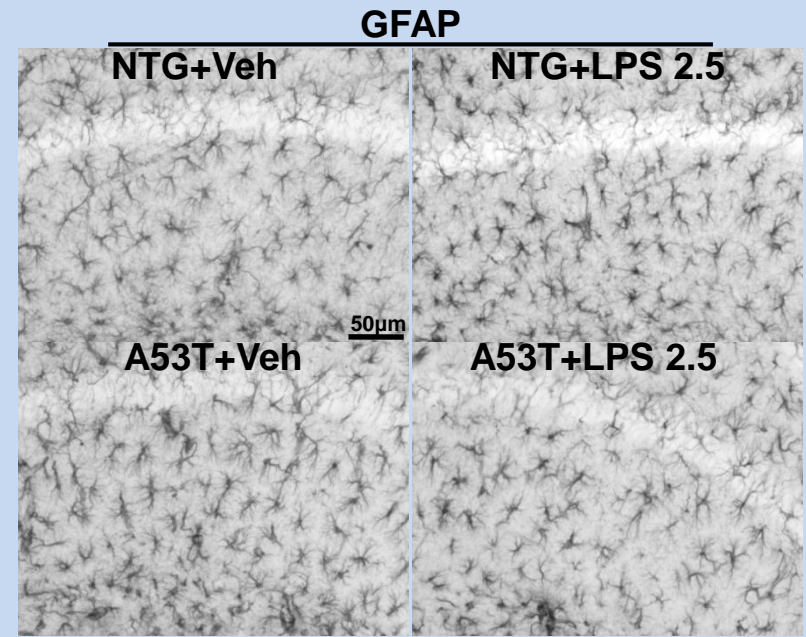
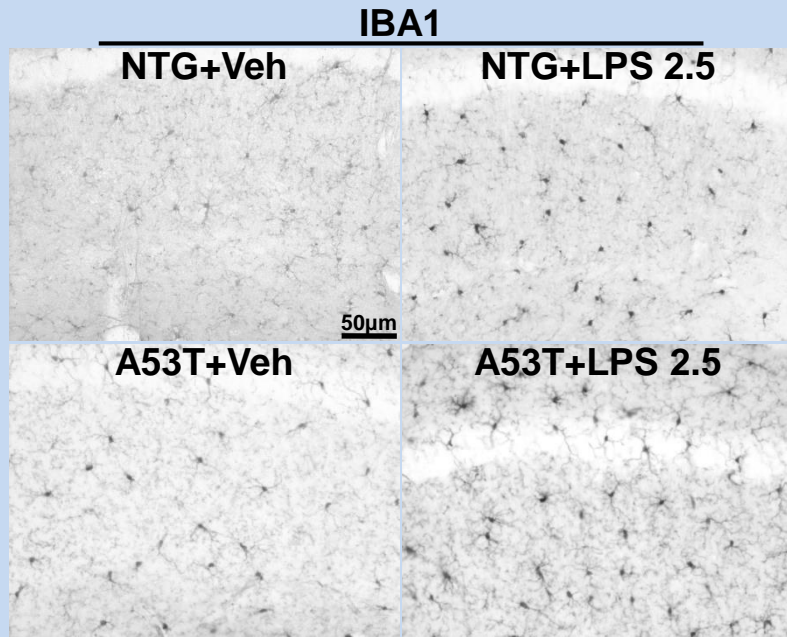
## Y-MAZE



## MWM



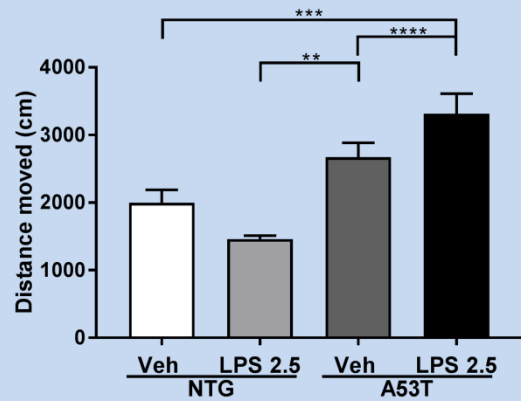
# Hippocampal neuroinflammation



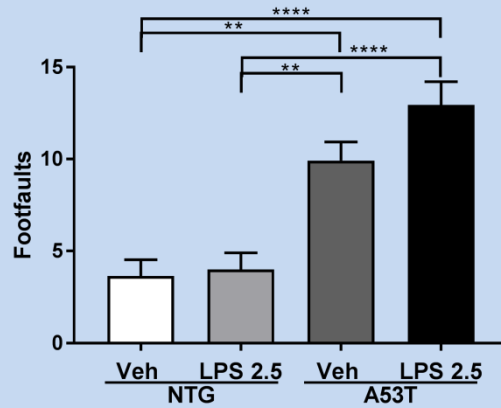


## Motor behavior

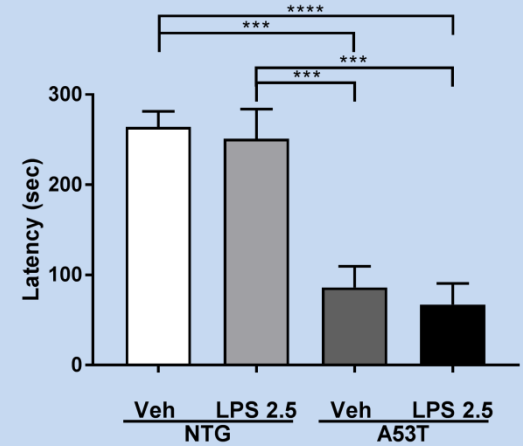
### OPEN FIELD



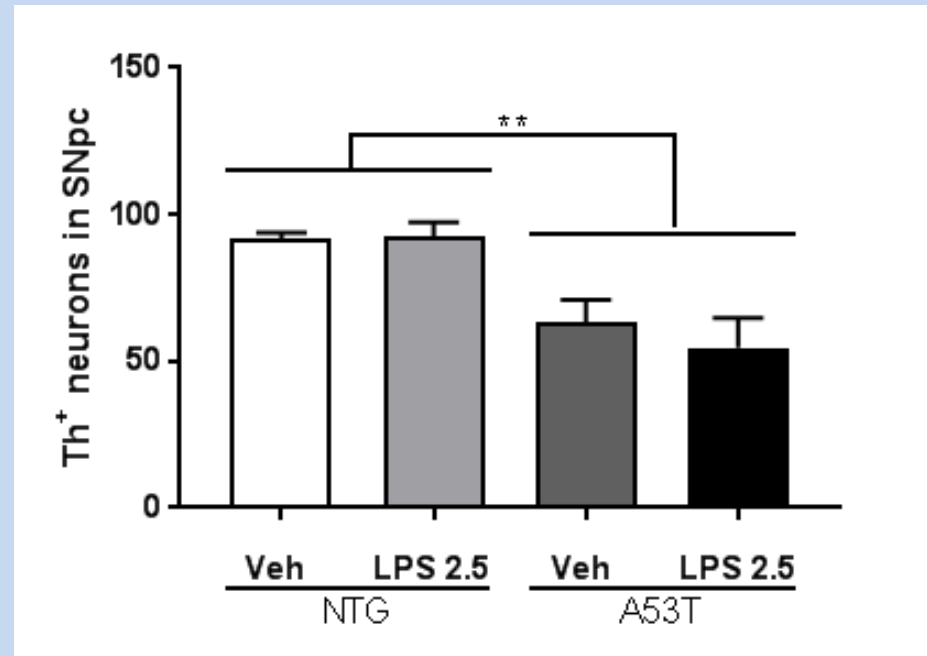
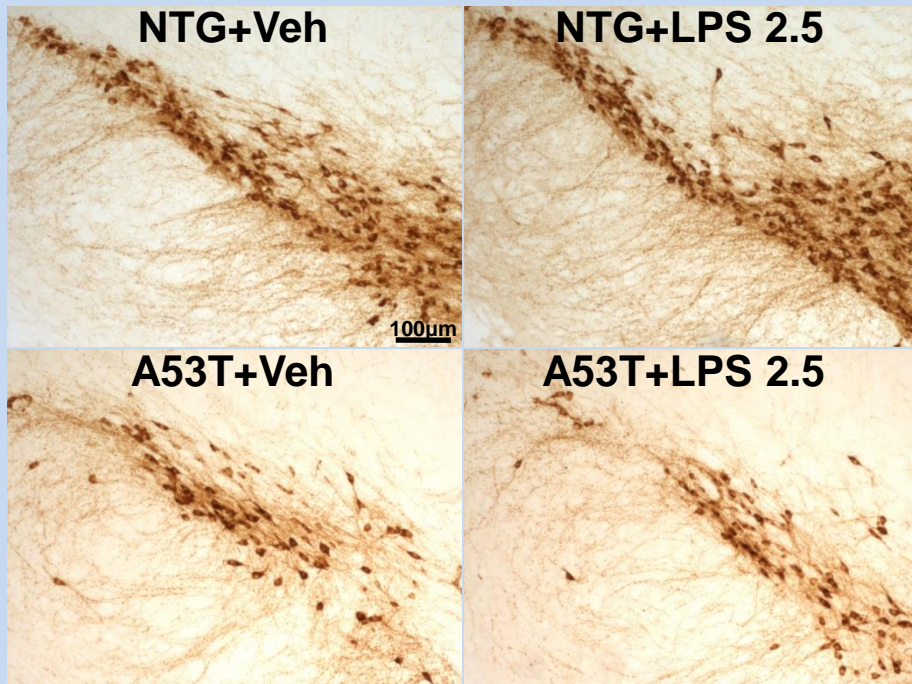
### BEAM WALK



### PAW GRID TEST

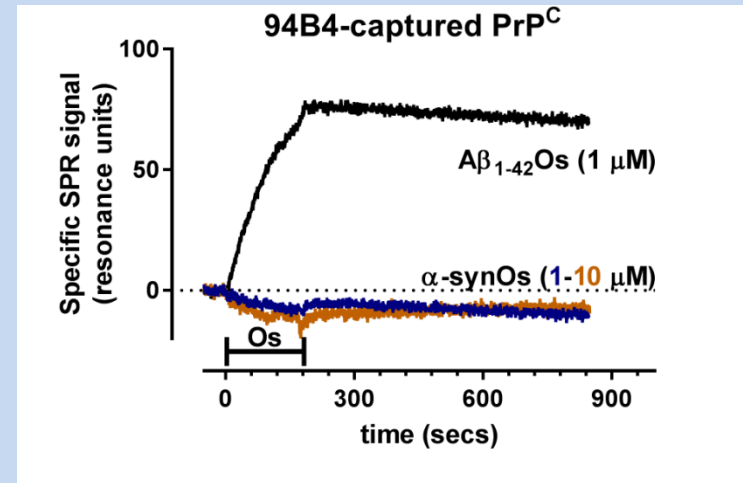
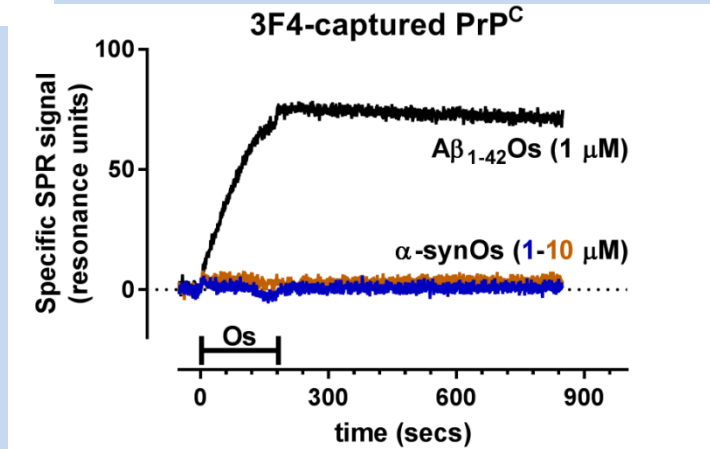


## Dopaaminergic neurodegeneraton in SNpc

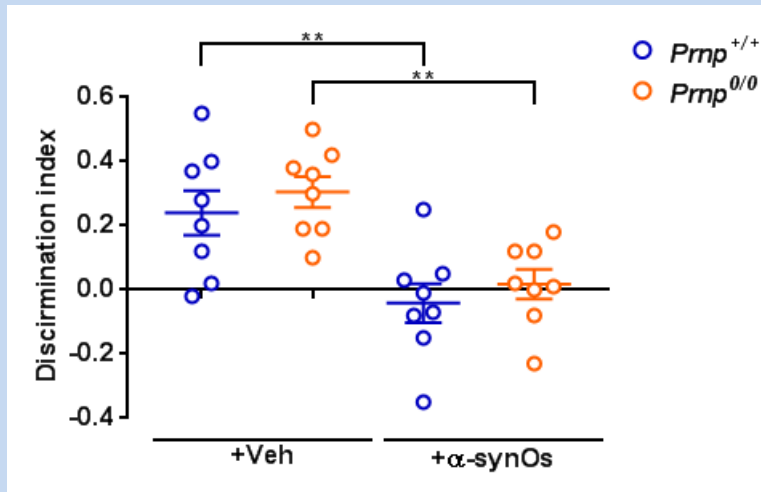


Cellular Prion protein neither binds to alpha-synuclein oligomers nor mediates their detrimental effects

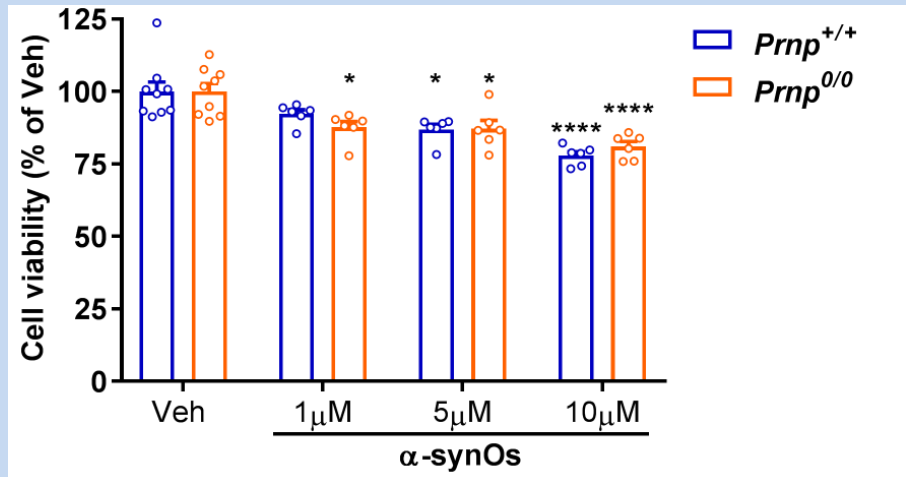
# SURFACE PLASMON RESONANCE



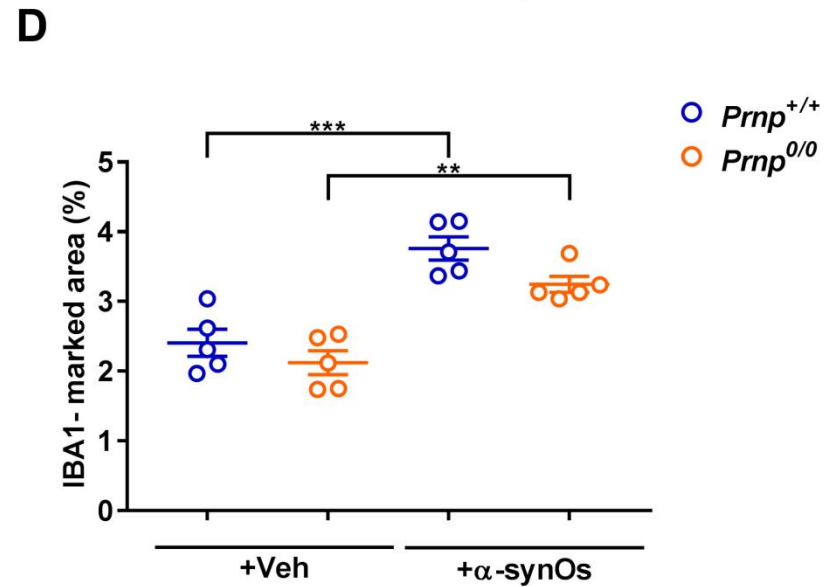
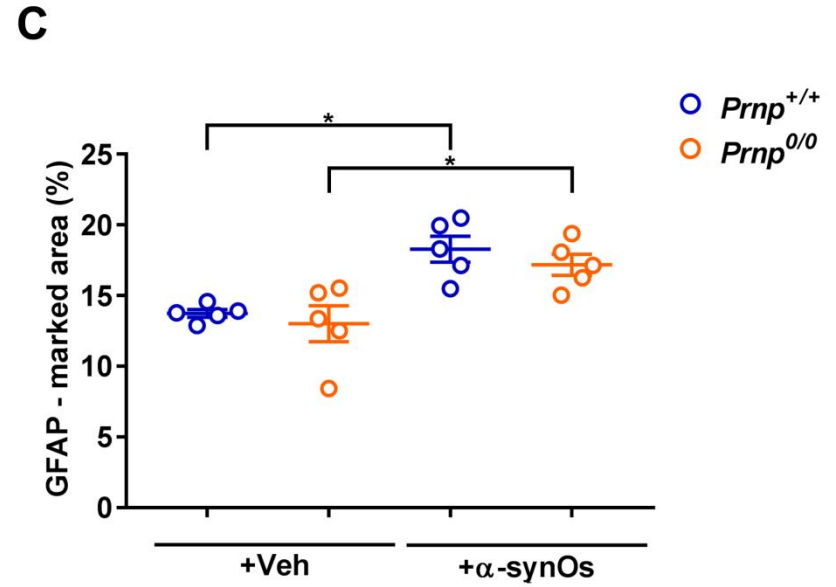
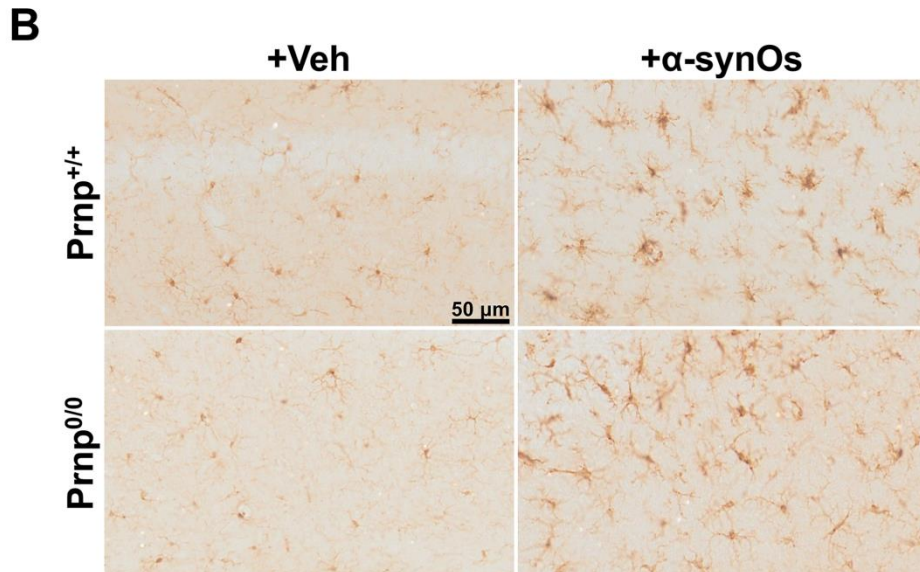
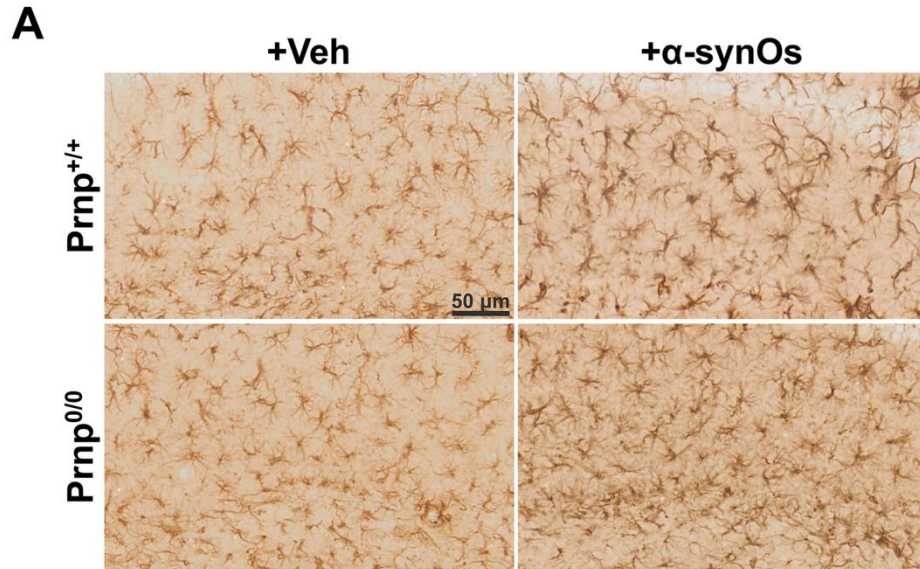
## NORT



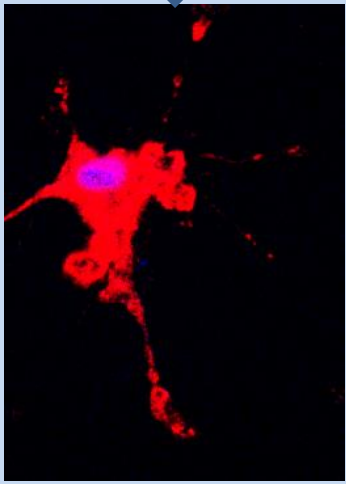
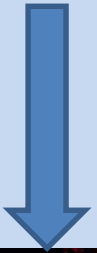
## CELL VIABILITY



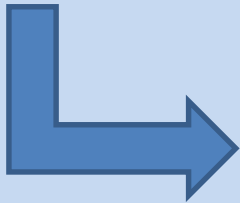
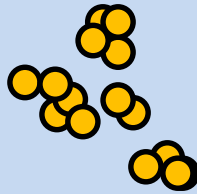
# HIPPOCAMPAL NEUROINFLAMMATION



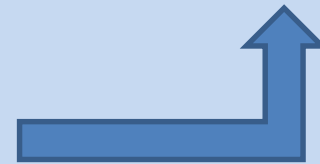
**Neuroinflammatory  
stimuli**

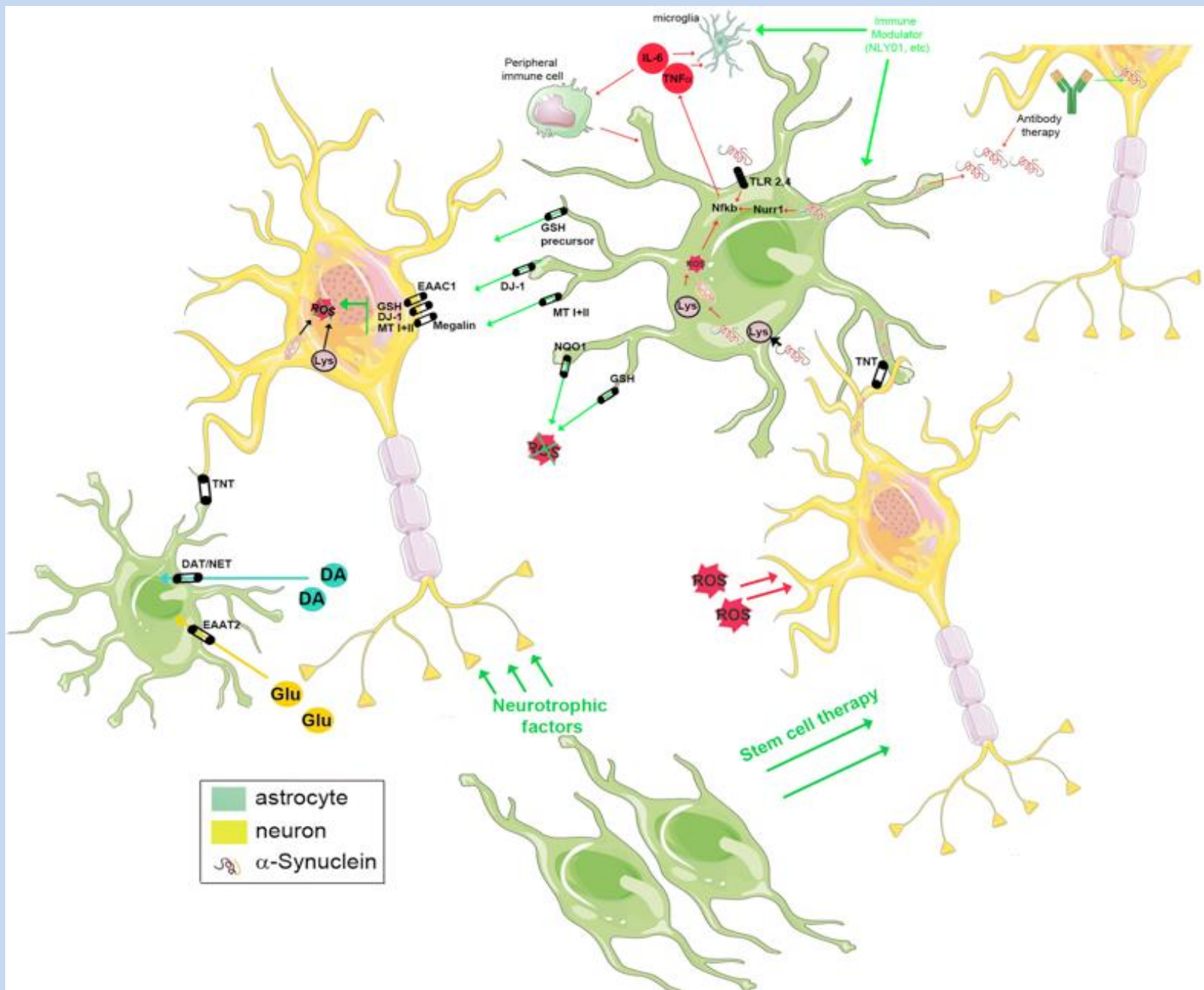


**$\alpha$ -synOs**



**Pro-inflammatory signals**





# ACKNOWLEDGEMENTS

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