

Assessing Synaptic Integrity In 4R Tauopathic Brains With UCB-J

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UCB-J selectively binds SV2A in PSP and CBD postmortem brains, revealing early and region-specific synaptic loss, supporting its potential as a reliable PET biomarker for 4R tauopathies.

INTRODUCTION

Synaptic loss is a key pathological feature of 4R tauopathies, including **Progressive Supranuclear Palsy (PSP)** and **Corticobasal Degeneration (CBD)**, two devastating neurodegenerative diseases with no available disease-modifying treatments.

There is an urgent need for reliable biomarkers to track disease progression.

SV2A, a synaptic vesicle protein widely expressed throughout the brain, can be targeted by **the novel PET tracer UCB-J**, which has shown great promise in tracking synaptic loss in tauopathies.

However, discrepancies between *in vivo* findings and a lack of mechanistic insight remain a critical barrier.

Therefore, without rigorous postmortem validation, the true utility of UCB-J as a synaptic biomarker in 4R tauopathies remains unresolved.

METHODS

Case Informations				
Group	n (cases)	Age (years)	Sex (M:F)	PMD
CN	7	77 ± 10.8	3:4	6:52 ± 2:48
PSP	7	76.9 ± 2.8	5:2	5:1 ± 0.5
CBD	8	68.4 ± 5.6	6:2	6:16 ± 1:14

Methods

Postmortem Human Brain Tissue

Homogenization

Cryosection

Tracer Incubation

Tracer Incubation

Radioligand Binding Assays

Autoradiography

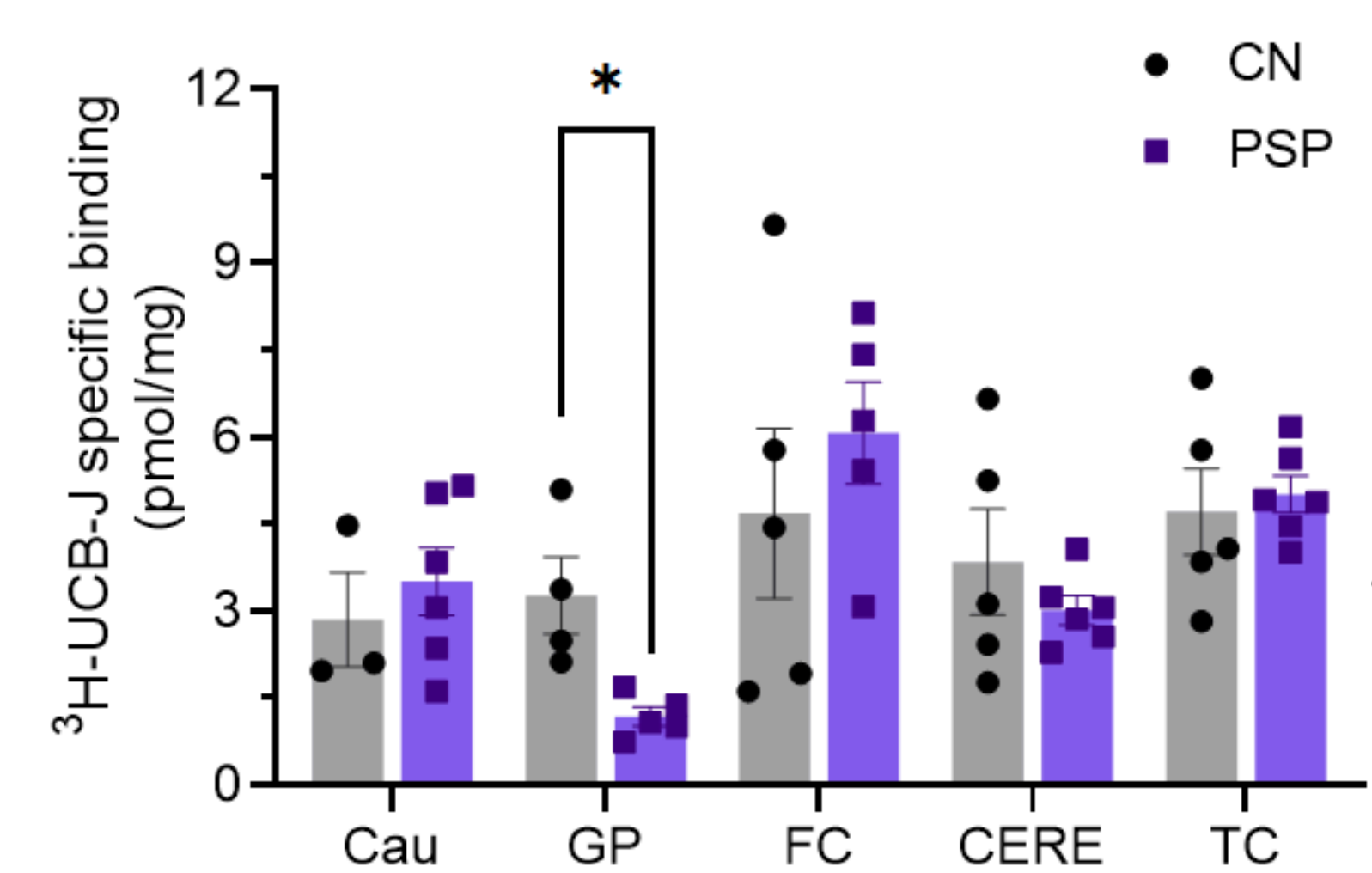
Liquid Scintillation Counter

Phosphor Imaging Scan

RESULTS

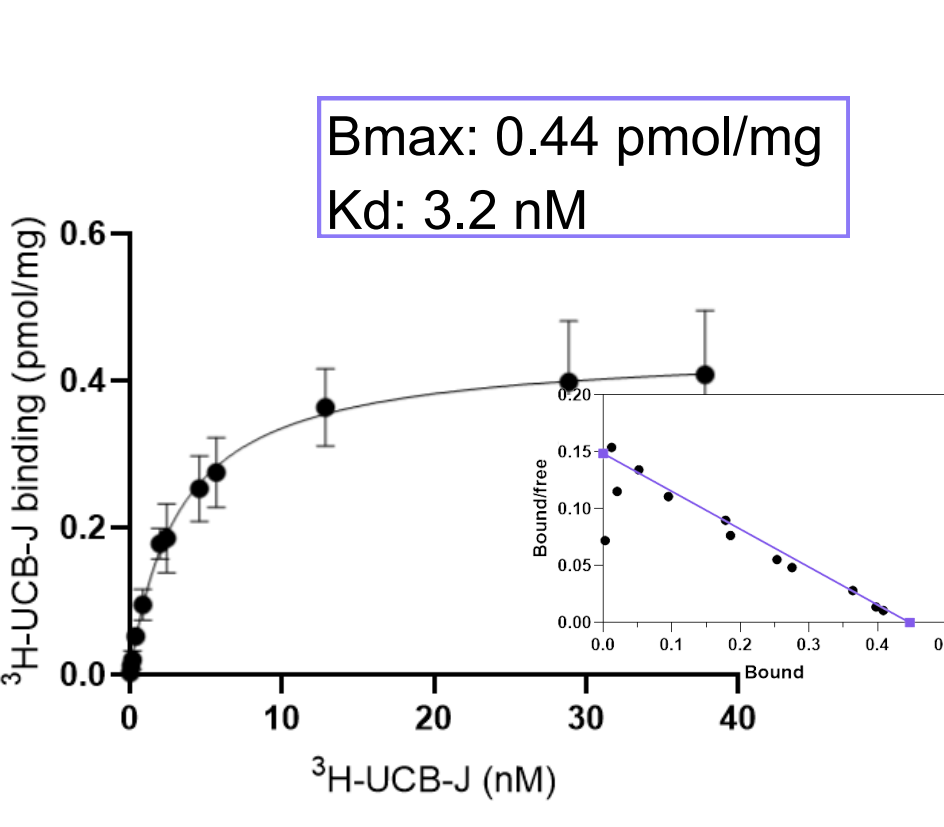
Radioligand Binding Assays in PSP and CBD

Brain Regional Binding Distribution in PSP



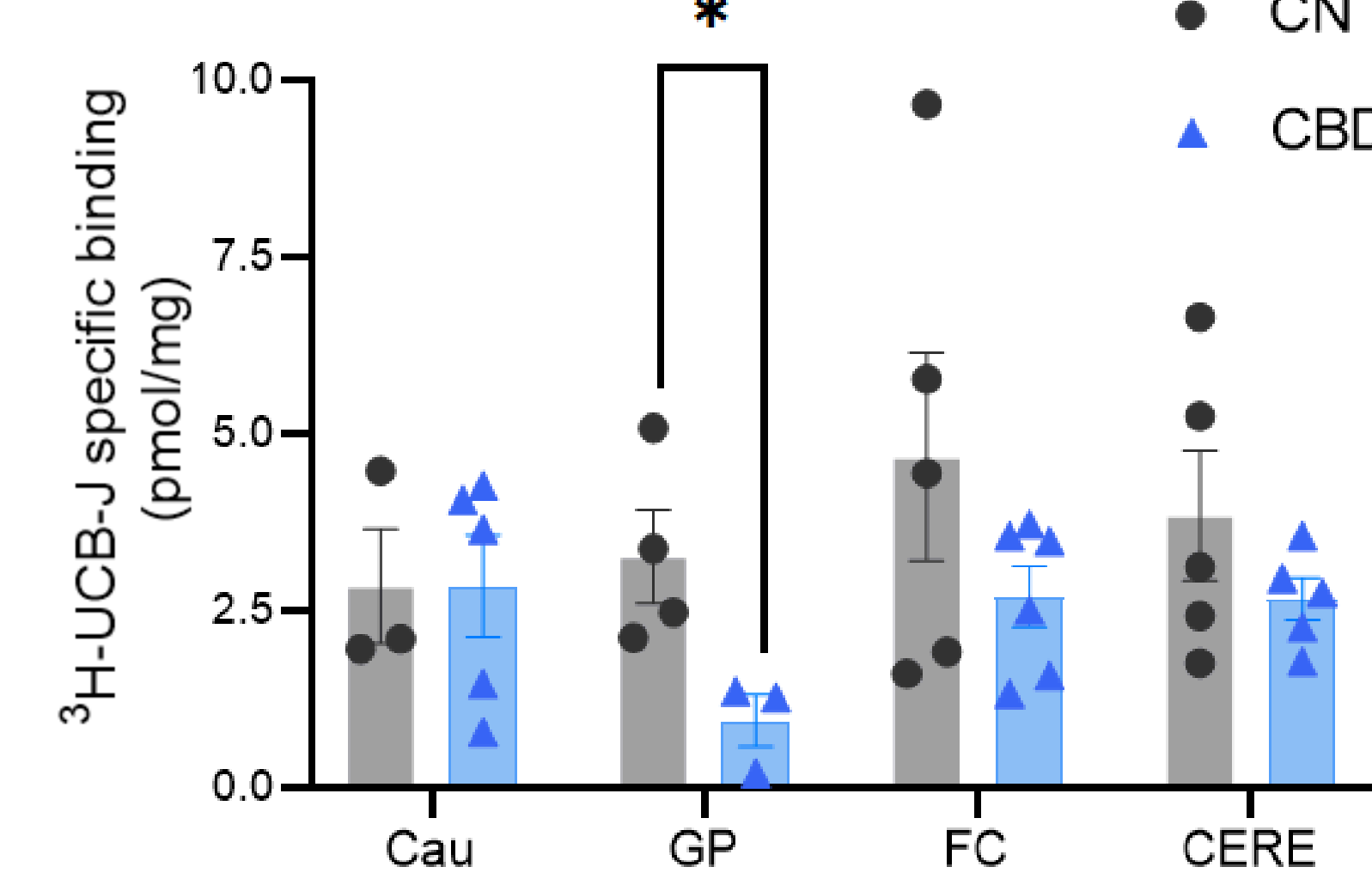
Region	CN (pmol/mg)	PSP (pmol/mg)
Cau	~3.0	~3.5
GP	~3.0	~1.0*
FC	~4.0	~6.0
CERE	~3.5	~3.0
TC	~4.0	~4.5

Saturation Binding in PSP



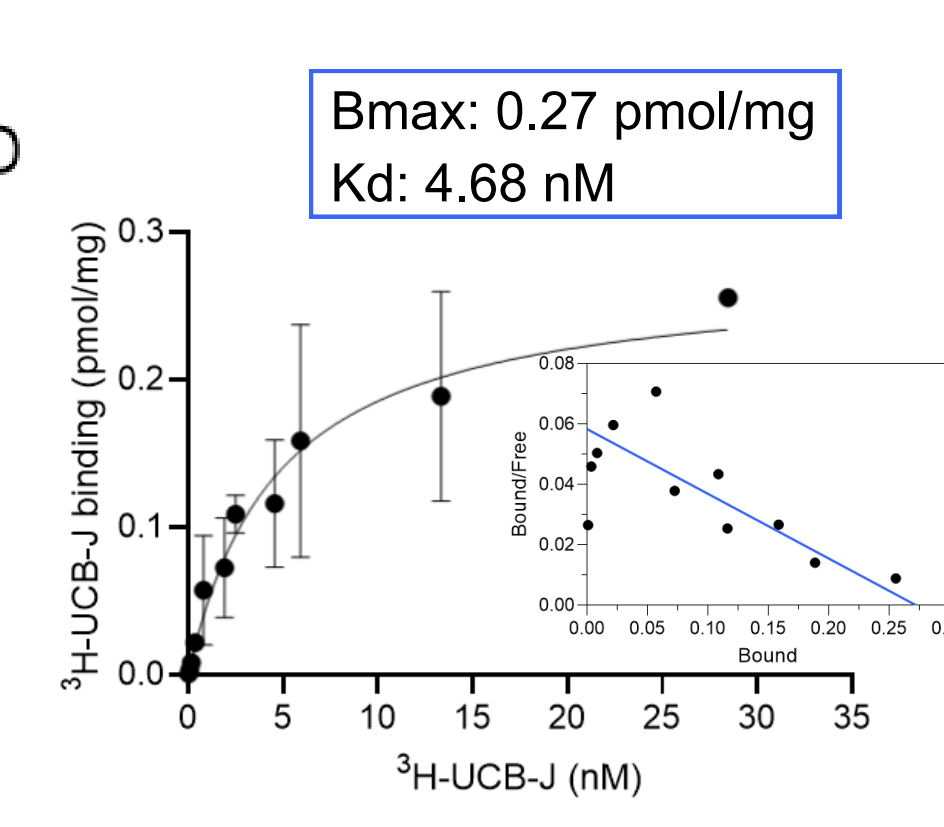
Bmax: 0.44 pmol/mg
Kd: 3.2 nM

Brain Regional Binding Distribution in CBD



Region	CN (pmol/mg)	CBD (pmol/mg)
Cau	~2.5	~2.5
GP	~3.0	~1.0*
FC	~4.5	~2.5
CERE	~3.5	~2.5

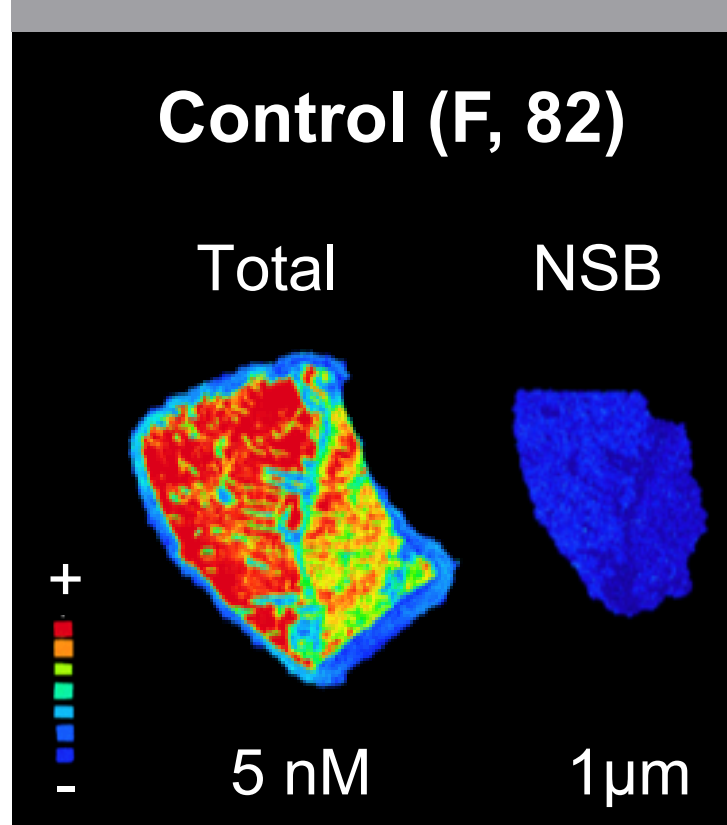
Saturation Binding in CBD



Bmax: 0.27 pmol/mg
Kd: 4.68 nM

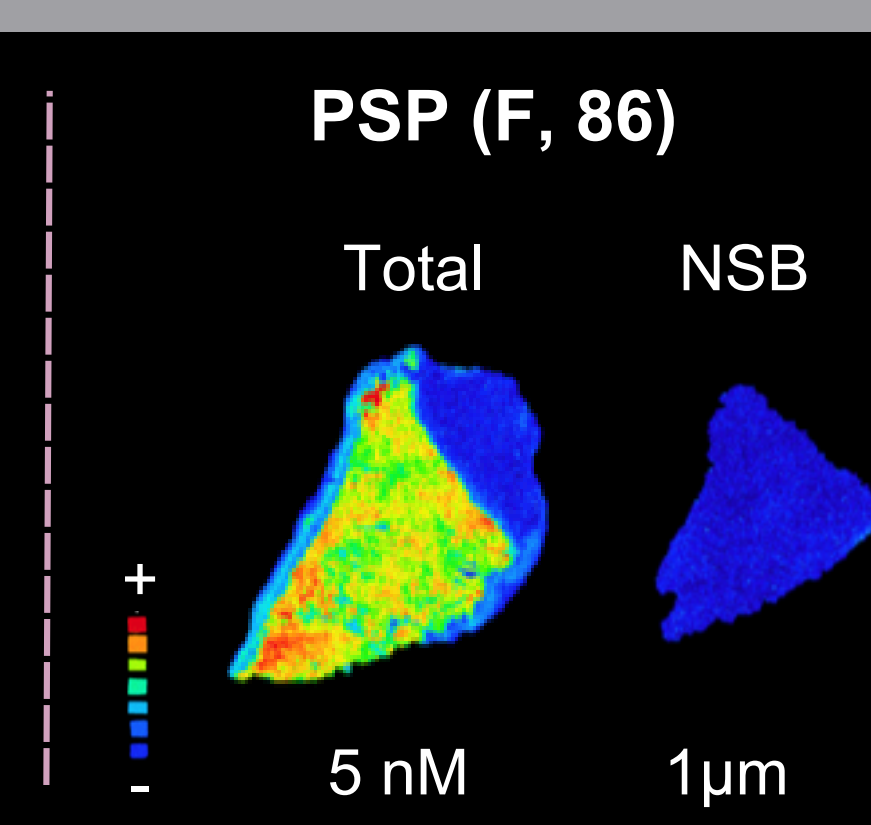
Postmortem Brain Imaging (Autoradiography)

Control (F, 82)



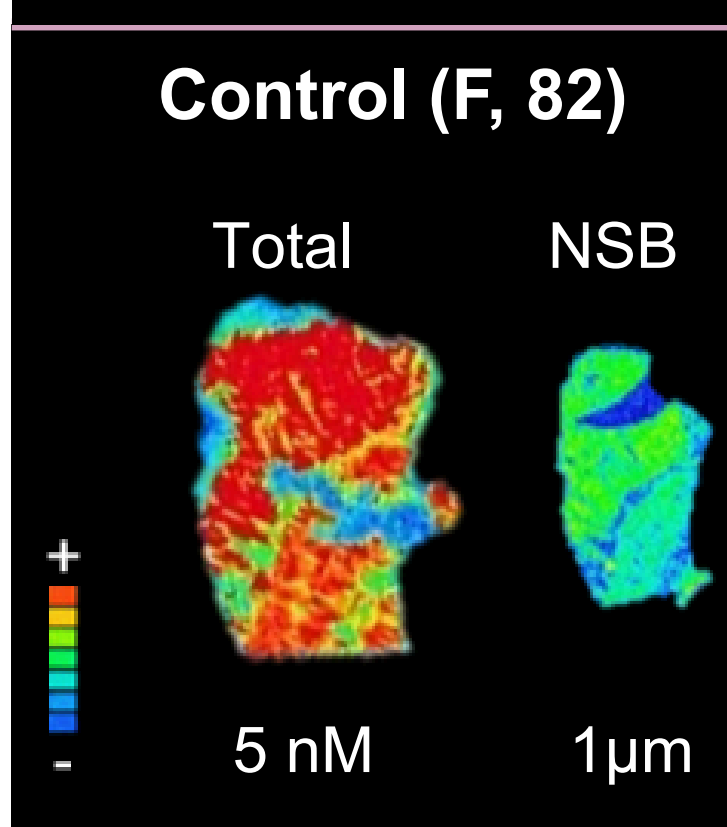
5 nM 1µm

PSP (F, 86)



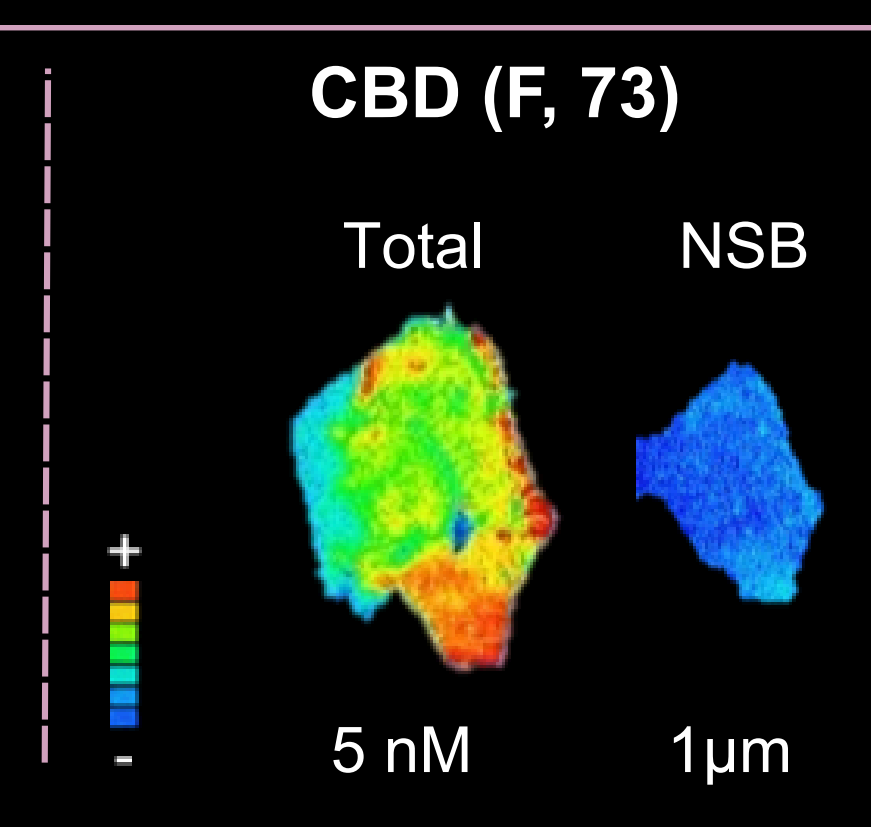
5 nM 1µm

Control (F, 82)



5 nM 1µm

CBD (F, 73)



5 nM 1µm

FUNDINGS & PUBLICATIONS

- Swedish Dementia Foundation (Demensfonden)
- Innovative ways to fight Alzheimer's disease - Leif Lundblad Family and others
- Tore Nilsons Stiftelse för Medicinsk Forskning
- Swedish Alzheimer Foundation (Alzheimerfonden)
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- KID

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- Stiftelsen Lars Hiertas Minne
- Ahlén Foundation

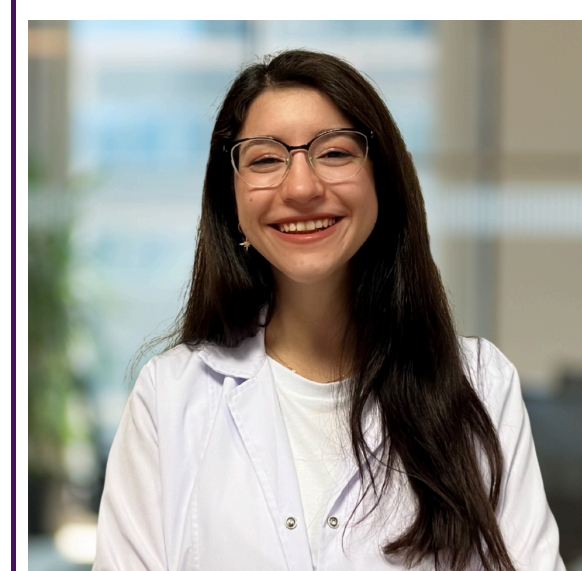


Relevant Publications

CONCLUSIONS

- UCB-J shows **high specificity** and **a single high-affinity** binding site for SV2A in both PSP and CBD brains.
- Significant synaptic loss was detected in the globus pallidus (**~60–72% reduction vs. controls**), consistent with known disease progression).
- UCB-J is a promising synaptic density marker in 4R tauopathies.

CONTACT



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