Association between thalamic atrophy and depression history in an Alzheimer's disease clinical cohort

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Introduction

There is evidence of a complex interplay between **depression**, **neurodegeneration**, and **Alzheimer's disease** (AD), but the underlying mechanisms are yet to be clarified.

Our group found that **44%** of clinical patients with confirmed Alzheimer's disease **(amyloid-positive; Aβ+)** have a lifetime history of depressive symptoms[1].

Previous studies have highlighted the **thalamus** as a region of interest for AD and depression:

- left lateralised atrophy in the ventral thalamus in an AD cohort, with greater atrophy in those with higher neuropsychiatric symptoms[2]
- significantly greater thalamic atrophy in a patient cohort with AD and depression, compared to an AD group without depression[3]

These studies, however, were carried out on selected research cohorts.

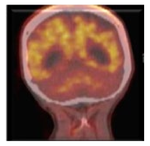
Aim

To examine the **association** between the grey matter volume and depression history in a clinical cohort with confirmed Alzheimer's disease.

Method

Subjects

- **69 amyloid-positive (Aβ+) patients** seen at Imperial Memory Clinic between 2013-2021



Positive API

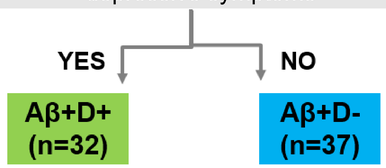
- underwent API following appropriate use criteria [4]
- clinical diagnosis of AD
- MRI ± 12 months of API

- **28 cognitively normal amyloid-negative** individuals without history of depression **(Aβ-D-)**

Depression assessment

Depression history information collected through structured review of clinical records.

- formal depression diagnosis
- history of previous/ongoing significant depressive symptoms



MRI

8 brain volumes [3] extracted from T1 images using FreeSurfer.

Results

Demographics

Demographics	Aβ-D-	Aβ+D-	Aβ+D+
Age years, M±SD	71.88 ± 5.99	67.54 ± 8.09	66.94 ± 8.89
Gender, %F	60.7	54.1	46.9

Comparison of 8 brain volumes

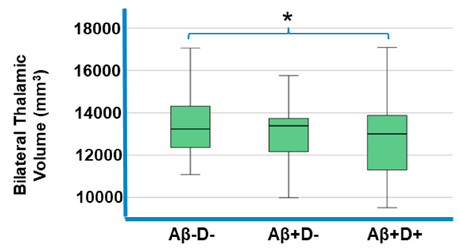
Association between 'group' and 'volume' for 7 regions, after controlling for age, gender and total intracranial volume.

- Thalamus[a]
- Amygdala[ab]
- Hippocampus[ab]
- Postcentral gyrus[ab]
- Precentral gyrus[b]
- Precuneus[ab]
- Posterior cingulate cortex
- Superior frontal gyrus[b]

Post-hoc Bonferroni: Significant difference between:
[a] Aβ+D+ & Aβ-D- (p<0.05)
[b] Aβ+D- & Aβ-D- (p<0.05)

Bilateral thalamus

Bilateral thalamic volume was the only region to differentiate Aβ+D+ (p=.016) but not Aβ+D- patients from controls (Aβ-D-) .

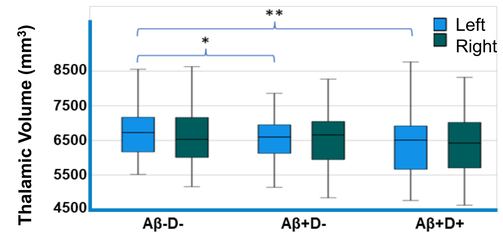


Boxplots of unadjusted bilateral thalamic volumes by group

Lateralized thalamus

Significant differences in the **left** but not the right thalamus between groups (F [2, 91] = 6.26, p=.003).

- **Lower volumes** in **Aβ+D-** (p=.032) and **Aβ+D+** (p=.003) groups compared to Controls (Aβ-D-).



Boxplots of unadjusted left & right thalamic volumes by group

Conclusion

In a clinical cohort, we found evidence of:

- **bilateral thalamic atrophy** in AD patients with history of depression
- **left thalamic atrophy** in both AD groups

Our results:

- support the clinical relevance of **asymmetrical thalamic atrophy** in AD
- suggest that depressive symptoms in AD are **associated** with thalamic volume loss

References

[1 Loreto et al., JAD subject to revision] [2 Low et al. 2019 Alz & Dem] [3 Karavasilis et al., 2017 J Neurol] [4 Johnson et al., 2013 Alz & Dem]

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