Neuropathologic Features of Antemortem Atrophy-Based Subtypes of Alzheimer Disease

Rosaleena Mohanty, PhD, Daniel Ferreira, PhD, Simon Frerich, MSc, et al., on behalf of the Alzheimer’s Disease Neuroimaging Initiative

Cite as: Neurology® 2022;99:e323-e333. doi:10.1212/WNL.0000000000200573

Study Question
Are the MRI-identified antemortem atrophy subtypes of Alzheimer disease (AD) related to postmortem AD and non-AD pathologies and does this subtype-to-pathology relationship vary by brain region?

What Is Known and What This Paper Adds
Brain atrophy in AD is considered downstream to accumulation of AD hallmarks (β-amyloid [Aβ] and tau) and non-AD (α-synuclein and TAR DNA-binding protein 43 [TDP-43]) pathologies. However, different atrophy subtypes are seen on MRI (typical, limbic predominant, hippocampal-sparing, and minimal atrophy AD) and their relationship with the AD and non-AD pathologies is not well understood. This investigation’s results indicate that atrophy subtypes are differentially associated with presence, burden, and region affected by the AD and non-AD pathologies.

Methods
This observational study includes data from 31 individuals enrolled in the Alzheimer’s Disease Neuroimaging Initiative (ADNI) study who had MRI done within the 2 years before death. All individuals had an antemortem diagnosis of AD dementia or mild cognitive impairment and postmortem-confirmed AD neuropathologic changes. Antemortem atrophy subtypes were modeled with continuous measures of typicality (hippocampus: cortex), spanning limbic-predominant to hippocampal-sparing AD, and severity (brain volume: CSF), spanning typical to minimal atrophy AD. Partial correlations (Spearman ρ) assessed associations between atrophy subtypes and neuropathologic outcomes (Aβ, tau, α-synuclein, TDP-43, and concomitance of multiple pathologies).

Results and Study Limitations
Antemortem typicality was significantly negatively associated with neuropathologic features of overall Aβ (ρ = −0.39), neuritic plaques (ρ = −0.4), and TDP-43 (ρ = −0.49) as well as regional tau (ρ = −0.38), α-synuclein (ρ = −0.39), and concomitance of pathologies (ρ = −0.59). This suggests that limbic-predominant AD was associated with higher pathology than hippocampal-sparing AD. Antemortem severity was significantly negatively associated with regional concomitance of pathologies (ρ = −0.43). This suggests that typical AD was associated with higher pathology than minimal atrophy AD. Limitations of this investigation include small sample size and the selective inclusion criteria of the ADNI study.

Study Funding and Competing Interests
This study did not receive targeted funding. Investigators report funding from governmental and foundation sources but report no additional competing interests. Go to Neurology.org/N for full disclosures.
Neuropathologic Features of Antemortem Atrophy-Based Subtypes of Alzheimer Disease
Rosaleena Mohanty, Daniel Ferreira, Simon Frerich, et al.
Neurology 2022;99:e323-e333 Published Online before print May 24, 2022
DOI 10.1212/WNL.0000000000200573

This information is current as of May 24, 2022

Updated Information & Services
including high resolution figures, can be found at:
http://n.neurology.org/content/99/4/e323.full

References
This article cites 47 articles, 5 of which you can access for free at:
http://n.neurology.org/content/99/4/e323.full#ref-list-1

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Alzheimer’s disease
http://n.neurology.org/cgi/collection/alzheimers_disease
MRI
http://n.neurology.org/cgi/collection/mri

Errata
An erratum has been published regarding this article. Please see next page or:
/content/early/2022/09/30/WNL.000000000201298.full.pdf

Permissions & Licensing
Information about reproducing this article in parts (figures,tables) or in its entirety can be found online at:
http://www.neurology.org/about/about_the_journal#permissions

Reprints
Information about ordering reprints can be found online:
http://n.neurology.org/subscribers/advertise
CORRECTION
Neuropathologic Features of Antemortem Atrophy-Based Subtypes of Alzheimer Disease
In the Research Article “Neuropathologic Features of Antemortem Atrophy-Based Subtypes of Alzheimer Disease” by Mohanty et al., the abbreviation for “Mini-Mental State Examination” should read “MMSE.” The authors regret the error.

REFERENCE