PREVALENCE AND CLINICAL ASSOCIATIONS OF ATROPHY SUBTYPES IN MCI USING QYSCORE® AND THE MEMENTO MEMORY CLINIC POPULATION

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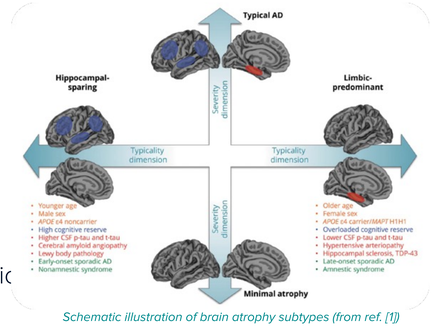
QYNAPSE

BACKGROUND

Three patterns of brain atrophy have been consistently identified in cases of Alzheimer's dementia[1]

- limbic-predominant (LP): atrophy of the hippocampus but relatively spared neocortex
- hippocampal sparing (HS): atrophy in the cortex (especially lateral temporal and parietal lobes) but sparing of the hippocampus
- typical/diffuse (TD): atrophy in both hippocampus and cortex

A recent study extended this concept to a less severely affected memory clinic population (the MEMENTO study)[2,3].



Schematic illustration of brain atrophy subtypes (from ref. [1])

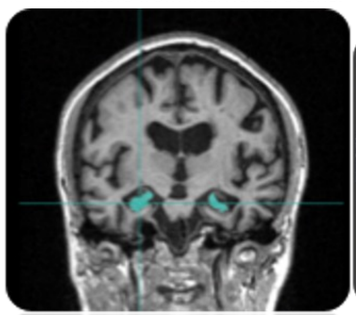
OBJECTIVES

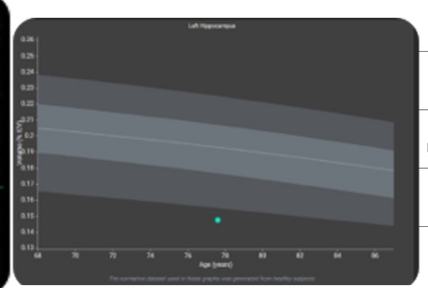
To assess atrophy subtypes in the MEMENTO population using a volumetric quantitative approach based on the automated output of QyScore® an FDA-approved and CE-marked image analysis software[4].

METHODS

IMAGING DATA

- **N=1642 3DT1 images** from mild cognitive impairment (MCI) participants from the MEMENTO cohort were included (Age=71±9, MMSE=27.8±2.0, CDR-SB=0.6±0.7)
- N=678 (41%) had amyloid status from CSF or PET, of which **193 (28%) were amyloid-positive (A+)**
- Neurodegeneration-positive (N+) atrophy subtypes (LP, HS or TD) were defined on individual scans using z-scores from parietal cortex and hippocampus volumes referenced to 1290 cognitively normal individuals using **QyScore® v1.10**
- Volumes were corrected by **intracranial volume** (ICV).
- QyScore® analytics with built-in normative database enables a definition of subtypes based on regional atrophy markers from individual scans:



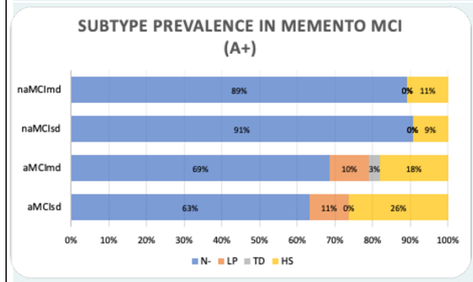


	N-	Limbic Predominant	Typical / Diffuse	Hippocampal Sparing
QyScore® Parietal Cortex	z ≥ -1.64	z ≥ -1.64	z < -1.64	z < -1.64
QyScore® Hippocampus	z ≥ -1.64	z < -1.64	z < -1.64	z ≥ -1.64

RESULTS

NEUROANATOMICAL PROFILE RESULTS

- N+ subtypes were more prevalent in the amnestic MCI (single domain (aMCIsd 18%), and multiple domain (aMCImd 17%)) presentations than non- amnestic (naMCIsd 8%, naMCImd 10%) presentations.
- N+ subtypes were more common in A+ participants, especially the amnestic presentations (aMCIsd 42%, aMCImd 29%)
- Overall, the HS subtype was the most common (8% of all cases, 16% of A+ cases), followed by LP (4%/6%) and TD (2%/3%)
- The LP subtype was more prevalent in amnestic presentations



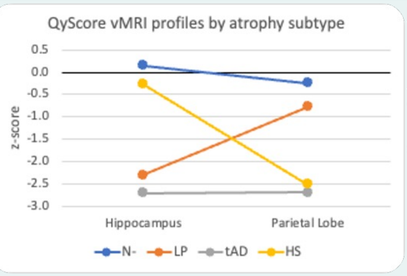


Figure 1: A) Subtype prevalence in the amyloid positive population in MEMENTO.
Figure 1: B) The z-score distribution of the full MEMENTO population used for subtype classification

aMCIsd = single-domain amnestic
aMCImd = multi-domain amnestic
naMCIsd = single- domain non-amnestic
naMCImd = multi-domain non-amnestic

- The relatively low prevalence of the TD subtype in this cohort is consistent with a previous report on the MEMENTO cohort, using a different methodology[3]
- The overall prevalence of N+ subtypes in MEMENTO by this method is intermediate between those previously reported[5] using a similar method for ADNI cognitively normal (CN), A+ and amnestic MCI (aMCI) A+ cohorts

Subtype	ADNI (CN, A+)	MEMENTO (aMCI & naMCI)	MEMENTO (aMCI & naMCI, A+)	MEMENTO (aMCI, A+)	ADNI (aMCI, A+)
N-	90%	86%	76%	68%	57%
LP	6%	4%	7%	10%	31%
TD	1%	2%	2%	2%	9%
HS	2%	8%	16%	19%	3%

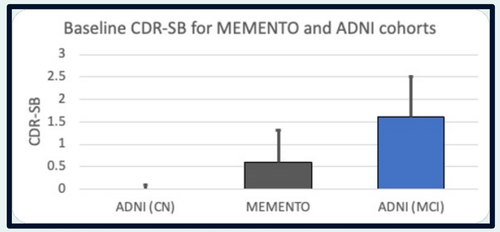


Figure 2: A) Comparison of neuroanatomical subtypes distribution across the MEMENTO MCI and ADNI CN and MCI populations
Figure 2: B) Baseline CDR-SB for MEMENTO and ADNI cohorts

CONCLUSIONS

- Automated quantification of atrophy subtypes was successfully performed in a large memory clinic population suggesting it's potential for application in wider clinical route imaging.
- This is particularly important given the increasing evidence that atrophy subtypes in MCI have prognostic value as the severity of cognitive and functional decline.[7]

References:
[1] Ferriera et al. (2020) Neurology 94:436; [2] Dufouil et al. (2017) Alz Res Ther 9:67; [3] Planche et al. (2021) Alz & Dem 17(4):651; [4] Cavedo et al. (2022) Eur Radiol 32(5):2949; [5] Charil et al. (2018) AAIC [6] Aisen et al. (2010) Alz & Dem 6(3):239; [7] Gordon et al (2022) AAIC