

maps were generated using MPnRAGE and subsequently skull-stripped, realigned and normalized to a 1mm<sup>3</sup> T<sub>1</sub>-weighted MNI template, and segmented by tissue type using gray and white matter MNI templates within SPM12. Average T<sub>1</sub> (in ms) was extracted from the resulting gray and white matter T<sub>1</sub> maps. Multiple regression models were estimated using R to determine relationships with CSF biomarkers (log transformed for normality). Primary analyses focused on markers of neurodegeneration including total tau, neurogranin, and neurofilament light protein (NFL). Secondary analyses examined relationships with AD biomarkers ptau and Aβ<sub>42</sub>/Aβ<sub>40</sub> ratio on quantitative T<sub>1</sub>, while controlling for age, sex, APOE status, and time between MRI and CSF sample collection. **Results:** Higher total tau was associated with higher T<sub>1</sub> in gray matter (b = 62.735 [4.22, 121.25], F(1, 39) = 4.703, p = 0.036). There were no significant relationships between phosphorylated tau, NFL, and Aβ<sub>42</sub>/40 ratio and quantitative T<sub>1</sub> in gray and white matter, although higher neurogranin was unexpectedly associated with higher T<sub>1</sub> in white matter (b = 94.346 [9.503, 179.188], F(1, 37) = 5.077, p = 0.03). **Conclusions:** We found that CSF tau—a marker of neurodegeneration—was associated with higher quantitative T<sub>1</sub>, potentially suggesting myelin loss and/or increased water content due to neurodegeneration. The relationship was measurable even among cognitively unimpaired adults, and when controlling for age. Additional studies with larger samples will determine whether quantitative T<sub>1</sub> may be useful for mapping neurodegeneration in the context of Alzheimer's, and the NIA-AA research framework.

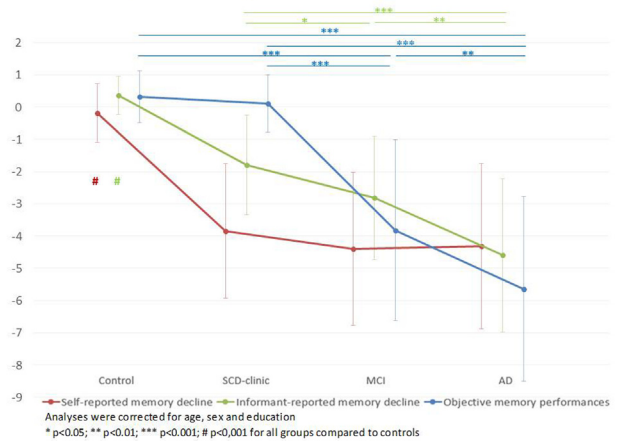
**IC-P-082 ASSOCIATION OF PERCEIVED MEMORY DECLINE WITH MULTIMODAL NEUROIMAGING AT DIFFERENT STAGES OF ALZHEIMER'S DISEASE**



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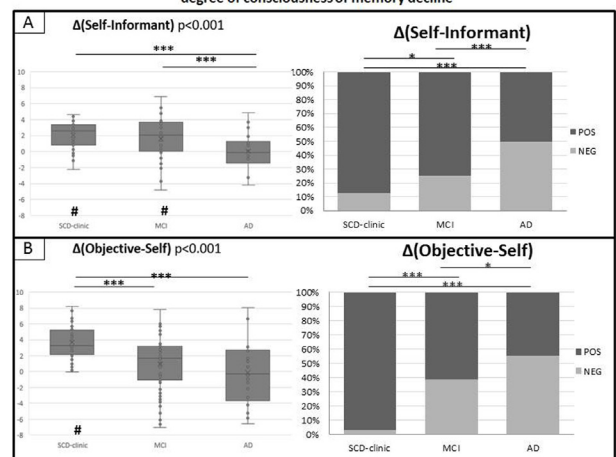
**Background:** Studies showed that both self- and informant-reported memory declines were associated with increased risk of conversion to Alzheimer's Disease (AD) in the preclinical (Subjective Cognitive Decline - SCD) and prodromal (Mild Cognitive Impairment - MCI) stages. This study aims at describing the evolution of self- and informant-reported versus objective memory declines through the different stages of the disease and their relationships with AD neuroimaging biomarkers. **Methods:** Thirty-five cognitively unimpaired older adults (controls), 36 SCD, 60 MCI and 37 AD patients underwent self-reported, informant-reported and objective memory decline examinations; along with neuroimaging

**Fig.1 Between-group differences in perceived memory decline.**

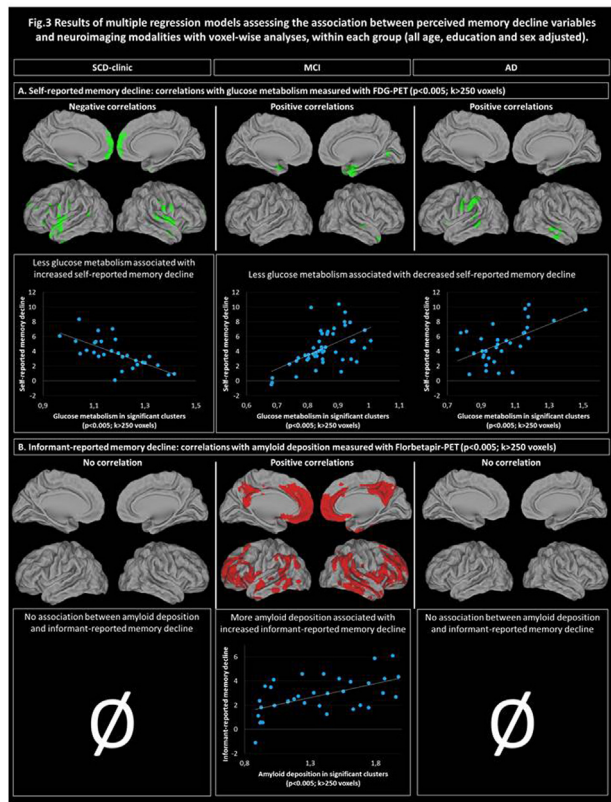


(anatomical MRI, FDG-PET and Flortetapir-PET) assessments. Delta scores (Δ(Self-Infomant) and Δ(Objective-Self)) and percentages of patients with a negative delta, interpreted as anosognosia, were computed. Scores were compared between groups and voxelwise multiple regressions were assessed between self- and informant-reported memory decline scores and neuroimaging data within each group (all age, education and sex adjusted). **Results:** Self-reported memory decline was higher in all patient groups versus controls but did not differ between patient groups, while the informant-reported score progressively increased between groups (controls<SCD<MCI<AD; Fig.1). Compared to controls, delta scores progressively decreased and the percentage of patients with a negative delta significantly increased from SCD to MCI to AD (Fig.2). Self-reported memory decline correlated to glucose metabolism in opposite directions in SCD (higher scores - lower metabolism) versus MCI and AD (lower scores - lower metabolism). Finally, informant-reported memory decline strongly (positively) correlated to amyloid deposition in MCI (Fig.3). **Conclusions:** Self-reported memory decline was present from the SCD stage but was not sensitive to increasing clinical stages by contrast to informant-reported score that progressively increased

**Fig.2 Between-group differences in the delta scores illustrating the degree of consciousness of memory decline**



# p<0.001 compared to control; † p<0.1 compared to controls  
 \* p<0.05; \*\* p<0.01; \*\*\* p<0.001; POS=positive delta; NEG=negative delta  
 Δ(Self-Infomant)=Difference between self- and informant-reported memory decline  
 Δ(Objective-Self)=Difference between objective and self-reported memory decline



in MCI and AD. Consistently, the gap increased across stages between self-reported and informant or objective scores, illustrating increased anosognosia. Neuroimaging findings suggest that higher self-reported score in SCD is a sign of decline associated with decreased glucose metabolism. By contrast in MCI and AD lower scores is associated with lower metabolism as it might reflect anosognosia. Our findings also highlight the relevance of informant-reported (rather than self-reported) memory decline in MCI patients as this score was specifically associated with amyloid deposition.

**IC-P-083 CORRELATION OF QUANTITATIVE SUSCEPTIBILITY MAPPING AND COGNITIVE DYSFUNCTION IN MIXED ALZHEIMER'S AND VASCULAR DEMENTIA**



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**Background:** The coexistence of Alzheimer's disease (AD) and vascular dementia (VaD) is the most common type of mixed dementia (MD). More than half of all clinically diagnosed AD cases show multiple pathologies at autopsy, but these are challenging to diagnose premortem. Hallmark features of MD are known to include white-matter disease (WMD) and deep grey matter

(dGM) microbleeds, but *in-vivo* imaging markers to identify and characterize these features are needed. Quantitative susceptibility mapping (QSM), a magnetic resonance imaging (MRI) measure that maps magnetic tissue properties and alterations (e.g. related to iron and myelin), may be able to fill this gap. Objective: To evaluate the relationship between QSM and clinical/cognitive measures in participants with clinically diagnosed MD, AD or subcortical VaD (SVaD). **Methods:** In this cross-sectional study, participants (N=17) were scanned at 3T (subtypes:7 MD/5 SvaD/5 AD; Sex:11M/6F; Age:75±8; MoCa:19±4 (range:12-28)). Multi-echo gradient echo data were acquired for QSM, including 5 echoes with 0.49x0.49x1mm<sup>3</sup> voxels. QSM data were processed using in-house developed software. Median QSM values were calculated within basal ganglia masks, containing the putamen, pallidum, accumbens and caudate as defined by the Harvard-Oxford subcortical atlas. Basal ganglia volumes were computed from the individual region-of-interest masks. Clinical/cognitive assessments included Clinical Dementia Rating (CDR) sum of boxes and Montreal Cognitive Assessment (MoCA) total score. We used a general linear model to predict clinical/neuropsychological assessment scores from basal ganglia QSM measurements. Covariates included age, sex, presence of cardiovascular conditions (to account for the effect of hypertension) and basal ganglia volumes. **Results:** Both increasing age ( $\beta=-0.4$ ;  $p=0.001$ ) and increasing basal ganglia QSM ( $\beta=-194$ ;  $p=0.002$ ) were significantly associated with lower MoCA total scores (model  $R^2=0.6$ ). The CDR sum of boxes measure was not significantly correlated with the basal ganglia QSM. There were no significant differences in basal ganglia volumes or QSM measures between MD, SVaD and AD after adjusting for age and sex. **Conclusions:** Our findings indicate that increasing dGM iron concentration, or the potential presence of microbleed-related pathologies, could be associated with cognitive deficits in dementia. Larger follow-up studies with sufficient power are warranted to separate MD from other dementias.

**IC-P-084 PREDICTING METABOLIC AND STRUCTURAL CHANGES IN DOMINANTLY INHERITED ALZHEIMER'S DISEASE**



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**Background:** Predicting changes in brain structure and metabolism in specific regions could allow for targeted therapy for individuals with Alzheimer's disease (AD). We propose an ensemble deep learning approach using multi-modal imaging to predict glucose hypometabolism and volumetric loss in autosomal dominant AD (mutations in APP, PSEN1, PSEN2). **Methods:** 131 mutation positive (M+) participants and 74 mutation negative (M-) controls with at least 2 separate fluorodeoxyglucose (FDG) and magnetic resonance imaging (MRI) sessions were obtained. (see Table 1 for demographics). Structural MRI over 160 Freesurfer brain regions of interest (ROIs) and metabolic activity (FDG) over 250 Freesurfer ROIs was acquired for each participant at each time point. Mutation