Baseline Amyloid ^{18}F-AV-45 PET Distributions by Consensus Diagnosis from the Alzheimer's Disease in Down Syndrome (ADDS) Consortium

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Introduction

Individuals with Down syndrome (DS) have an increasing age-related prevalence of Alzheimer's disease (AD). In DS, the triplication of amyloid precursor protein on chromosome 21 contributes to a life-long accumulation of brain amyloid. *Dementia increases with age to over 75% prevalence after age 65 years.*

In non-demented adults with DS, PET studies have shown increased amyloid uptake. However, the relationship between amyloid uptake and cognitive decline in DS has not been determined. *This study compares brain amyloid distribution by consensus diagnosis in patients with DS using ^{18}F-AV-45 PET.*

Methods

- 85 participants with DS were assessed with 18F-AV-45 PET scans, acquired across 3 sites.
- Participants were given a baseline diagnosis of: 1) Non-demented (i.e., cognitively stable), 2) Mild cognitive impairment (MCI), or 3) Dementia
- PET units were converted to standardized uptake value ratios (SUVR) using the cerebellum reference region[1]. Reference regions were derived using Freesurfer 6.0[2].
- PET region of interest (ROI) averages were partial volume corrected (PVC) using PETSurfer[3] prior to analysis.
- ROI averages were adjusted for age, gender, and region volume prior to statistical analysis.
  - PET $ROI_{SUVR(CB)}$ ~ Diagnosis + Age + Gender + MRI ROI_{Volume}
- For voxelwise analysis, co-registered PET data was warped to MNI space using the SPM12[4].

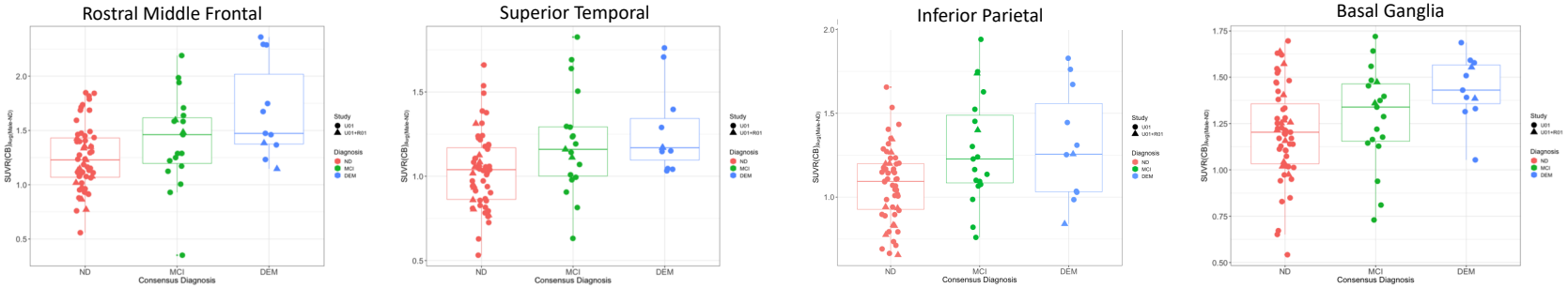
Results

Diagnosis	N	Gender	Age@PET(yrs.) [min,max]
Non-Demented (ND)	55	33 M / 22 F	48.4 +/- 5.9 [40, 62]
MCI	19	17 M / 2 F	53.8 +/- 6.4 [44, 66]
Dementia	11	5 M / 6 F	55.4 +/- 6.6. [45, 65]

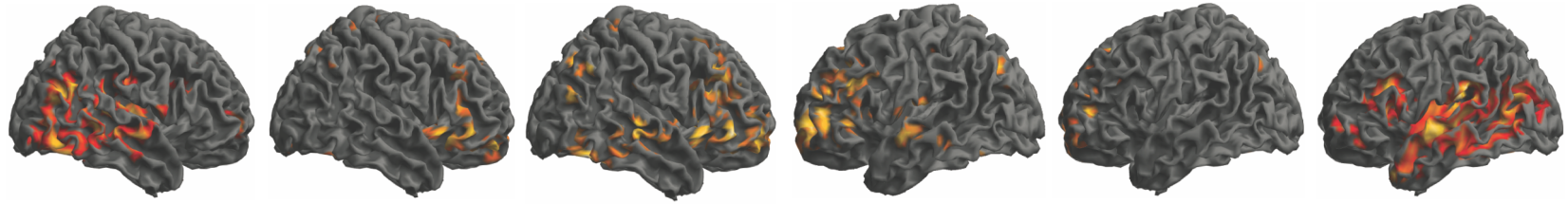
Significant Regional Increases in Amyloid Burden by Diagnosis

Dementia > MCI	MCI > ND	Dementia > ND	
• Rostral middle frontal*	• Inferior parietal*	• Rostral middle frontal*	• Medial orbitofrontal*
• Inferior temporal	• Superior temporal*	• Superior frontal*	• Orbitofrontal*
• Basal ganglia	• Superior frontal*	• Middle temporal*	• Inferior temporal*
• Middle temporal	• Middle temporal	• Basal ganglia*	• Anterior cingulate
	• Anterior cingulate	• Superior temporal*	• Lateral orbitofrontal
	• Rostral middle frontal	• Inferior parietal*	• Posterior cingulate
	• Basal ganglia	• Lateral occipital*	

*. **p < 0.05 FDR (1-tailed),** p < 0.05 unc. otherwise



Significant Voxelwise Increases in Amyloid Burden by Diagnosis



MCI > ND t=2.37; p<0.01unc | DEM > MCI t=2.37; p<0.01unc | DEM > ND t=3.31; p<0.05 FDR | DEM > ND t=3.31; p<0.05 FDR | DEM > MCI t=2.37; p<0.01unc | MCI > ND t=2.37; p<0.01unc

Conclusions

1. MCI in DS is primarily characterized by increased amyloid burden in superior and middle temporal and inferior parietal regions.
2. Alternatively when comparing DEM to MCI groups in participants with DS we see increased amyloid burden in predominantly frontal regions along with increased variability.
3. None of the regions tested completely separated the diagnostic groups by AV-45 amyloid burden alone likely a result of mapping a continuous disease process to categorical diagnoses.

References

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