The relationship of neuroimaging measures to dementia status and cognition in older adults with Down Syndrome
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Target audience: This research is of interest to those involved in research with Down Syndrome, Alzheimer’s disease, and other dementias.

Purpose: Individuals with Down Syndrome (DS) show earlier and more frequent diagnosis of Alzheimer’s (AD)-like dementia than the general population1. The increased incidence of dementia and the difficulty of diagnosis in this population highlight the need for both markers of disease onset and progression and an understanding of AD pathology in DS. The objective of the current work is to determine if neuroanatomical and proton magnetic resonance spectroscopy (1H-MRS) measures are related to level of cognitive functioning and dementia in individuals with DS.

Methods: 15 adults with Down Syndrome (mean age 44.6 ± 6.9, 6 males) were scanned in an IRB-approved protocol at 3T, in a 12-ch receive head coil. Scans included T1-MPRAGE and single voxel point resolved spectroscopy (TE 30 ms, TR 3000 ms, 96 data averages) at the left dorsal lateral prefrontal cortex (DLPFC) with and without water suppression.

1H-MRS data analysis using jMRUI software package1 involved (i) zero order phase correction using residual water signal, (ii) residual water suppression using HLSVD filter3, (iii) apodization with a 5 Hz Gaussian filter, (iv) zero filling and (v) baseline correction. QUEST algorithm4 was used for metabolite quantification. The basis set for QUEST was calculated using product-operator based NMR-SCOPE5 with spin Hamiltonian parameters from [6]. Gray matter (GM), white matter (WM) and CSF contribution to the voxel composition was calculated using FAST7 with the T1-MPRAGE as the base image and used in the calculation of metabolite levels.

Total tissue volume and a volumetric scaling factor were estimated with the FSL program SIENAX8, and more detailed anatomical volumes were estimated using the program Freesurfer9. All volumes were corrected for head size using the volumetric scaling factor.

Cognitive functioning was measured using the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS–IV). The Dementia Questionnaire for Learning Disabled Persons (DLD) was used to determine dementia status.

Discussion: In the current study, Cho is the only measure which shows a relationship with measures of cognition. Prior research has shown increased Cho in individuals with DS, suggesting metabolic abnormalities10,11, though our study is the first to suggest a relationship with cognition or dementia. We found no relationship between DLPFC myo-inositol (mI) and neuropsychological measures, though previous studies suggest hippocampal mI is related to both overall cognitive ability and to dementia status in DS12,13. We also find that measures of total white matter and ventricular volume are related to a measure of dementia and that cortical and subcortical grey matter volumes are related to age. The complex relationship between cognition, dementia, and age is highlighted in these results, particularly as subcortical grey matter volume has previously been found to relate to dementia status14.

Conclusion: In individuals with DS, we find a relationship between DLPFC Cho and dementia status and overall cognitive ability, and between neuroanatomical measures and dementia status. These results highlight the need for longitudinal studies of this population, to clarify the relationship between imaging measures, baseline cognitive ability, and dementia.


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