

## **Title:** Employment and the Biomarkers of Early Alzheimer's Disease in Down Syndrome

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**Introduction:** Individuals with Down syndrome (DS) experience an accelerated aging process in that medical conditions and physical and functional declines associated with aging occur earlier as compared to the general population (Lott & Dierssen, 2010). One of the aging conditions, Alzheimer's disease (AD), occurs at extremely high rates in the DS population and is thought to be initiated by the deposition of brain  $\beta$ -amyloid (A $\beta$ ) (Mann & Esiri, 1989). Nearly all adults with DS begin showing evidence of brain A $\beta$  plaques by the age of 40 years (Wiseman et al., 2015), due to a third copy of chromosome 21, which contains the gene for the amyloid precursor protein. Despite this genetic similarity among individuals with DS, there is marked variability in the timing of A $\beta$  accumulation and in the age of onset of dementia in DS (McCarron, McCallion, Reilly, Dunne, Carroll, & Mulryan, 2017), suggesting that environmental factors may play a role in AD pathophysiology and/or its effects in DS. Employment complexity is one environmental factor that has been posited to serve as a protective factor against AD in the general population (Smart, Gow, & Deary, 2014). The extent to which employment complexity is associated with A $\beta$  accumulation and cognitive decline in DS is not known. Our study aims were to: 1) describe employment variability among individuals with DS; 2) determine whether employment is related to variability in A $\beta$  accumulation and/or cognitive performance.

**Methods:** Participants were part of the larger ongoing study, Neurodegeneration in Aging Down Syndrome (NiAD). Fifty-nine adults aged 25-52 years ( $M = 36.27$ ,  $SD = 6.90$ ) with DS participated in a supplemental study on lifestyle, which included an assessment of employment opportunities and work-related tasks. Participant occupations were coded into complexity scores using the Dictionary of Occupational Titles (DOT; United States Employment Service, 1977). Data complexity (range: [0-6]), people complexity (range: [0-8]), and things complexity (range: [0-7]) were coded in order to determine associations between job complexity, cognition, and A $\beta$  accumulation. DOT ratings are coded so that lower scores reflect higher occupational complexity. Participants were also administered direct measures of executive functioning and memory, and underwent PET scans using Pittsburgh compound B (PiB) to assess A $\beta$  accumulation. Pearson correlations were utilized to examine associations between job complexity, A $\beta$  accumulation, and six measures of cognitive functioning.

**Results:** Descriptive statistics revealed that of the  $n = 41$  participants with employment status data, 25% ( $n = 15$ ) of participants are employed part time, 5% ( $n = 3$ ) are employed full time, 32% ( $n = 19$ ) work in a supported workshop, 2% ( $n = 1$ ) attend day treatment programs, 3% ( $n = 2$ ) volunteer, and 2% ( $n = 1$ ) are not employed. In regards to job complexity scores, Data complexity yielded a mean of 5.41 ( $SD = .95$ ), People complexity indicated a mean of 7.02 ( $SD = 1.34$ ), and Things complexity yielded a mean of 5.89 ( $SD = 1.83$ ). People complexity was significantly associated with striatal A $\beta$  accumulation after controlling for mental age ( $r = -.335$ ,  $p = .012$ ). Data complexity was associated with the Down Syndrome Mental Status Exam total score ( $r = -.265$ ,  $p = .049$ ) and People complexity was associated with the Block Design task ( $r = -.275$ ,  $p = .040$ ) in models controlling for level of intellectual disability. However, there were no other significant associations.

**Discussion:** We found important variability in both employment status and in job complexity in adults with DS; employment may be an important lifestyle variable that explains differences in aging outcomes in DS. The positive association between Data and People complexity scores and cognitive functioning indicates that adults with DS in more complex jobs have better cognitive functioning, possibly suggesting a benefit of employment. Our findings also suggest that adults with DS in jobs with more complex interpersonal interactions may be able to maintain high cognitive functioning despite early AD-related changes (i.e., A $\beta$  accumulation); however, longitudinal research is needed to explore these possibilities.

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**Acknowledgement:** The research was funded by the National Institute of Aging (R01AG031110, U01AG051406; R01AG70028) and the National Institute on Child Health and Human Development (U54 HD090256).

