**Title**: Longitudinal investigation of gait and Alzheimer’s disease in adults with Down syndrome

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**Introduction**: Gait abnormalities are associated with AD in the general adult population (Pedersen et al., 2014; Sheridan & Hausdorff, 2007), but it is unclear if gait impairments are a feature of DSAD. To explore this relationship in the DS population, the specific study aims were to: 1) examine gait across 32 months in relation to baseline biomarkers of PET amyloid-beta (Aβ), neurofibrillary tangles of tau (NFT) PET, and MRI-hippocampal volume; 2) determine whether change in gait across 32 months is related to change in cognitive functioning; and 3) compare changes in gait across 32 months based on clinical AD status.

**Method**: Participants included 218 adults with DS (aged 25 to 72) who were part of the Alzheimer Biomarkers Consortium for Down Syndrome (ABC-DS; Handen et al., 2020). Participants and their study partner completed a multi-day visit at baseline and 32 month follow-up. The adults with DS underwent structural MRI (hippocampal volume) and PET (Aβ, NFT) scans and completed cognitive (DSMSE), memory (mCRT), and gait functioning (Tinetti) assessments. The Tinetti Gait assessment includes two 15 foot walks and is scored in 8 domains, with a maximum of 12 points. The study partner reported on the participant’s medical history and functioning, including any dementia symptoms (NTG). Clinical AD status of cognitively stable, mild cognitive impairment (MCI) or dementia was determined based on a case consensus conference involving a psychologist, physician, and at least two research staff who were blind to neuroimaging data. A series of residual change regression models examined the relation between neuroimaging, cognitive functioning, and clinical AD status with change in gait performance across the 32 months. Age, intellectual disability level, and medical history of seizures, cataracts, and bone health conditions were associated with baseline gait and included in models as covariates.

**Results**: Results indicated participants with dementia at 32 months had significantly lower gait scores than those who remained cognitively stable. Declines in cognitive ability on the DSMSE, mCRT, and informant-reported dementia symptoms (NTG) across the 32 months were associated with greater impairments in gait performance across that same period. Finally, higher baseline PET Aβ and NFT PET and lower MRI-hippocampal volume were associated with greater impairments in gait 32 months later.

**Discussion:** Findings suggest thatgait impairments are a key feature of DSAD and begin early in disease development. Thus, gait assessments should be part of early AD screenings with adults with DS. Identifying a broad array of observable functional declines that are part of early symptomatic AD is important for screening efforts, especially for adults with DS who may have limited verbal abilities. The Tinetti gait assessment may offer a quick, cost-effective, non-invasive screen for gait impairments that occur as part of AD symptomology in adults with DS.

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