Title: Sleep, Cognitive Functioning, and β-amyloid in Adults with Down Syndrome

Authors: Brianna Piro-Gambetti1, Iulia Mihaila2, Ben Handen3, Brad Christian1, Patrick Lao4, Karly Cody1, Dana Tudorascu1, Annie Cohen3, William Klunk3, and Sigan L. Hartley1

1University of Wisconsin-Madison; 2University of Illinois-Chicago; 3University of Pittsburgh Medical Center; 4Columbia University Medical Center

Introduction: Individuals with Down syndrome (DS) have an increased prevalence of sleep disorders. Sleep disorders such as obstructive sleep apnea and behavioral sleep disturbances are associated with executive functioning and memory difficulties (Breslin et al., 2014) and have been linked to Alzheimer’s disease (AD) in the general population (Chen et al., 2017). Individuals with DS have an increased risk for AD due to their third copy of chromosome 21, which contains the gene for the amyloid precursor protein. As a result, individuals with DS have an overproduction of brain β-amyloid. The extent to which sleep disruptions are linked to executive functioning and memory in adults with DS, and may be associated with variability in AD onset and trajectory in the DS population is not known. Our study aims were to: 1) determine the feasibility of collecting sleep data via actigraph accelerometers in adults with DS; 2) evaluate the reliability and validity of sleep data via actigraph accelerometers in adults with DS; 3) examine the association between sleep and executive functioning and memory and a biomarker of early AD (β-amyloid).

Methods: Participants were part of a larger ongoing Neurodegeneration in Aging Down Syndrome (NiAD) project. Thirty-nine adults with DS (aged 26-56 years) wore an actigraph accelerometer wristband continuously over a 7-night period. Approximately half were male (n = 20) and half were female (n = 19). Participants, together with caregivers, also completed a daily diary, reporting on the quality and quantity of their sleep. Actigraph variables of interest included: total sleep time (TST), wake after sleep onset (WASO), Sleep Fragmentation Index (SFI), and Number ofAwakenings (NOA). Prior to the daily diary, adults with DS were administered direct measures of executive functioning and memory, and underwent MRI and PET scans using the imaging agent [11C] Pittsburgh compound B (PiB) to assess β-amyloid in the neocortex.

Results: All adults with DS wore the actigraph for at least one night, and 77% of the adults with DS wore the actigraph for at least 6 nights (n = 30). Pearson correlations indicated significant associations between TST and self-reported hours of sleep (r = .64, p <.01) and SFI and self-reported hours of sleep (r = -.45, p = .01). There was a significant association between self-reported minutes awake and Digit Span Backwards (r = -.57, p = .01), and between NOA and Cat/Dog Switch (r = -.50, p = .01). There were trend level negative associations between self-reported hours of sleep and Story Recall (r = -.38, p = .06) and between WASO and Cat/Dog Switch (r = -.34, p = .08). These associations were maintained after controlling for chronological age and IQ. There were significant positive associations between PET β-amyloid and mean WASO (r = -.42, p = .02) and NOA (r = -.36, p = .05).

Discussion: Our findings suggest that actigraph accelerometers are a feasible way to assess sleep in adults with DS. Sleep data collected through the actigraph accelerometer was associated with caregiver/self-reported daily diary data in expected directions. Findings suggest that there may be important links between sleep, executive functioning and memory, and early AD neuropathology in adults with DS. This information is critical for informing intervention efforts for healthy aging.

References:

Acknowledgement:
R01AG031110, U01AG051406, P30HD03352, U54HD090256