preclinical women showed more stable Immediate Recall than men (beta=6.24, SE=.82, p<.0001), they were more likely to be in the Immediate Recall accelerated decline class (23.4% vs. 16.25%; female:male; Chi-square=36.29, p<.00001). On average, preclinical women and men did not differ in Delayed Recall trajectories (beta=.31, SE=.30, p=.28); however, preclinical women were more likely to be in the stable Delayed Recall class (11.04% vs. 6.5%; Chi-Square=19.19, p<.0001). Within the MCI group, 2-class models representing a stable decline group and an accelerated decline group provided optimal fit for both outcomes. Whereas, on average, MCI women showed more stable Immediate Recall than men (beta=3.55, SE=.79, p<.0001), they were more likely to be in the Immediate Recall accelerated decline class, although not significantly. Women and men did not differ, on average, in their Delayed Recall trajectories; however, women were significantly more likely to be in the Delayed Recall accelerated decline class (Chi-square=32.24, p<.0001).
Conclusions: Our findings indicate that sex is an important determinant of the variability observed in early-stage AD trajectories; however, sex differences varied by Immediate versus Delayed Recall likely due, in-part, to psychometric test properties. Our results suggest that, when looking at sex differences in AD trajectories on average, women's superior stability in verbal learning masks their higher likelihood of rapid decline. Our findings have implications for our ability to optimally diagnose and track disease progression in both sexes.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: dementia - Alzheimer's disease
Keyword 2: mild cognitive impairment
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Paper Session 02: Aging topics: section 1

9:00 - 10:30am
Thursday, 2nd February, 2023
Town & Country Ballroom D

Moderated by: Anna Egbert

1 Subjective Cognitive Concerns, Neuropsychological Test Performances, and Frontoparietal Thickness and Connectivity in High-Functioning Older Adults

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Objective: Neuropsychologists have difficulty detecting cognitive decline in high-functioning older adults, in whom substantially greater neurological change may need to occur before performance on cognitive tests are low enough to indicate cognitive impairment. For high-functioning older adults, subjective cognitive concerns (SCC) may indicate decline that is not detected by the presence of low cognitive test scores but may be related to the absence of high scores and the presence of latent neurological changes. We hypothesized that high-functioning older adults with SCC would have fewer high scores than those without concerns, but a comparable number of low scores. These findings would indicate that objective decline has occurred but would not be detected by a traditional focus on low scores. We also hypothesized that SCC would be associated with lower frontoparietal network volume, thickness, and connectivity, indicating latent neurological change underlying subjective cognitive concerns.
Participants and Methods: Participants from an imaging sub-study of an ongoing longitudinal aging study were selected if they had high estimated premorbid functioning, defined as either (a) estimated intelligence ≥75th percentile on the North American Adult Reading Test (n=48) or (b) having a college degree (n=62). This resulted in 68 participants subdivided based on SCC, defined as one or more self-reported SCC on the Medical Outcomes Study Cognitive Functioning Scale (MOS-Cog). Participants with SCC (n=35; 73.9 years-old, SD=9.6, range: 60-95; 62.9% female; 94.3% White) and without SCC (n=33; 71.0 years-old, SD=7.2, range: 61-85, 75.8% female; 100% White) completed a neuropsychological test

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battery of memory and executive functions, including the Rey Auditory Verbal Learning Test, Trail Making Test Parts A and B, Controlled Oral Word Association Test, Digit Span, and Letter-Number Sequencing, and underwent structural MRI. MR images were analyzed for frontoparietal network volume, thickness, and connectivity.
Results: Participants with and without SCC were compared on the number of low test scores (i.e., at or below the 16th percentile) and high test scores (i.e., at or above the 75th percentile), finding a comparable number of low scores, t=1.66, p=.103, d=.40, but a lower number of high scores among participants with SCC, t=2.95, p=.004, d=.71. Participants with SCC had lower bilateral mean frontoparietal network volumes (left: t=2.98, p=.004, d=.74; right: t=2.63, p=.011, d=.66) and cortical thickness (left: t=2.65, p=.010, d=.66; right: t=2.18, p=.033, d=.54), but did not differ from those without SCC in terms of network connectivity.
Conclusions: SCC have been reported as a potential risk factor for dementia in older adults. High-functioning older adults with SCC presented with fewer high scores than those without SCC but had a comparable number of low scores. Among high-functioning older adults, subjective cognitive decline may correspond with objective cognitive change not detected by the traditional emphasis on low scores, but rather the absence of high scores. SCC were also related to underlying changes in the volume and thickness of the frontoparietal network, but not connectivity. In high-functioning older adults, subjective cognitive decline may correspond with a reduction from high average functioning in some domains and underlying neurological changes.

Categories: Aging
Keyword 1: aging disorders
Keyword 2: neuropsychological assessment
Keyword 3: neuroimaging: structural
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2 Cognitive Heterogeneity and Risk of Progression in Data-Driven Subtle Cognitive Decline Phenotypes

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Objective: There is increasing recognition of cognitive and pathological heterogeneity in early-stage Alzheimer's disease and other dementias. Data-driven approaches have demonstrated cognitive heterogeneity in those with mild cognitive impairment (MCI), but few studies have examined this heterogeneity and its association with progression to MCI/dementia in cognitively unimpaired (CU) older adults. We identified cluster-derived subgroups of CU participants based on comprehensive neuropsychological data and compared baseline characteristics and rates of progression to MCI/dementia or a Dementia Rating Scale (DRS) of ≤129 across subgroups.
Participants and Methods: A hierarchical cluster analysis was conducted using 11 baseline neuropsychological test scores from 365 CU participants in the UCSD Shiley-Marcos Alzheimer's Disease Research Center (age M=71.93 years, SD=7.51; 55.9% women; 15.6% Hispanic/Latino/a/x/e). A discriminate function analysis was then conducted to test whether the individual neuropsychological scores predicted cluster-group membership. Cox regressions examined the risk of progression to consensus diagnosis of MCI or dementia, or to DRS score ≤129, by cluster group.
Results: Cluster analysis identified 5 groups: All-Average (n=139), Low-Visuospatial (n=46), Low-Executive (n=51), Low-Memory/Language (n=83), and Low-All Domains (n=46). The discriminant function analysis using the neuropsychological measures to predict group membership into these 5 clusters correctly classified 85.2% of the participants. Subgroups had unique demographic and clinical characteristics. Relative to the All-Average group, the Low-Visuospatial (hazard ratio [HR] 2.39, 95% CI [1.03, 5.56], p=.044), Low-Memory/Language (HR 4.37, 95% CI [2.24,

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