

## ABSTRACT

Sex/Gender Differences in Serial Position Profiles in Patients with Mild Cognitive Impairment and Healthy Controls  
by

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**Introduction:** Alzheimer's disease disproportionately affects more women, but paradoxically, men have a higher incidence of Mild Cognitive Impairment (MCI). Researchers have suggested that women's verbal memory advantage across the lifespan reflects better premorbid skills, which then require more neurodegeneration to manifest early clinical impairment. To date, measurement of sex differences in verbal memory have used total list scores. We proposed that a granular examination of serial position effects (SPE) in list-learning can refine the source of sex/gender differences.

**Methods:** A cross-sectional analysis of participants with Mild Cognitive Impairment (MCI) and Healthy Controls (HC) was examined from the Alzheimer's Disease Neuroimaging Initiative-1 dataset. We first determined whether there were robust sex/gender differences in serial position profiles (Aim 1). Second, we examined whether there were significant neuroanatomical correlates to these sex-specific SPE profiles, particularly focused on hippocampal integrity and prefrontal integrity (Aim 2). Multiple linear regression analyses were stratified by diagnosis (HC and MCI) and conducted for each brain region (prefrontal brain integrity and hippocampal integrity) to determine Sex/gender by brain region interactions at each SPE position (Primacy, Middle, Recency) and Time Point (Learning, Short Delay, Long Delay). All analyses covaried for Age, Education, and *APOE-ε4* carrier status.

**Results:** Sex/gender differences in learning and recall were localized to better recall of Middle and Recency items in HC women, and better recall of Primacy and Middle items in women with MCI. Interestingly, for these serial positions, sex/gender did not significantly interact with hippocampal integrity across HCs and patients with MCI. Rather, women with MCI demonstrated a significant association of dorsolateral prefrontal cortex volume ratio with Middle item recall, such that with more volume, women performed better at this position across all Time Points.

**Conclusion:** Our findings support our hypothesis that the sex-specific verbal memory advantage for women manifests for Primacy and Middle items, possibly through engagement of deep semantic processing. Furthermore, at early stages of cognitive decline (MCI), women demonstrate a reliance on brain regions other than hippocampus, possibly reflecting an alternate organization of verbal information, and thus a different list learning strategy.