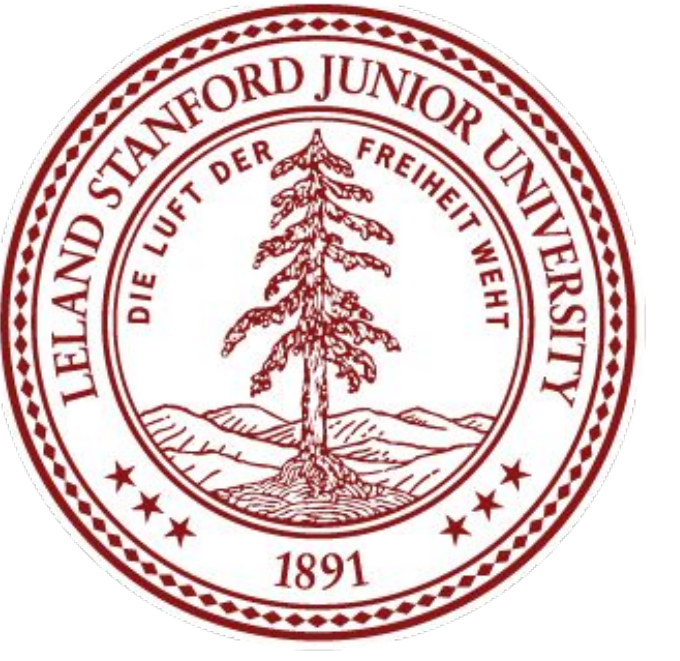


Sex Differences in Alzheimer's Disease Plasma Biomarkers, Neuroimaging, and Cognition in Down Syndrome

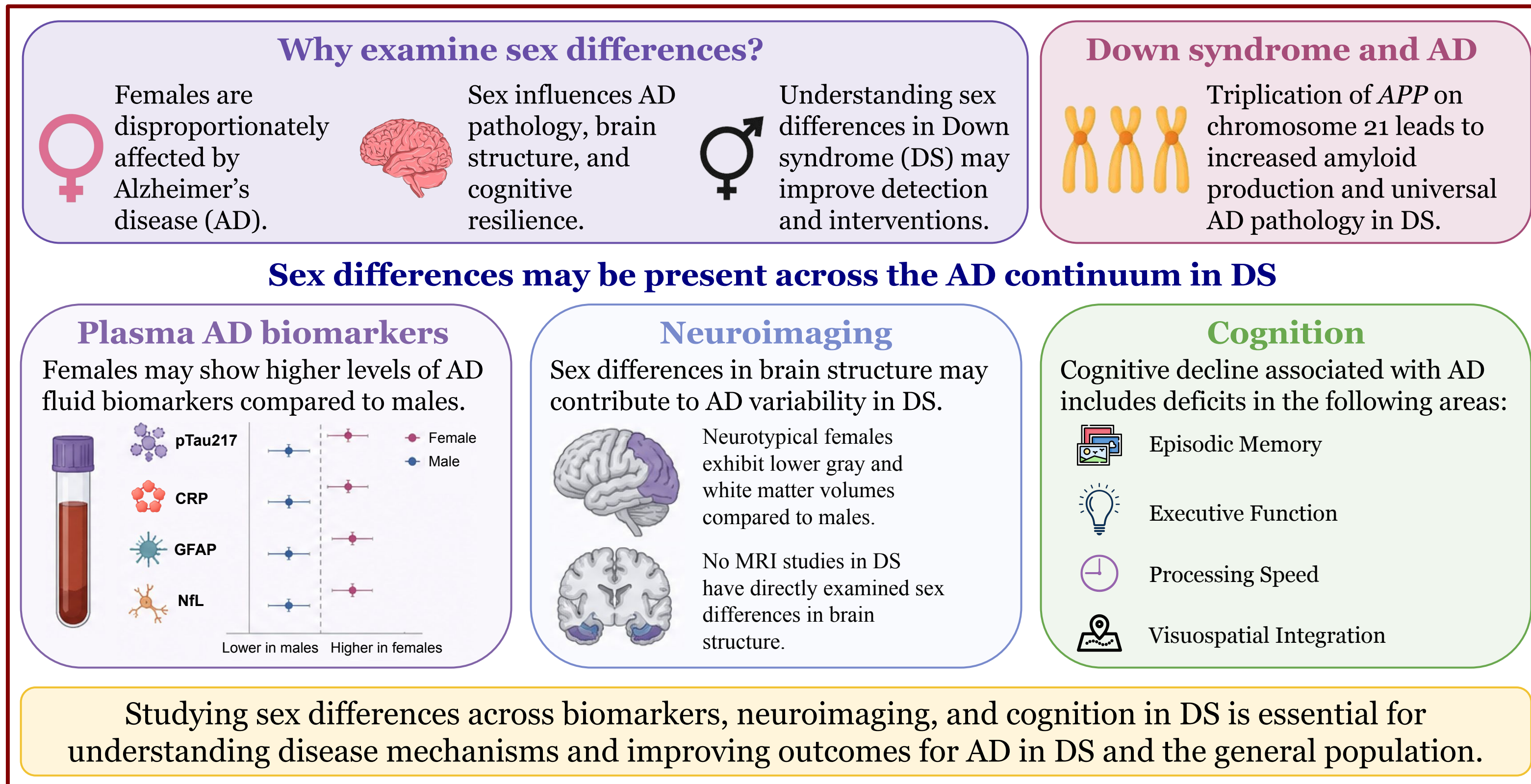
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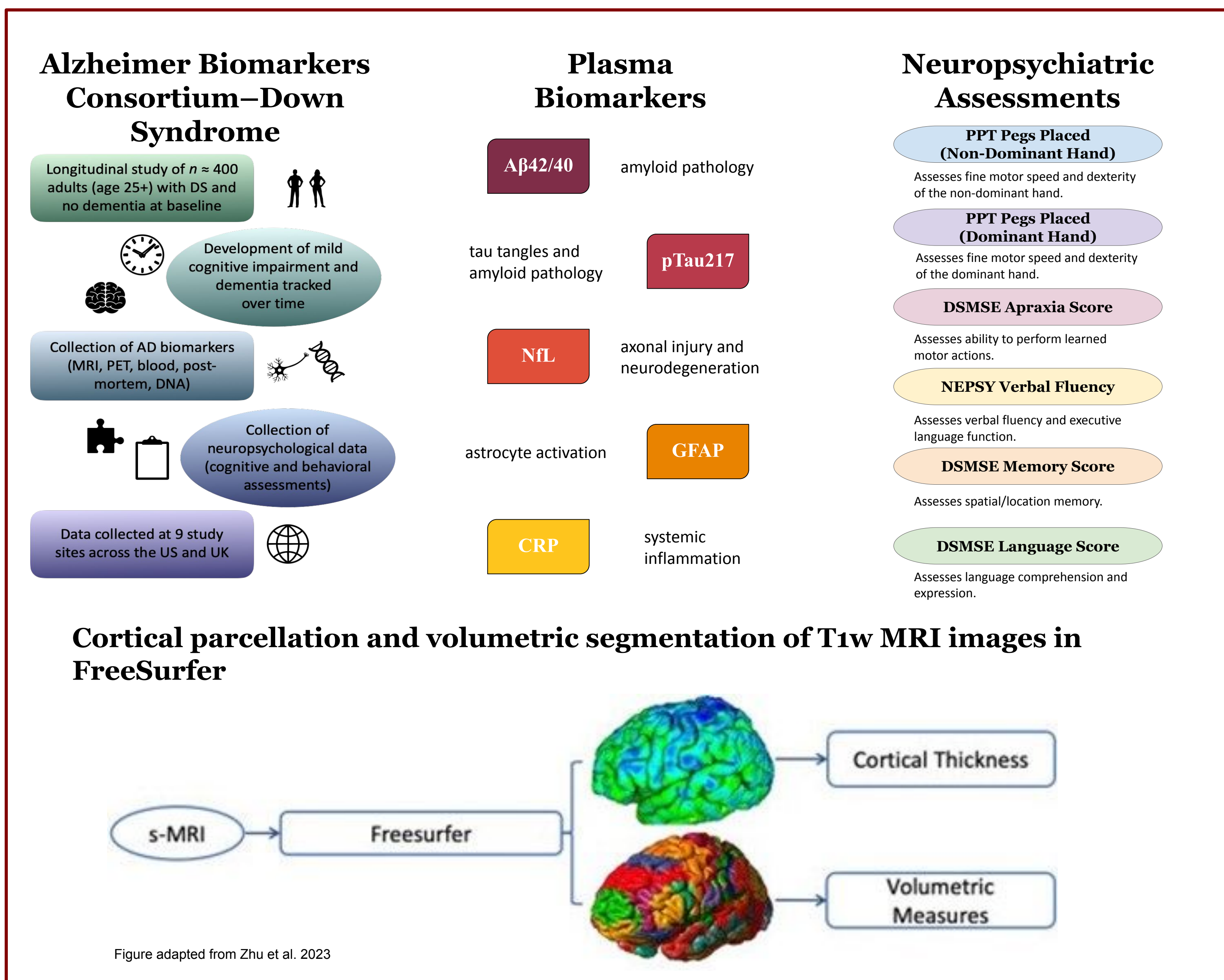
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Introduction



Methods



References

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- Zhu X, Kim Y, Ravid O, et al. Neuroimaging-based classification of PTSD using data-driven computational approaches: A multisite big data study from the ENIGMA-PGC PTSD consortium. *Neuroimage*. 2023;283:120412. doi:10.1016/j.neuroimage.2023.120412

Results

Brain structural measures differ significantly based on diagnosis group and sex.

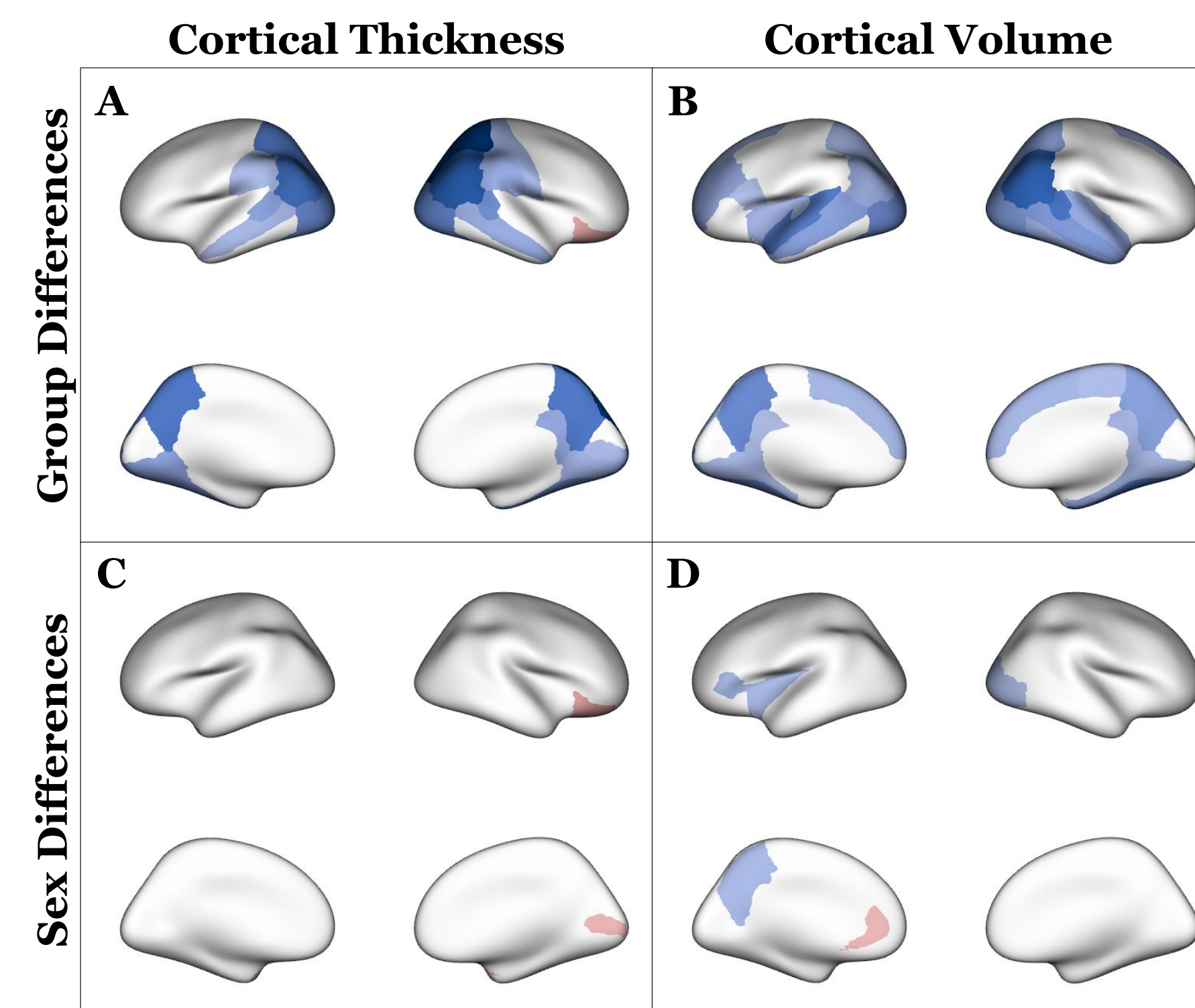


Figure 1. Differences in structural measures are shown between cognitively stable DS participants and MCI/dementia participants in (A) and (B), and between cognitively stable males and females with DS in (C) and (D) ($p < .05$). In (A) and (B), blue regions represent areas with higher values for the cognitively stable DS group; in panels (C) and (D), blue regions represent areas with higher values for males. Analyses (A) and (B) controlled for sex, age, and site; (C) and (D) for age and site.

NfL, GFAP, and CRP are significantly elevated in females with DS.

	Male	Female	β	SE	t	p
Aβ42/40			-0.001	0.001	-0.81	0.417
N	146	134				
Mean (SD)	0.036 (0.010)	0.036 (0.007)				
pTau217			-0.022	0.14	-0.15	0.878
N	43	35				
Mean (SD)	-1.083 (0.641)	-0.924 (0.802)				
NfL			0.151	0.07	2.16	0.032
N	105	105				
Mean (SD)	2.236 (0.555)	2.443 (0.611)				
GFAP			0.109	0.053	2.06	0.041
N	137	131				
Mean (SD)	5.098 (0.588)	5.199 (0.571)				
CRP			0.65	0.213	3.06	0.003
N	66	73				
Mean (SD)	15.058 (1.126)	15.783 (1.320)				

Table 1. Blood-based biomarkers by sex. Analyses controlled for age and study site.

Cognition significantly varies between males and females with DS.

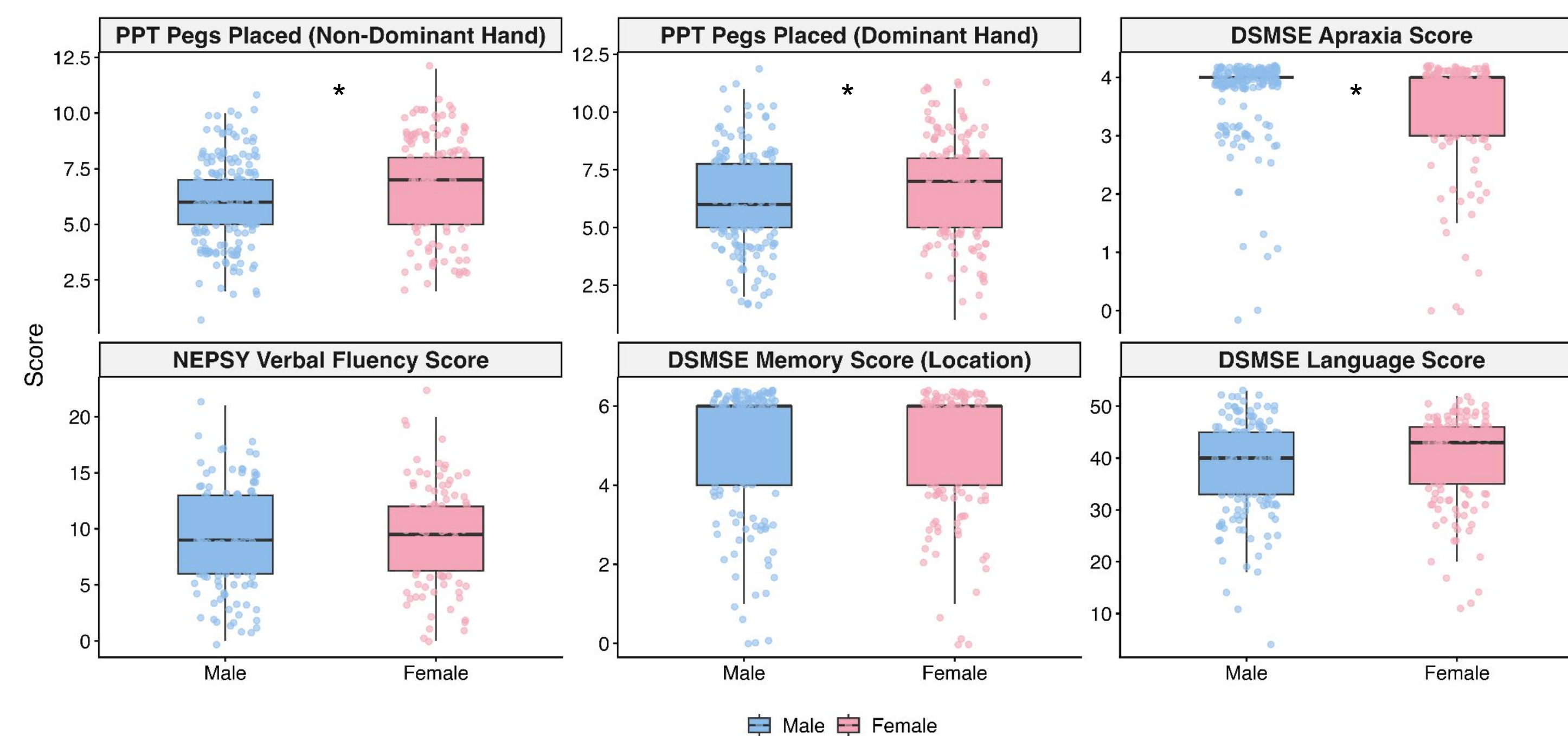


Figure 2. Differences in cognitive scores are shown between cognitively stable males and females with DS. Analyses controlled for age and study site. * $p < .05$. PPT = Purdue Peg Board. DSMSE = Down Syndrome Mental Status Examination.

Conclusions, Limitations, & Future Directions

- Sex differences in plasma biomarkers, cortical brain structure, and selected cognitive domains were identified among cognitively stable adults with Down syndrome, supporting the presence of sex-specific neurobiological variation prior to Alzheimer's disease dementia.
- The cross-sectional design limits inference regarding the temporal progression of sex-specific changes, and smaller sample sizes for select plasma biomarkers may have reduced statistical power.
- Future work will incorporate longitudinal analyses to determine how sex influences trajectories of biomarker change, cortical atrophy, and cognitive decline, and further investigate the biological mechanisms underlying sex-specific differences in Alzheimer's disease pathology.