

Glial Fibrillary Acidic Protein And Ptau181 As Biomarkers Of Visuospatial And Visuomotor Ability In Down Syndrome

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Background

- Down syndrome (Trisomy 21) may function as a model to understand biological factors affecting aging and cognitive decline given the high incidence of Alzheimer's disease (AD) in individuals with Down syndrome (DS).¹
 - By age 40, over 90% of individuals with DS have brain changes related to AD.
 - Identifying biomarkers linked to cognitive functioning in this group may help clarify mechanisms of decline and inform earlier detection, monitoring, and intervention efforts.
 - Patients with DS are qualified for treatment trials for AD, classified as AD stage 0.
- GFAP and pTau181 are promising plasma biomarkers of AD-related pathophysiology in DS, with GFAP reflecting astrocytic activation/neuroinflammation and pTau181 reflecting amyloid and tau-related disease processes.²
- Examining GFAP and pTau181 together may clarify whether these biomarkers show broad or domain-specific relationships with visuospatial and visuomotor performance in DS.

Methods

- We examined the association between plasma GFAP and pTau181 levels and cognitive ability using baseline cognitive assessment data from ABC-DS.
- Participants included 336 adults with Down syndrome spanning cognitively stable, MCI, and dementia classifications.
- MCI/dementia participants showed higher plasma GFAP and pTau181 levels than cognitively stable participants with DS.
- Hierarchical linear regressions tested whether biomarker levels predicted visuospatial and visuomotor performance after controlling for age, sex, and APOE-4 status.
 - Cognitive outcomes included visuospatial construction, visuomotor integration, sequential processing and motor planning.
- Analyses were repeated within cognitively stable adults to examine whether biomarker associations were present prior to overt clinical impairment.

Data Set

Alzheimer's Biomarker Consortium-Down Syndrome:

Longitudinal study of $n = 400$ adults (age 25+) with DS and no dementia at baseline



Development of mild cognitive impairment and dementia tracked over time



Collection of AD biomarkers (MRI, PET, blood, post-mortem, DNA)



Collection of neuropsychological data (cognitive and behavioral assessments)

Data collected at 9 study sites across the US and UK



Results

Plasma Biomarkers and Visuospatial/Visuomotor Performance in Down Syndrome (* p<0.01, p<0.05)

Biomarker	Outcome	β -coefficient	p-value (β)	R ² change	F(range)=value
GFAP	Visuospatial Construction (Haxby Block Design)	-0.388	<.001	.085	F(4,304) = 21.00
GFAP	Visuomotor Integration (Beery VMI)	-0.348	<.001	.069	F(4,303) = 19.17
GFAP	Sequential Processing and Motor Planning (RADD Hand Movements)	-0.360	<.001	.097	F(4,150) = 10.89
pTau181	Visuospatial Construction (Haxby Block Design)	-0.142	0.028	.013	F(4,331) = 14.94
pTau181	Visuomotor Integration (Beery VMI)	-0.144	.025	.013	F(4,330) = 13.59

Key Findings:

- Across the full DS sample, higher GFAP was associated with poorer performance on Haxby Block Design, Beery VMI, and RADD Hand Movement.
- Higher pTau181 was associated with poorer Haxby Block Design and Beery VMI performance, but was not significantly associated with RADD Hand Movement.
- In analyses restricted to cognitively stable adults with Down syndrome, higher GFAP remained significantly associated with poorer Block Design performance ($p = .002$).
- Models adjusted for age at visit, sex/gender, and APOE $\epsilon 4$ status. pTau181 Block Design coefficient is scaled per 1,000 units for readability. RADD = Rapid Assessment for Developmental Disabilities.

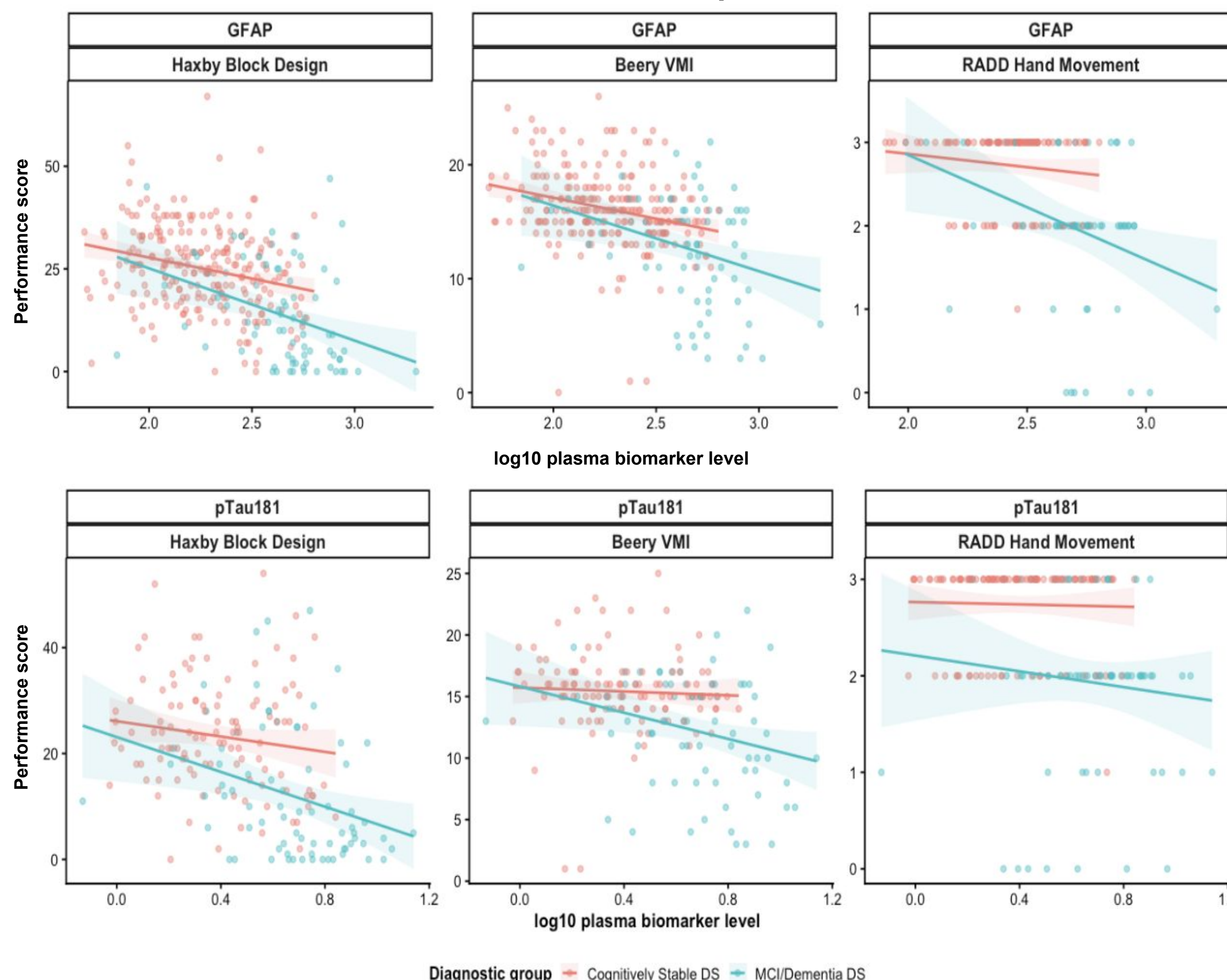
Conclusions

- Together, these findings suggest that GFAP may capture broader cognition-motor vulnerability across clinical stages, whereas pTau181 may show more selective associations with visuospatial construction and visual-motor integration.
- GFAP showed broad associations across visuospatial construction, visuomotor integration, sequential processing and motor planning, suggesting that astrocytic activation may relate to cognition-motor vulnerability across clinical stages.
- pTau181 showed more selective associations with visuospatial construction and visuomotor integration, but not sequential processing and motor planning, suggesting possible domain-specific biomarker effects.
- In cognitively stable adults, GFAP remained significantly associated with poorer performance on visuospatial construction tasks, suggesting that GFAP may capture early visuospatial vulnerability prior to overt clinical impairment.
- Future longitudinal research should examine whether GFAP and pTau181 predict cognitive and functional decline over time in adults with Down syndrome.

References

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Plasma Biomarker Associations with Visuospatial and Visuomotor Performance



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