

Visual MRI Atrophy Scales and Amyloid, Tau, and Neurodegeneration Biomarkers in Down Syndrome

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INTRODUCTION

- Down syndrome (DS) is considered a genetically determined form of Alzheimer’s disease (DSAD)
- Visual rating scales of brain atrophy (VAS) are a low-cost metric used in clinical neuroradiology
- Relationship of VAS and *in vivo* biomarkers in DSAD remains incompletely understood.
- We aimed to investigate the association between commonly used VAS and biomarkers in the aging process of individuals with DS**

METHODS

- Two-center retrospective study including adults with DS and non-DS controls from early adulthood underwent 3T brain MRI, and biomarkers assessment with PET and CSF
- Amyloid positivity was defined as an Aβ42/40 ratio <0.062 or visually by [11C]PiB-PET
- CSF biomarkers included phosphorylated tau (pTau-181), total tau (tTau), and NfL
- MRI VAS used were:
 - medial temporal atrophy (**MTA**), entorhinal cortex atrophy (**ERICA**), posterior cortical atrophy (Koedam), and global cortical atrophy (**GCA**), with maximum hemispheric scores used for analysis.
- Group comparisons were performed, followed by multivariable logistic regression models adjusted and Spearman correlation

RESULTS

- N = 235 Down Syndrome (DS) individuals/ 130 non-DS controls.**
- DS →** substantially higher prevalence of amyloid positivity (42.3% vs 4.6%, p<0.001); significantly higher CSF pTau-181, total tau, and NfL levels.
 - MTA ≥1.5 was significantly more frequent in DS, whereas other VAS did not differ significantly between groups (Table 1).**
 - In multivariable analyses (Fig 1), all VAS were independently associated with amyloid positivity.
 - MTA was associated with amyloid positivity (OR 2.8; p<0.001); ERICA showed the strongest associations with amyloid (OR 5.3, p<0.001), followed closely by Koedam (OR 4.8).
 - CSF biomarkers (Fig 2) →** all VAS correlated significantly with levels of NfL, p-Tau 181, and t-Tau (p<0.001). Koedam had a robust association with NfL (p=0.51), and with p-Tau 181 (p=0.43). Correlations with t-Tau were generally more modest across all scales, with MTA and Koedam showing similar performance (p=0.39).

	Down syndrome (n = 235)	Non-DS (n=130)	p-value
Age (Years)	49 (19-73)	58 (22-89)	0.003
Gender			< 0.001
Male	143 (60.9%)	41 (31.5%)	
Female	92 (39.1%)	89 (68.5%)	
Nationality			< 0.001
Spanish	201 (85.5%)	88 (67.7%)	
Brazilian	34 (14.5%)	42 (32.3%)	
Amyloid positive	99 (42.3%)	6 (4.6%)	< 0.001
Age groups			
≥ 40yo	179 (76.2%)	106 (81.5%)	0.235
≥ 45yo	153 (65.1%)	99 (76.2%)	0.029
MTA ≥ 1.5	70 (29.8%)	5 (3.8%)	< 0.001
ERICA ≥ 1.5	13 (5.5%)	1 (0.8%)	0.023
Koedam ≥ 1.5	32 (13.6%)	11 (8.5%)	0.143
GCA ≥ 1.5	20 (8.5%)	5 (3.8%)	0.091
CSF Aβ 42/40 ratio	0.063 (0,041)	0.103 (0,014)	<0,001
CSF pTAU-181 (pg/mL)	47.60 (87,5)	32.3 (14.5)	0.005
CSF tTAU (ng/mL)	367 (445)	239 (101)	<0,001
CSF nFL (pg/mL)	507.6 (540.2)	396.5 (243.1)	<0,001

Table 1. Demographic characteristics, age distribution, cerebrospinal fluid (CSF) biomarkers, amyloid and tau status, and frequency of pathological visual atrophy scores in individuals with Down syndrome (DS) and non-DS controls

CONCLUSION

- Visual atrophy scales demonstrate complementary and stage-dependent associations with amyloid deposition, tau pathology, and neurodegeneration in DS
- MTA and ERICA were closely linked to amyloid pathology
- Koedam and GCA showed stronger associations with neurodegenerative burden

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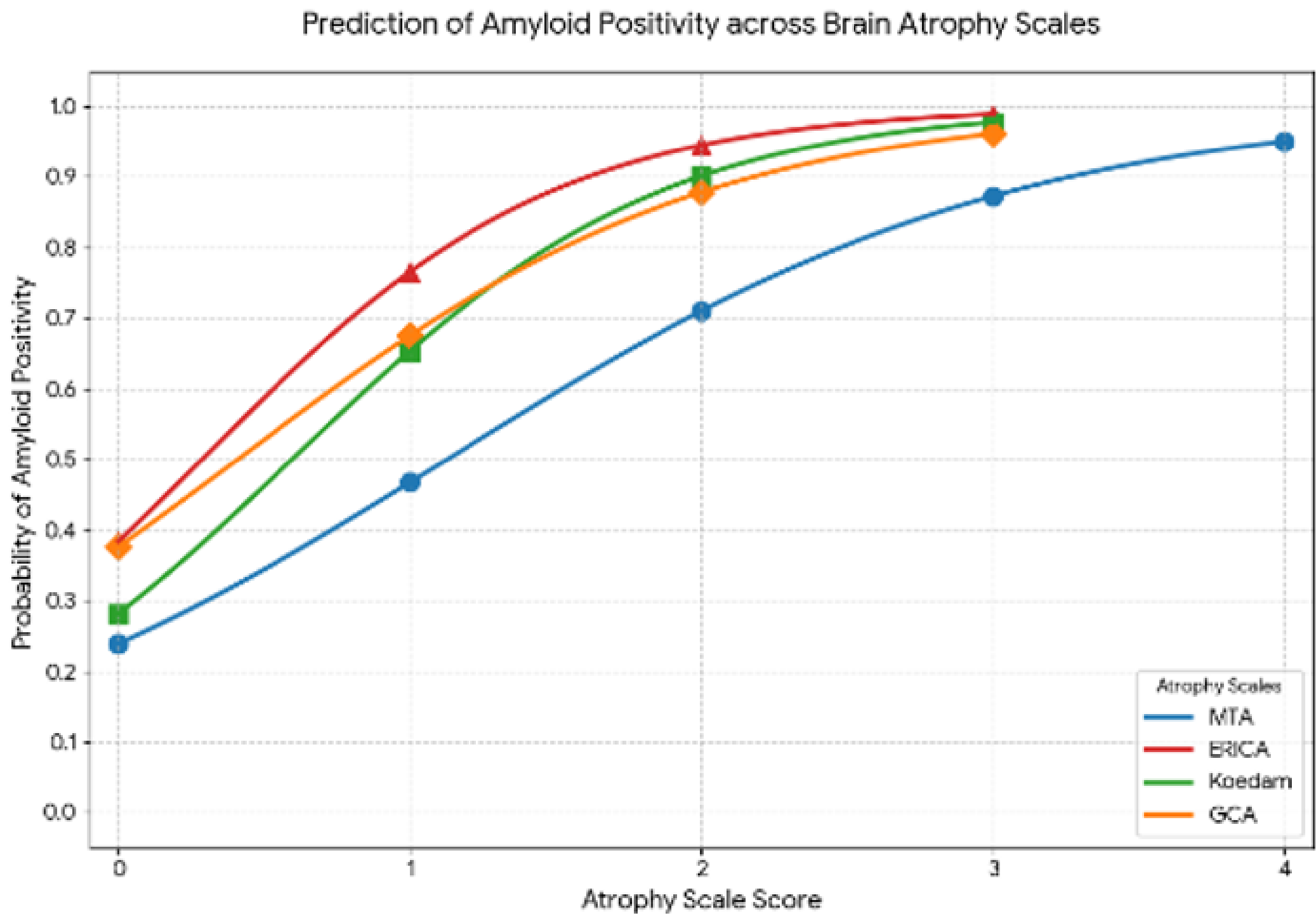


Figure 1. Logistic regression models for amyloid positivity. Curves demonstrate the predicted probability of biomarker positivity across atrophy scores. ERICA showed the highest odds ratios (OR=5.3; all p < 0.001).

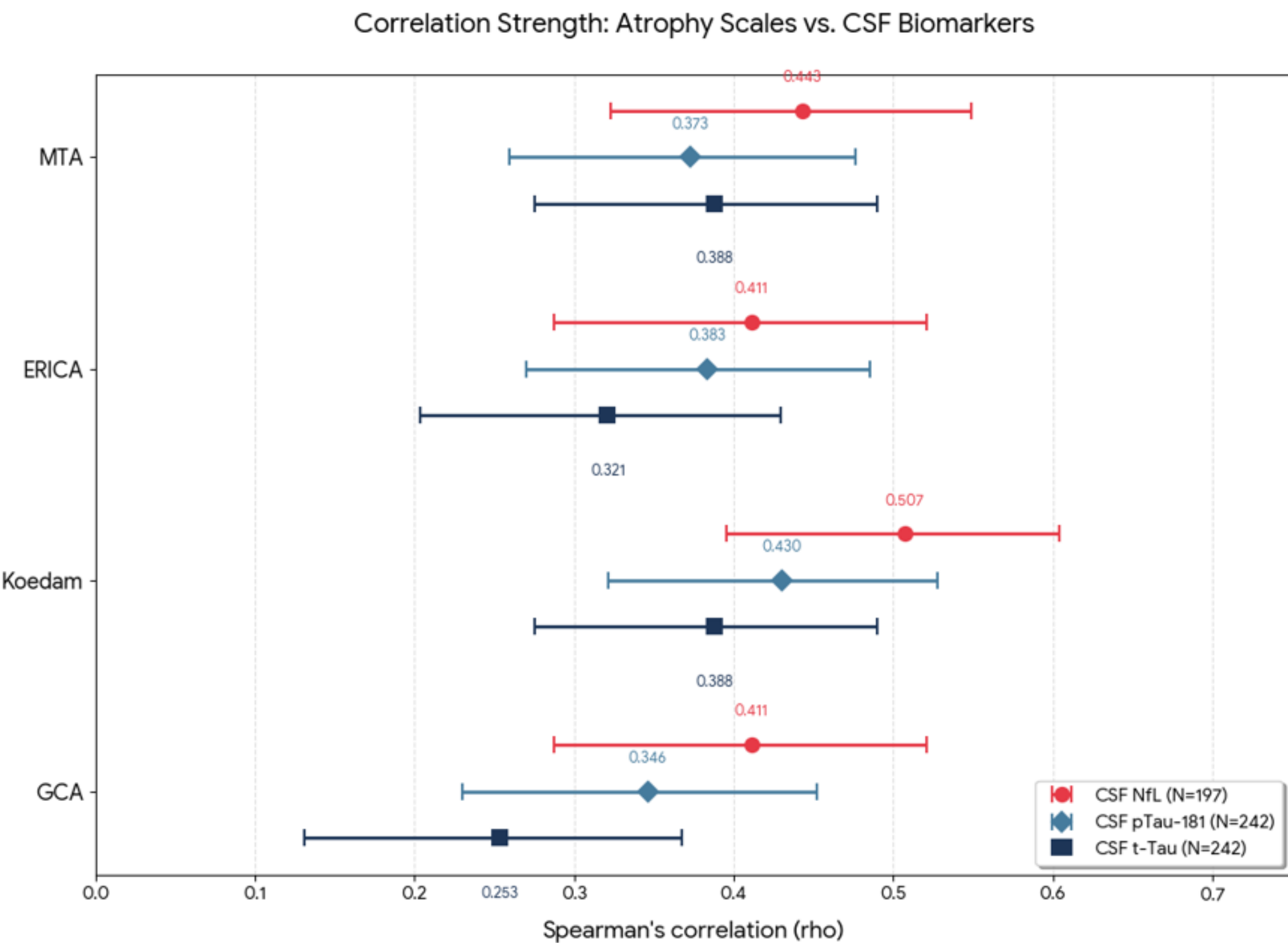


Figure 2. Spearman correlations between atrophy scales and CSF biomarkers (NfL, pTau-181, t-Tau). Points represent p coefficients; error bars indicate 95% CI. Red: NfL (N=197); Light Blue: pTau-181 (N=242); Dark Blue: t-Tau (N=242). All correlations were significant (p < 0.001). The Koedam scale consistently showed the highest correlation across all biomarkers, particularly with NfL (p = 0.51).