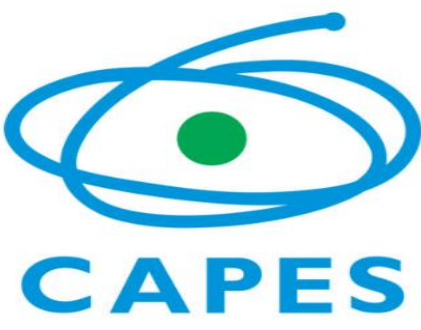


Gait and Balance as Clinically Accessible Functional Biomarkers of Cognitive Status in Adults with Down Syndrome

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This cross-sectional study demonstrates an association between functional performance, assessed using the Performance-Oriented Mobility Assessment (POMA), and cognitive status in adults with Down syndrome (DS), supporting the potential of gait and balance as clinically accessible functional biomarkers of cognitive impairment.

INTRODUCTION

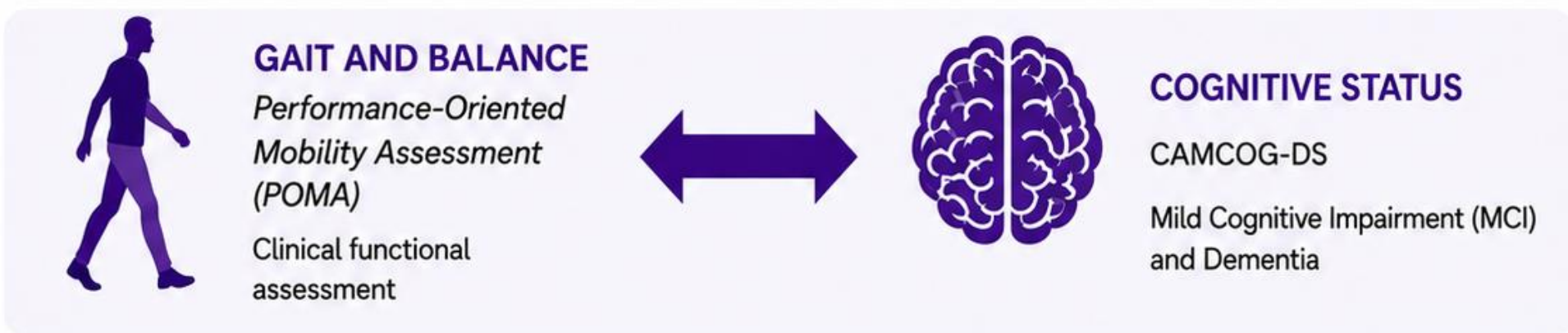
Adults with Down syndrome (DS) are at high risk for Alzheimer's disease (AD) due to APP gene overexpression and accelerated cerebral β -amyloid accumulation¹. Gait and balance impairments have emerged as potential functional biomarkers of neurodegeneration^{2,3}; however, their association with cognitive performance³ and AD biomarkers in DS remains poorly understood. This study investigated these associations using the Performance-Oriented Mobility Assessment (POMA)⁵, CAMCOG-DS Total⁶ and PET-PiB⁷.

OBJECTIVE

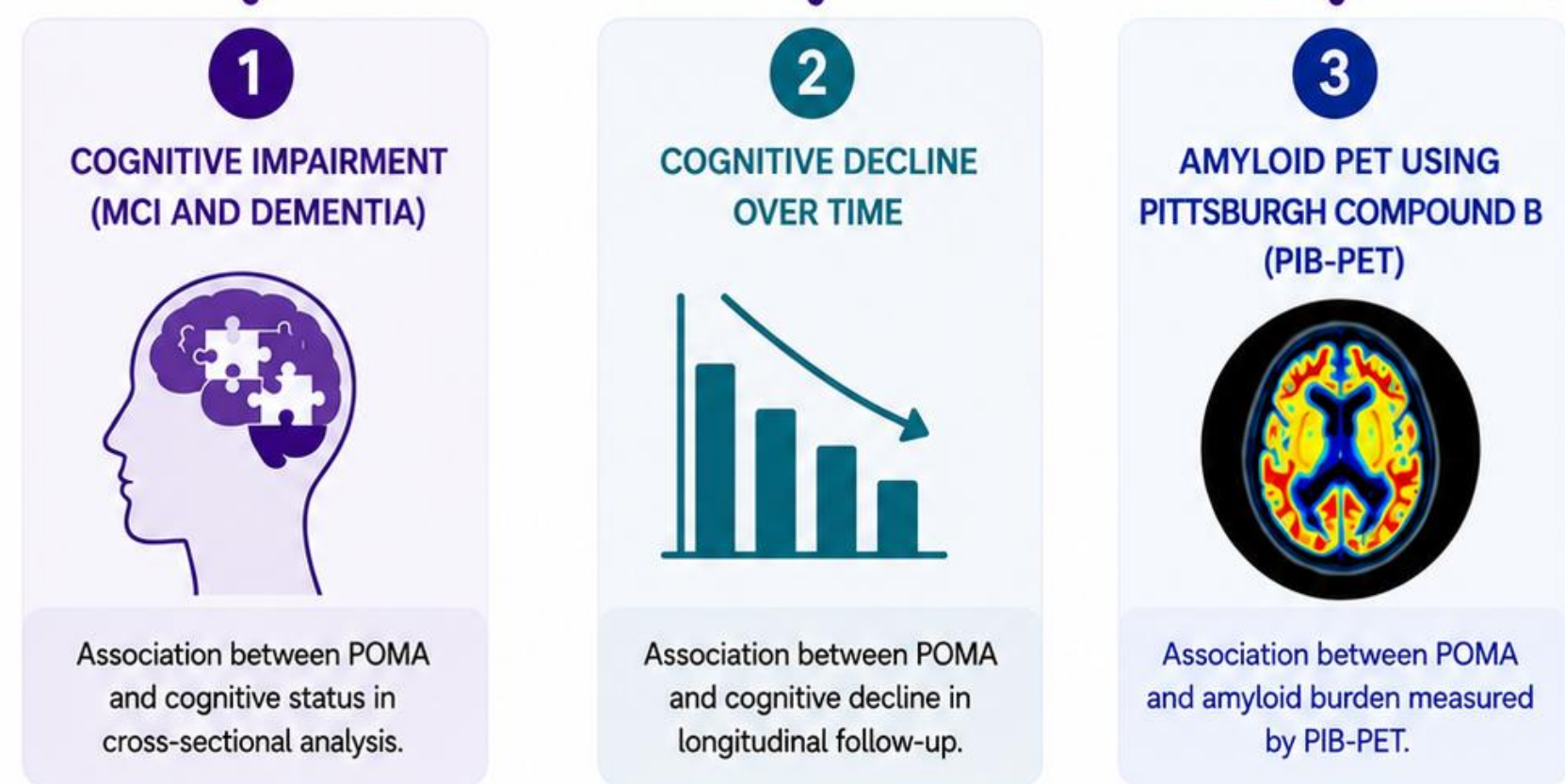
PRIMARY OBJECTIVE



To evaluate whether gait and balance impairments, measured by the *Performance-Oriented Mobility Assessment (POMA)*, are associated with cognitive and biological markers of Alzheimer's disease in adults with Down syndrome.



KEY COMPONENTS OF THE PRIMARY OBJECTIVE



COHORT OF ADULTS WITH DOWN SYNDROME
Cross-sectional sample: N = 135
Longitudinal sample: N = 42



This cross-sectional investigative study aims to identify associations between functional performance (gait and balance), cognitive status, and Alzheimer's disease biomarkers, contributing to the early identification of individuals at higher risk.

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All authors involved in this study declare no conflict of interest
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METHODS

METHODS — ASSESSMENTS

Cognition	CAMCOG-DS
Gait	Performance-Oriented Mobility Assessment (POMA)
Anthropometry	Body Mass Index (BMI)
Diagnosis	Multidisciplinary consensus diagnosis
Neuroimaging biomarkers	Amyloid PET using Pittsburgh Compound B (PET-PiB)

STATISTICAL ANALYSIS

- Descriptive analysis:** Continuous variables: mean $\pm$ SD or median (IQR). Categorical variables: frequency (%).
- Association analyses:** Pearson or Spearman correlation coefficients to assess associations between POMA and cognitive domains, and between POMA and biomarkers.
- Regression modeling:** Multivariable logistic regression to examine the association between POMA performance and MCI/dementia. Models adjusted for age, sex, and intellectual disability level.
- Statistical significance:** Two-tailed analyses with significance level set at $p < 0.05$.

RESULTS

Table 1. Baseline demographic and clinical characteristics

Characteristic	Value
Participants, n	135
Age (years), mean $\pm$ SD	37.7 $\pm$ 11.5
Male sex, n (%)	74 (54.8)
Body mass index (kg/m ²), mean $\pm$ SD	28.97 $\pm$ 5.85
BMI classification	
Normal weight	13 (27.1)
Overweight	16 (33.3)
Obesity	19 (39.6)
Clinical diagnosis	
Cognitively stable	80 (74.8)
Mild cognitive impairment	10 (9.3)
Dementia	17 (15.9)
Intellectual disability level	
Mild	41 (48.8)
Moderate	37 (44.0)
Severe	6 (7.1)

Abbreviations: BMI, body mass index; SD, standard deviation; MCI, mild cognitive impairment.

Table 2. Association between POMA performance and cognitive impairment at baseline

POMA	Cognitively Stable n (%)	MCI/Dementia n (%)	Adjusted OR (95% CI)	p-value
Total score (mean $\pm$ SD)	21.1 $\pm$ 5.4	17.0 $\pm$ 6.7	0.89 (0.82-0.97)	0.005
Low fall risk	26 (89.7)	3 (10.3)	Reference	—
Moderate fall risk	30 (78.9)	8 (21.1)	2.24 (0.54-9.40)	0.268
High fall risk	23 (63.9)	13 (36.1)	4.71 (1.19-18.67)	0.027

Footnote. Odds ratios were obtained from multivariable logistic regression adjusted for age, sex, body mass index, and level of intellectual disability.

Figure 1. Frequency of observed cognitive and functional decline during follow-up

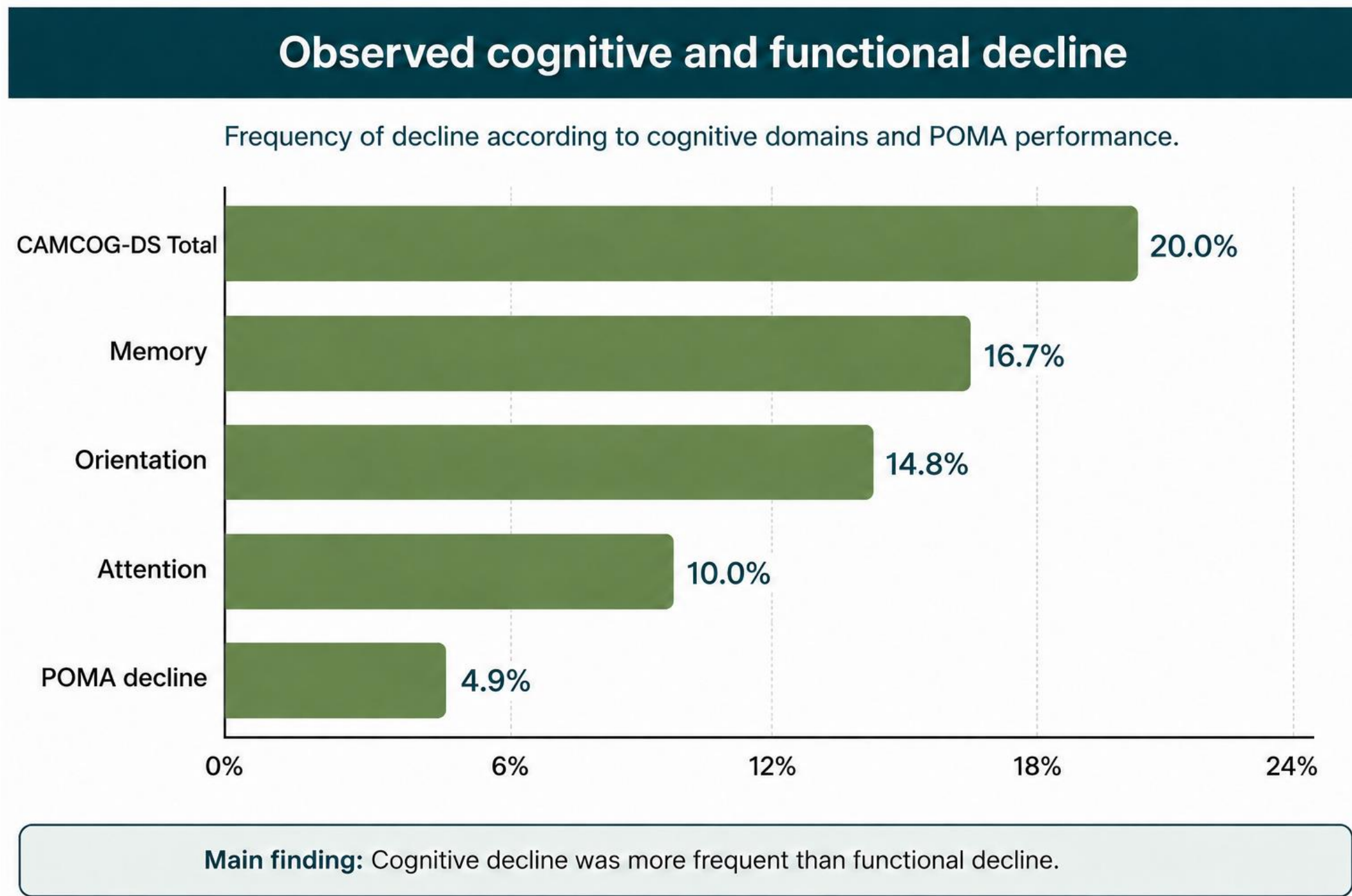


Figure 2. Multivariable Regression Analysis of Amyloid PET Positivity

Variable	Coefficient (β)	Standard Error (SE)	p-value
Intercept	-4,090	1,105	0,001
POMA – moderate risk (ref: high risk)	0,628	0,596	0,308
Age (years)	0,092	0,024	<0,001

Only age was significantly associated with amyloid PET positivity after adjustment for sex and POMA risk category.

CONCLUSIONS

Gait and balance performance, assessed using the POMA, was associated with cognitive status in adults with DS, supporting its potential as a clinically accessible functional biomarker of cognitive status. Cognitive decline was more frequent than functional decline during follow-up. Functional performance was not associated with cerebral amyloid PiB-PET, whereas age was independently associated with greater amyloid burden, as expected. Larger longitudinal studies are needed to determine whether gait and balance alterations predict cognitive decline and AD progression in adults with DS.