Online keyboard tapping as a digital biomarker for frontotemporal dementia (FTD)

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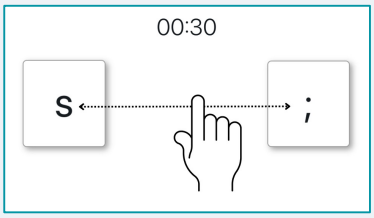
Background

Frontotemporal dementia (FTD) is primarily characterised by behavioural or language impairments but shows notable clinical and genetic overlap with amyotrophic lateral sclerosis (ALS) and parkinsonism, including shared genetic causes such as the *C9orf72* repeat expansion. There remains a need for early and objective markers of FTD, which has led to the development of digital investigations for frequent and precise assessment.

Methods



BRAIN Tap Test
Outcome Measures

- Kinesia score (KS; number of taps)
- Akinesia time (AT; mean dwell time)
- Incoordination score (IS; variance in travelling time)
- Slope (change in velocity)

All computed as the mean across both hands.

The online BRadykinesia Akinesia INcoordination (BRAIN) Tap Test, originally developed for Parkinson's disease, involves alternate tapping between two keys of a computer keyboard for 30 seconds. The test was completed by 269 participants whose motor function, cognition, behaviour, language, and neuropsychiatric symptoms were assessed using the CDR® plus NACC FTLD-NM scale (0=normal, 0.5=minimally impaired, and ≥0.5=impaired). Participants included healthy controls (HC; n=157), asymptomatic (n=23) and prodromal (n=54) genetic carriers, and people with symptomatic behavioural variant FTD (bvFTD, n=19) and ALS (n=16). The aim was to investigate whether the BRAIN Tap Test could be used across the FTD-ALS spectrum to detect early changes in motor function by assessing its associations with established metrics including plasma neurofilament light chain (NfL) levels and CDR plus NACC FTLD-NM, and using ROC analysis to assess discriminative ability between groups.

	0	0.5	bvFTD	ALS	Total
HC	0	0	0	0	157
Familial	0	0	0	0	96
C9orf72	13	32	5	6	56
MAPT	4	13	7	0	24
GRN	6	8	0	0	14
SOD1	0	0	0	1	1
TBK1	0	1	0	0	1
Sporadic	0	0	7	9	16
Total	23	54	19	16	112

Table 1: Study population.

Results

Correlations with Plasma NfL and Sum of Boxes (SOB)

The mean KS ($p = 0.0011$) and AT ($p = 0.0136$) significantly correlated with plasma NfL levels (n=85). Three of the four BRAIN Tap Test metrics significantly correlated with the CDR plus NACC FTLD-NM SOB, a measure of clinical severity (KS $p < 0.0001$; AT $p < 0.0001$; IS $p = 0.0160$).

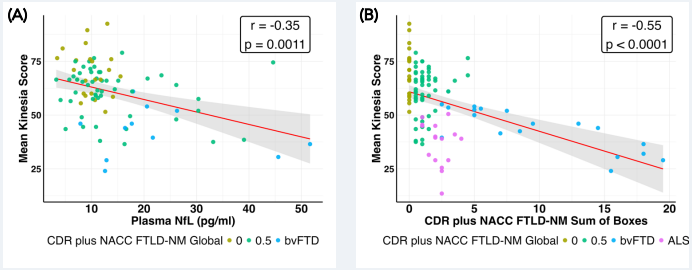


Figure 1: Mean KS correlates with **(A)** plasma NfL levels and **(B)** the Sum of Boxes (SOB) score calculated using the CDR plus NACC FTLD-NM scale.

Results

Kinesia Score ROC Curves

ROC analysis showed excellent discrimination for HC vs. bvFTD (AUC = 0.92) and HC vs. ALS (AUC = 0.97), while discrimination for HC vs. prodromal genetic carriers was modest (AUC = 0.69).

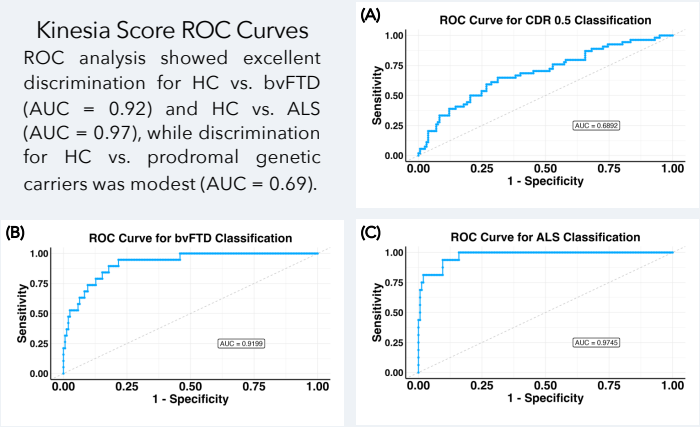


Figure 2: ROC curves for mean KS discriminating HC from **(A)** prodromal genetic carriers with CDR plus NACC FTLD-NM Global score of 0.5, **(B)** bvFTD, and **(C)** ALS.

CDR plus NACC FTLD-NM Global Analysis

After adjustment for age, sex, and education, both mean KS and AT significantly differentiated HC from symptomatic individuals with bvFTD (KS $p < 0.001$; AT $p < 0.001$) and ALS (KS $p < 0.001$; AT $p = 0.001$). The mean IS differentiated between HC and ALS only (IS $p = 0.028$).

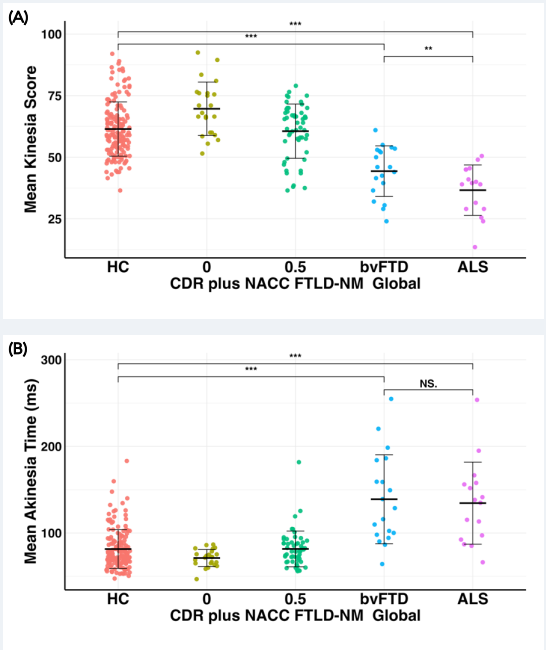


Figure 3: (A) Mean KS and **(B)** AT differentiate HC from symptomatic individuals with bvFTD and ALS.

Conclusion

The BRAIN Tap Test, particularly its KS and AT metrics, shows promise as a sensitive, digital tool to detect motor changes in both bvFTD and ALS. It demonstrated significant correlations with other physiological and clinical markers, including plasma NfL levels and the CDR plus NACC FTLD-NM SOB. These findings align with observed upper limb motor deficits across the FTD-ALS spectrum and underline the value of monitoring motor function in bvFTD.

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