

The Ignite computerised assessment: comparing sensitivity of outcome measures for cognitive tests in frontotemporal dementia.

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BACKGROUND

Traditional neuropsychological tests have demonstrated insufficient sensitivity in detecting early cognitive changes in frontotemporal dementia (FTD). Consequently, digital biomarkers such as the iPad-based Ignite cognitive app, have emerged to enhance the early detection of impairments. While Ignite presents as a promising alternative, its efficacy relies on the ability of its outcome measures to capture these subtle changes. This study evaluated the sensitivity of outcome measures for two Ignite tests of processing speed and executive function: Colour Mix (Levels 1-4) and Path Finder (Levels 1- 2), which are digital adaptations of the Stroop task (Levels 1-4) and Trail Making Test (parts A and B), respectively.

METHODS

This study employed a data-driven approach to assess the diagnostic utility of the Colour Mix and Path Finder tests for detecting cognitive decline in FTD. A cross-sectional analysis was conducted on 236 participants from the GENetic Frontotemporal Dementia Initiative (GENFI) study, including 85 mutation-negative controls and 151 mutation carriers. The carriers were categorised into CDR+NACC-FTLD stages: 0=asymptomatic (n=71), 0.5=prodromal (n=63), and ≥1=fully symptomatic (n=17), see Table 1. All participants completed the Ignite app, alongside standardised clinical assessments, during their annual GENFI visit.

Table 1. Participant Demographics

	Non-carriers (n=85)	Mutation carriers (n=151)			
		ALL (n=151)	CDR=0 (n=71)	CDR=0.5 (n=63)	CDR≥1 (n=17)
Male	37 (44%)	64 (42%)	31 (44%)	23 (37%)	10 (59%)
Age	48.8 (12.7)	46.8 (12.8)	42.9 (12.4)	47.5 (11.9)	60.6 (6.13)
Education	15.4 (3.24)	15.0 (4.11)	14.9 (4.52)	15.7 (3.72)	13.3 (3.14)
% of total carriers	-	-	46%	41%	11%

Validated outcome measures of the Stroop and Trail Making Tasks were identified from the literature and modified to fit the Ignite test protocol. The study classified outcomes as direct (derived from a single task level) or contrast (derived from multiple task levels), see Table 2.

Table 2. Outcome Measures for Path Finder and Colour Mix Ignite tasks

Task and Outcome Measure		Formula/Description	
Path Finder	DIRECT	Completion time (L1-2) Prorated (L2) Efficiency (L2)	The total time taken to complete the trial. $PF-pr = \text{Completion time} / \text{no. of completed circles} \times 19$ $PF-e = (\text{Total time}/(\text{correct number of moves} - \text{errors made}) + \text{correct moves completed})$
	CONTRAST	Difference (PF-d) Ratio (PF-r)	$PF-d = L2 \text{ completion time} - L1 \text{ completion time}$ $PF-r = L2 \text{ completion time} / L1 \text{ completion time}$
	DIRECT	Speed-accuracy trade-off (SAT) (L1-4) Average reaction time (RT) (L1-4)	$SAT = \text{total correct} / \text{average RT}$ RT is summed up and then divided by the number of completed trials.
	CONTRAST	Accuracy (L1-4) Difference (CM-d) Ratio (CM-r)	The total number of correct trials completed $CM-d = \text{average RT in L3} - \text{average RT in L1}$ $CM-r = \text{average RT in L3} / \text{average RT in L1}$ $CM-GI = CW - [(W \times C) / (W + C)]$
Colour Mix		Golden's Interference (CM-GI)	Where: GI = Golden's interference score; CW = total number of items named in Level 3 (60 seconds); Total number of items named in 30 seconds for: W = Level 1 and C = Level 2

A receiver operating characteristic (ROC) curve with area under the curve (AUC) analysis was performed to assess the diagnostic ability of various outcome measures in distinguishing non-carrier controls from FTD mutation carriers at different disease stages. Bootstrapped logistic regression models, adjusted for age, were conducted for each outcome measure. The primary analysis compared non-carriers with both prodromal and symptomatic carriers, while the secondary analysis compared non-carriers to only symptomatic carriers.

RESULTS

ROC curve regression analyses with AUC and 95% bias-corrected confidence intervals (CI) were generated (see Table 3). When comparing CDR≥0.5 with non-carriers, AUC values for Path Finder outcomes ranged from 0.54 to 0.72, with the highest predictive ability shown by completion times for Level 1 (AUC = 0.72) and Level 2 (AUC = 0.71), as well as the PF-pr outcome (AUC = 0.70). In the Colour Mix task, AUC values ranged from 0.53 to 0.69, with the highest predictive ability shown by the level 4 SAT score, Level 3 average RT score, CM-GI score, and Level 4 accuracy (all AUC = 0.69). The most predictive outcome measures are displayed in Figure 1 (A and C).

Table 3. ROC curve analysis of each outcome measure for comparing mutation carrier groups against controls

Outcome Measure		Control versus CDR≥0.5		Control versus CDR≥1	
		AUC	95% CI BC	AUC	95% CI BC
Path Finder	Completion Time L1	0.72	[0.63, 0.79]	0.91	[0.76, 1.00]
	Completion Time L2	0.71	[0.62, 0.79]	0.90	[0.78, 0.99]
	Prorated L2	0.70	[0.62, 0.77]	0.91	[0.79, 0.99]
	Efficiency L2	0.56	[0.57, 0.75]	0.91	[0.75, 1.00]
	Difference	0.60	[0.52, 0.69]	0.76	[0.60, 0.92]
Colour Mix	Ratio	0.54	[0.44, 0.62]	0.79	[0.69, 0.87]
	SAT L1	0.65	[0.56, 0.73]	0.87	[0.73, 0.96]
	SAT L2	0.66	[0.58, 0.74]	0.86	[0.72, 0.96]
	SAT L3	0.68	[0.58, 0.76]	0.86	[0.69, 0.97]
	SAT L4	0.69	[0.60, 0.77]	0.89	[0.81, 0.96]
	Average RT L1	0.66	[0.57, 0.74]	0.86	[0.70, 0.97]
	Average RT L2	0.66	[0.57, 0.74]	0.86	[0.69, 0.98]
	Average RT L3	0.69	[0.60, 0.78]	0.84	[0.64, 0.96]
	Average RT L4	0.66	[0.58, 0.74]	0.79	[0.60, 0.93]
	Accuracy L1	0.65	[0.56, 0.74]	0.86	[0.72, 0.96]
	Accuracy L2	0.67	[0.58, 0.75]	0.86	[0.72, 0.96]
	Accuracy L3	0.69	[0.59, 0.77]	0.85	[0.66, 0.97]
	Accuracy L4	0.69	[0.61, 0.78]	0.91	[0.82, 0.97]
	Difference	0.53	[0.45, 0.63]	0.75	[0.61, 0.86]
	Ratio	0.55	[0.46, 0.63]	0.64	[0.46, 0.81]
	CM-GI	0.69	[0.60, 0.76]	0.84	[0.66, 0.98]

For discriminating symptomatic FTD only (CDR≥1), all Path Finder outcome measures had AUC values >0.75, with completion time, PF-pr, and PF-e showing AUCs over 0.90. In the Colour Mix tasks, the CM-GI score showed an AUC of 0.84, while direct measures ranged from 0.79 to 0.91. The outcomes with the greatest discriminative ability in the primary analysis are displayed for symptomatic FTD participants in Figure 1 (B and D).

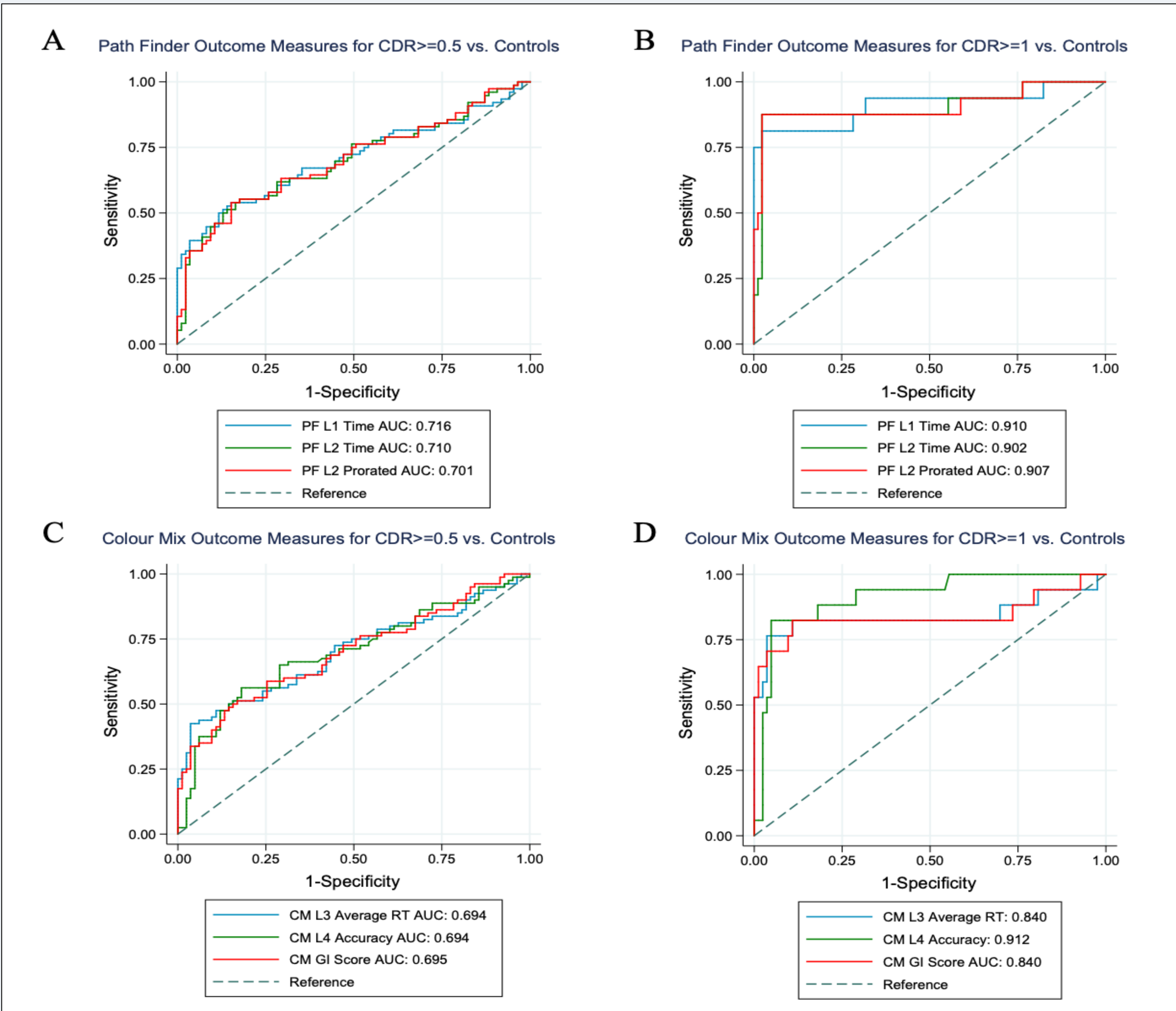


Figure 1(A-D). Diagnostic performance of the selected outcomes measures with the greatest AUC for the Path Finder and Colour Mix tasks at different disease stages of FTD.

CONCLUSION

ROC analyses highlighted the most sensitive measures for detecting FTD-related cognitive impairment. For Path Finder, these were completion times and PF-pr; for Colour Mix, Level 4 SAT and accuracy, Level 3 average RT, and the CM-GI measure. The predictive power notably increased when comparing symptomatic FTD individuals with controls. Overall, direct measures derived from a single test condition outperformed contrast measures from multiple conditions, though substantial overlap was observed. This study supports the use of Colour Mix and Path Finder tests in detecting cognitive dysfunction in presymptomatic FTD mutation carriers, validating Ignite as a robust outcome measure for clinical trials.

Acknowledgements: We thank the research participants for their contribution to the study. RSC and JDR acknowledge the support of the Rosetrees Trust and the National Brain Appeal. This work was also supported by the MRC UK GENFI grant (MR/M023664/1), the Bluefield Project, and the JPND GENFI-PROX grant (2019-02248). Please see GENFI website (www.genfi.org) for further acknowledgements.

