Ignite – a novel computerized cognitive assessment battery for frontotemporal dementia

Convery RS[1], Goldsmith S[1], Nicholas JM[2], Moore KM[1], Russell LR[1], Rohrer JD[1]

[1]Dementia Research Centre, UCL Queen Square Institute of Neurology, London, UK; [2]London School of Hygiene and Tropical Medicine, London, UK

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Background

There are currently no curative treatments for frontotemporal dementia (FTD), and early detection in the presymptomatic phase may guide interventions to slow disease progression. Computerised cognitive testing provides an opportunity to overcome the lack of sensitivity in current pen and paper psychology tests. Ignite is a novel tablet-based battery, designed for more sensitive detection of cognitive impairment in FTD. Ignite includes 12 different tests measuring aspects of executive function and social cognition, as well as other cognitive domains, in 25 minutes or less.

Methods

Ignite has been tested in a clinically normal cohort (N=2,004) aged 20-80 to generate a normative database. Outcome measures of speed (average reaction time), accuracy (total number of correct trials), and a combined speed-accuracy trade-off (SAT) score (accuracy/speed) were generated for each test. Spearman correlations were used to compare demographic variables and Ignite outcome measures. To generate a normative calculator, estimated Z-scores were calculated for all tests based on multiple linear regressions that adjusted for the demographic predictors of age, sex, and years in education. Percentile ranks were calculated from the normal distribution of each Z-score. Test-retest reliability and concurrent validity were also investigated through Intraclass (ICC's) and Spearman correlations, respectively, in a separate group of healthy controls (N=100).
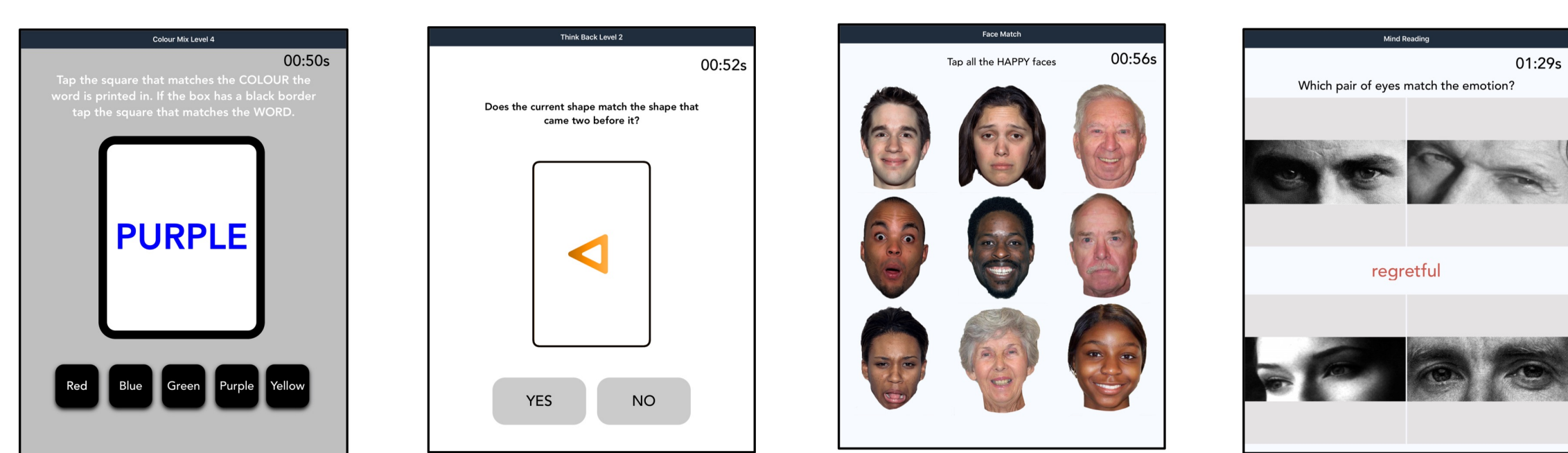

Figure 1. Ignite tests from left to right: Colour Mix (Stroop task), Think Back (N-back task), Face Match (Simple Emotion Processing) and Mind Reading (Reading the Mind in the Eyes)

Ignite was subsequently administered in a group of at-risk participants from the Genetic FTD Initiative (GENFI) study. Analysis has been performed in an initial subset of executive function and social cognition tasks (Figure 1) in a cohort of 48 mutation carriers and 20 non-carriers. Linear regression models were used to investigate differences in performance between carriers and non-carriers on the Ignite tests. To compare performance between GENFI participants and the normative sample, raw Ignite scores were entered into the normative calculator and age-, sex- and education-adjusted normative values were calculated for carriers and non-carriers.
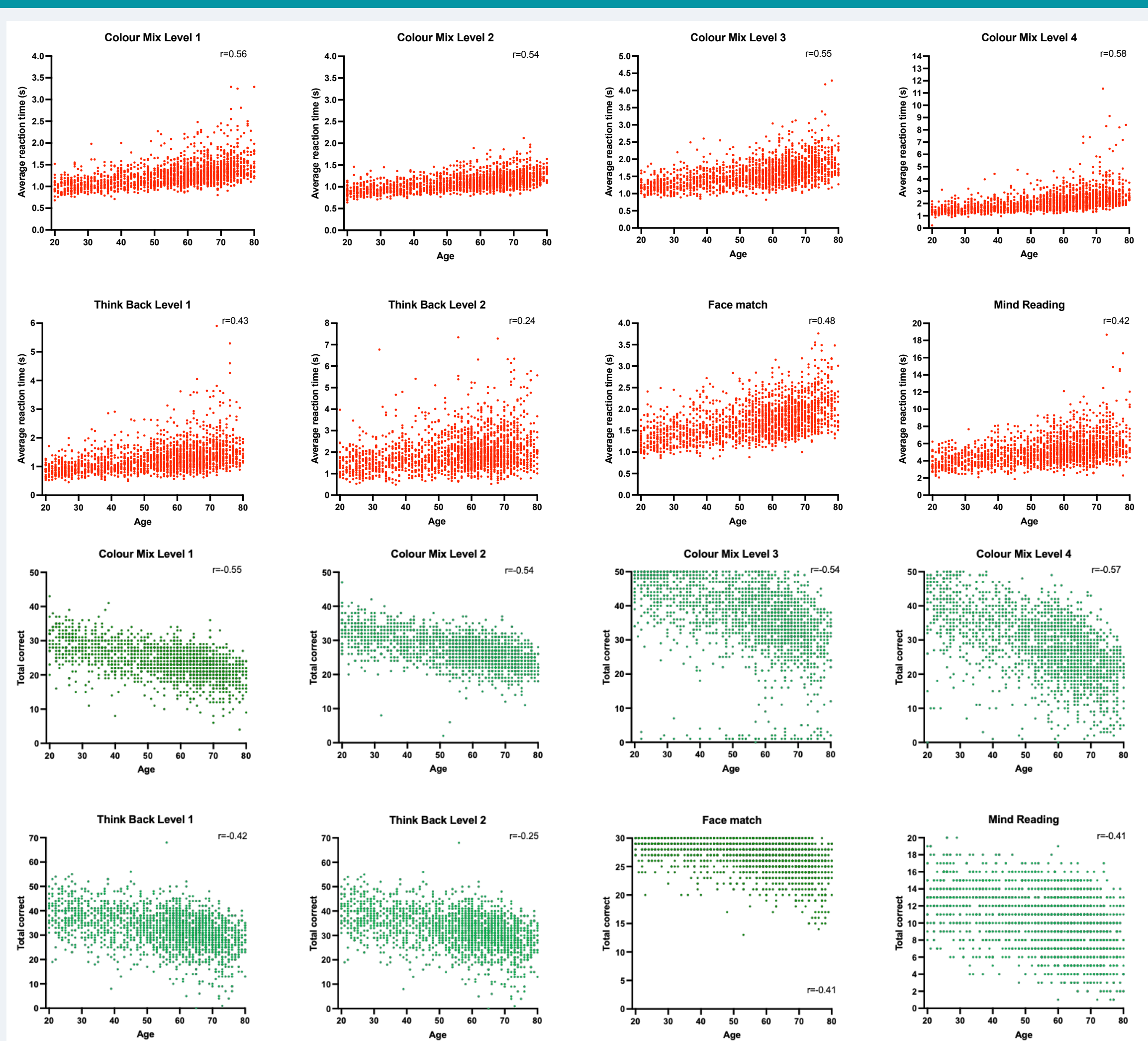
Results

Figure 2. Scatterplots of average reaction time (top two rows) and total number of correct items (bottom two rows) with age in the normative sample. r=Spearman Rho coefficient.

Results *continued*

Validation data

The Ignite tests were shown to be sensitive to expected age-, sex-, and education-related effects in the normative population. Performance was impacted by age across all the Ignite tests, with an age-related decline observed for speed (r=0.24 to 0.58, p<0.001) as shown by an increase in the average reaction times, and for accuracy (r=-0.25 to -0.57, p<0.001) demonstrated by a decrease in the total number of correct items; see Figure 1. Ignite tests also displayed moderate to excellent test-retest reliability when administered at two timepoints one week apart (ICC's=0.62 to 0.90) and showed significant correlations with corresponding traditional tests (r=0.29 to 0.75, p<0.01).

Carriers vs. Non-carriers

Demographic characteristics of the GENFI participants are shown in Table 1. Carriers scored lower, on average, than non-carriers on all the Ignite tests (Table 2). Linear regressions showed a significant difference in performance on the Mind Reading task of social cognition, with carriers achieving fewer correct items (M=11.0, SD=3.11) than non-carriers (M=12.6, SD= 2.99, p=0.03), and having a significantly lower speed-accuracy trade-off (SAT) score (carriers: M=2.40, SD=1.08; non-carriers: M=3.05, SD=1.20, p=0.02). No other significant differences were observed at the group level.

	N	Sex (% Male)	Age	Education
Non- carriers	20	55.0	45.5 (10.4)	15.7 (4.46)
Carriers	48	43.7	42.6 (9.60)	16.3 (3.71)

Table 1. GENFI participant demographics, unless specified values denote means (standard deviations).

Percentile scores

For individual scores, more presymptomatic mutation carriers scored below the 5th percentile compared to non-carriers, particularly for SAT scores. The greatest impairment was seen on the Face Match task (measuring social cognition), with 22.9% of carriers scoring in the bottom 5th percentile, compared to 0% of controls. A greater proportion of carriers also performed worse on complex executive function tasks, including Colour Mix Level 4 (inhibition/set-shifting) and Think Back Level 2 (working memory), with 18.8% and 16.7% scoring in the bottom 5th percentile of the population on these tests respectively (compared to 0% of controls).

Ignite test	Outcome measure	Carriers – means (SD)	Non-carriers-means (SD)	p-value	95% CI's	Carriers (% below 5th percentile)	Non-carriers (% below 5th percentile)
Colour Mix Level 1	Total correct	24.5 (5.1)	25.0 (3.4)	0.59	-2.62 - 1.48	12.5	0.0
	Average RT (s)	1.26 (0.3)	1.19 (0.2)	0.21	-0.04 - 0.2	10.4	0.0
	SAT score	21.2 (7.8)	21.7 (5.7)	0.77	-3.84 - 2.85	14.6	0.0
Colour Mix Level 2	Total correct	27.5 (4.6)	27.9 (3.6)	0.69	-2.01 - 1.22	12.5	10.0
	Average RT (s)	1.10 (0.2)	1.06 (0.2)	0.37	-0.04 - 0.12	10.4	10.0
	SAT score	26.6 (8.2)	27.0 (6.5)	0.79	-3.43 - 2.6	12.5	0.0
Colour Mix Level 3	Total correct	39.4 (8.8)	42.6 (5.7)	0.09	-6.75 - 0.43	2.1	0.0
	Average RT (s)	1.50 (0.2)	1.40 (0.2)	0.11	-0.02 - 0.23	8.3	5.0
	SAT score	28.5 (11.2)	31.5 (8.1)	0.21	-7.57 - 1.65	10.4	0.0
Colour Mix Level 4	Total correct	29.9 (10.6)	31.5 (9.1)	0.58	-5.64 - 3.16	18.8	0.0
	Average RT (s)	2.05 (0.8)	1.78 (0.4)	0.07	-0.02 - 0.55	12.5	5.0
	SAT score	17.6 (9.9)	18.8 (8.4)	0.58	-5.64 - 3.16	18.8	0.0
Think Back Level 1	Total correct	31.3 (8.9)	31.3 (7.1)	1.00	-3.87 - 3.86	20.8	15.0
	Average RT (s)	1.35 (0.2)	1.34 (0.5)	0.96	-0.24 - 0.25	14.6	10.0
	SAT score	26.9 (14.6)	28.4 (13.1)	0.67	-5.51 - 8.58	16.7	10.0
Think Back Level 2	Total correct	18.9 (7.3)	22.2 (7.2)	0.07	-6.74 - 0.3	18.8	5.0
	Average RT (s)	2.39 (1.5)	1.98 (0.9)	0.15	-0.15 - 0.98	12.5	0.0
	SAT score	11.3 (8.2)	14.5 (9.2)	0.15	-7.64 - 1.17	16.7	0.0
Mind Reading	Total correct	11.0 (3.1)	12.6 (2.9)	**0.03**	-3.03 - -0.15	6.3	0.0
	Average RT (s)	5.04 (1.2)	4.54 (1.2)	0.09	-0.08 - 1.09	14.6	5.0
	SAT score	2.40 (1.1)	3.05 (1.3)	**0.02**	-1.21 - -0.1	8.3	0.0
Face Match	Total correct	27.1 (2.5)	27.1 (1.6)	0.94	-0.97 - 1.05	10.4	0.0
	Average RT (s)	1.91 (0.6)	1.87 (0.4)	0.75	-0.18 - 0.25	20.8	0.0
	SAT score	15.0 (4.8)	15.1 (3.7)	0.68	-1.63 - 2.51	22.9	0.0

Table 2. Mean (standard deviations) scores of carriers and non-carriers on each outcome measure of the Ignite tests, as well as the proportion of each group that scored below the 5th percentile compared to the normative sample (adjusting for age, education, and sex). P-values indicate results from linear regressions between groups, significant differences are in bold. RT=reaction time, SAT=speed-accuracy trade-off, CI's = confidence intervals.

Conclusion

The Ignite normative data displays an age-related decline in the tests similar to well-described data from pen and paper equivalents. Preliminary data shows the Mind Reading test can detect differences in social cognition between presymptomatic mutation carriers and non-carriers at the group level. However, individual raw scores input into the normative calculator showed more carriers scored below the 5th percentile than non-carriers, across all the Ignite tests. The greatest differences were seen on social cognition and higher-order executive function tasks when a combined SAT score was used. These results mirror the pattern of cognitive decline in FTD and demonstrate the utility of a measure that combines both speed and accuracy when teasing apart performance in carriers and non-carriers. Ignite is a validated tool which appears promising in the detection of presymptomatic cognitive impairment in genetic FTD.

GENFI — GENETIC FTD INITIATIVE — PRINTED BY SCIENCEPOSTERS