Neurocognitive Evaluation from the Home: Validation of the Cumulus Platform in FTD And ALS Populations

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PRECISION ALS · BEAUMONT HOSPITAL · Cumulus

Cumulus Platform for Use in Real-World Settings

Cumulus cognitive and EEG tests are designed to be highly repeatable, with large banks of non-repeating stimuli.

- Objectively administered and automatically scored
- Results available in minutes, enabling remote monitoring
- Suitable for detecting change over time
- Designed to be an approachable and friendly experience for patients, minimising assessment burden
- A variety of behavioural, EEG and hybrid test paradigms are available

Background

People living with ALS (plwALS) and/or FTD (plwFTD) often experience cognitive change. However, detection can be confounded in one-off clinical/research visits due to factors including fatigue and testing anxiety.

Furthermore, cognitive decline in these population is hard to characterize as ALS and FTD are fast-progressing disorders that are difficult to study longitudinally and often present high and non-random attrition rate.

Home-based digital assessments may address this problem by offering a less burdensome assessment, eliminating the need to travel to clinics, while also offering an ecologically valid measure of cognitive function.

The Cumulus platform, consisting of a hand-held tablet with gamified cognitive tasks, and a portable dry electroencephalography (EEG) device, enables ecologically valid data collection from the home and better estimates of true performance.

Study objective: Assessment of the Cumulus platform feasibility and comparison of the Cumulus digital tasks against traditional pen and paper neuropsychological tests

Methods

Three 25-min sessions every two weeks completed autonomously in the home on the Cumulus platform for 8 months.

Traditional in-person evaluation in the clinic at month 0, 4 and 8. Participants completed the Edinburgh Cognitive and Behavioural ALS Screen (ECAS) and a full neuropsychological assessment.

The digital task suite included behavioural tasks (Picture Description, Digit Symbol Substitution Task, Facial Emotion Recognition, Task/FERT, Psychomotor Speed) and 3 EEG tasks (Resting State/RS, Mismatch Negativity/MMN, Visual Oddball).

The Cumulus platform discriminatory power at baseline was assessed using one-way Analyses of Variance (ANOVAs). Baseline performance on Cumulus tasks was defined as the average score of participants first 3 cycles (6 weeks) following familiarisation. ALS, FTD and Control groups were compared using both Cumulus digital tasks and conceptually similar benchmark neuropsychological tests.

Linear mixed effects models examined cognitive performance over time, as measured by both Cumulus and benchmark cognitive tests.

Individual case studies are presented to illustrate how individual cognitive change can be captured by the measures of the platform.
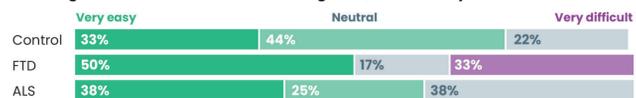
Table 1. Participant demographic and clinical characteristics.

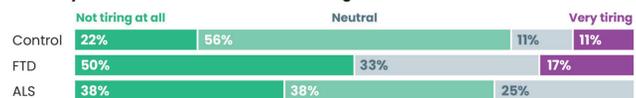| Demographics	ALS	FTD	Controls
Number of participants	11 recruited 2 withdrawals	8 recruited 1 withdrawal 1 screen fail	10 recruited 0 withdrawals
Age in years [mean, (std, range)]	62.9 (8.8, 47-74)	65.6 (8.6, 54-76)	63.7 (9.7, 42-75)
Gender	9 females/ 2 males	2 females/ 6 males	6 females/ 4 males
ECAS at baseline [mean, (std)]	102.4 (7.9)	86.9 (22.7)	115.8 (9.8)
Years in education [mean, (std)]	17.14 (4.14)	17.14 (2.91)	18.35 (3.06)
Age of onset in years [mean, (std)]	60.82 (9.16)	60 (8.53)	NA
Diagnostic delay in months [mean, (std)]	14.5 (5.12)	40 (37.73)	NA
Site of onset: Spinal [n, (%)]	7 (64%)	NA	NA
Site of onset: Bulbar [n, (%)]	4 (36%)	NA	NA
Baseline ALSFRS-R [mean, (std)]	38.7 (6.33)	NA	NA

How much support was needed to enable you to complete each session?
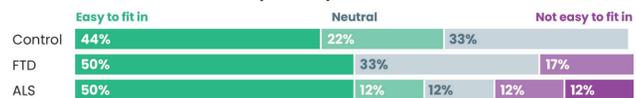
	No/little support	Neutral	A lot of support
Control	78%	11%	11%
FTD	50%	17% 17%	17%
ALS	62%	25%	12%

Thinking about the headset and tablet together, how would you rate ease of use?

	Very easy	Neutral	Very difficult
Control	33%	44%	22%
FTD	50%	17%	33%
ALS	38%	25%	38%

How do you find each session in terms of fatigue?

	Not tiring at all	Neutral	Very tiring
Control	22% 56%	11%	11%
FTD	50%	33%	17%
ALS	38%	38%	25%

How well does the session fit into your daily schedule?

	Easy to fit in	Neutral	Not easy to fit in
Control	44%	22%	33%
FTD	50%	33%	17%
ALS	50%	12% 12%	12% 12%

Now that the study is over, what is your opinion of the technology used in this study?

	Very positive	Neutral	Very negative
Control	33%	33%	33%
FTD	33% 17%	17%	17% 17%
ALS	50%	25%	25%

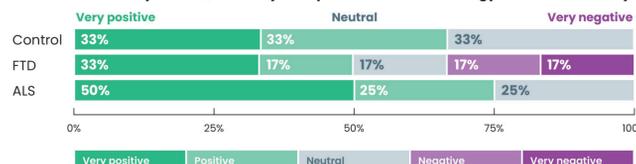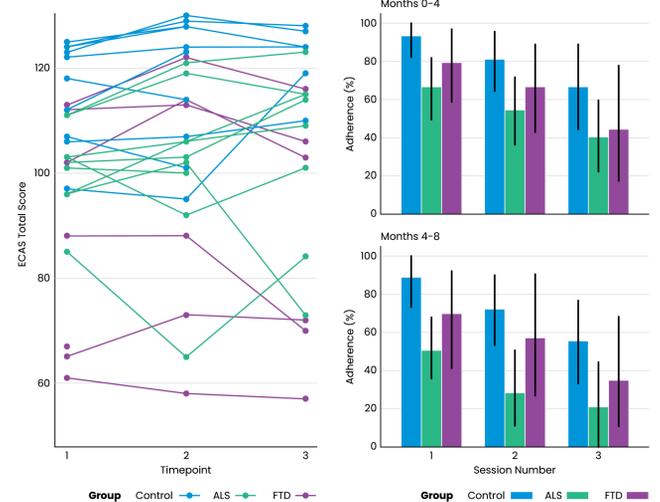Very positive · Positive · Neutral · Negative · Very negative

Figure 1. Usability Feedback collected at the end of the 8 months.

Results

There was no statistically detectable difference in progression between ALS, FTD and Control groups in terms of their cognitive performance over time on any of the traditional neuropsychological assessments.

On four Cumulus digital tasks, ALS, FTD and Control groups had different slopes of performance over time.

- For the psychomotor ($x2(2)$=7.61, p=0.02) and Flanker tasks ($x2(2)$=11.97, p=0.003), the significant interaction effects were driven by FTD group, who started with a lower baseline, and then improved over time relative to ALS and control groups.

- For FERT ($x2(2)$=8.12, p=0.02) and the speech fluency tasks ($x2(2)$= 11, p=0.004), the significant effects were driven by decline in the ALS group whilst controls and FTDs stayed stable or improved.

Research Questions

Q1: Is the cumulus platform useable and feasible for pwALS and pwFTD ?

The Cumulus Neuroscience platform was found to be both feasible and usable for participants to use, with moderate to high adherence and positive user feedback.

Q2: How do at-home frequent measures compare to traditional neuropsychological batteries at baseline?

Baseline cross-sectional analyses revealed that the Cumulus platform could emulate benchmark neuropsychological tasks in comparing groups, with similar effect sizes and patterns of differences on post-hoc comparisons.

Q3: Can at-home frequent measurements capture longitudinal declines in pwALS and pwFTD and how does this compare to traditional approaches?

Longitudinally, benchmark neuropsychological tests showed no evidence of cognitive decline in any group. Cumulus tasks, benefitting from a much larger number of repeated samples, found several significant differences between groups in their slopes of change over time.

Individual case studies analyses revealed that the Cumulus assessments can capture and reveal sometimes large session-to-session variability that are typically not captured by less frequent traditional assessments.

Table 2. ANOVA summaries comparing the cross-sectional discriminatory power of Cumulus and similar benchmark assessments at baseline.

Assessment method	Task	df	F	p	η2
Cumulus Task	Symbol Swap, total correct	2, 23	7.19	0.004	0.38
Benchmark Task	ECAS Executive functioning	2, 25	6.08	0.007	0.33
Cumulus Task	Memory Match, total correct	2, 19	1.65	0.22	0.15
Benchmark Task	WMS LM Immediate recall	2, 23	6.89	0.005	0.37
Cumulus Task	Double take, % correct	2, 24	13.46	<.001	0.54
Benchmark Task	DKEFS Digit Span total	2, 24	8.61	0.002	0.42
Cumulus Task	Astrotrap, reaction time	2, 22	7.09	0.004	0.39
Benchmark Task	CWIT Inhibition errors	2, 21	7.3	0.004	0.41
Cumulus Task	Go with the Flow, BIS	2,19	5.32	0.01	0.36
Benchmark Task	CWIT Switching errors	2, 21	4.97	0.02	0.32
Cumulus Task	P1vital FERT, % correct	2,19	6.42	0.007	0.4
Benchmark Task	ACS Emotion Recognition	2,25	5.37	0.01	0.3
Cumulus Task	Rapid Response, reaction time	2, 24	13.5	<.001	0.53
Benchmark Task	RCFT Copy time	2,23	2.19	0.14	0.16
Cumulus Task	Winterlight Lingo, MATTR_10	2,19	3.26	0.06	0.26
Benchmark Task	Verbal Fluency Index score	2, 21	6.81	0.005	0.39
Cumulus Task	P1vital FERT misclassification	2,19	2.43	0.12	0.2
Benchmark Task	PHQ-9 total score	2,23	19.38	<.001	0.63

Figure 2. Individual participant ECAS total score trajectories over time.

Fig 3. Adherence to the schedule of Cumulus sessions
Session 1 included Rapid Response, Relaxation, Sonic Cinema, Symbol Swap, and Lingo; Session 2 included Rapid Response, Relaxation, Astrotrap and Double Take; Session 3 included Rapid Response, Relaxation, Memory Match, Go with the flow and FERT.

Figure 4: Case Study 1 (plwALS)
Decline observed in executive functioning as measured by Cumulus DSST task (A) and ECAS executive score (B). PlwALS (green) is compared with a gender, age and education matched control (blue).
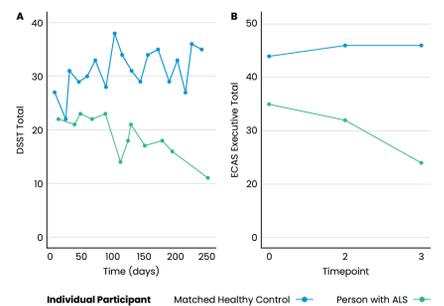
Figure 5: Case Study 2 (plwALS)
Individual decline in emotion recognition as measured by Cumulus FERT task (A) and ACS Emotion-Prosody matching task (B). PlwALS (green) is compared with a gender, age and education matched control (blue).
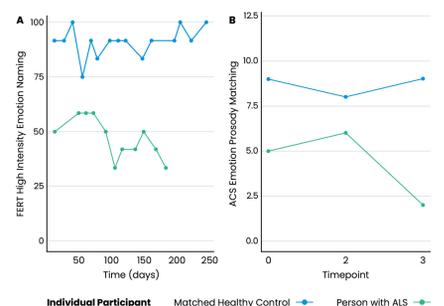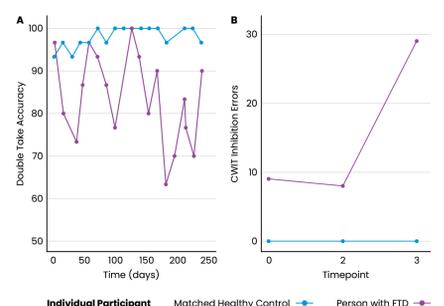
Figure 6: Case Study 3 (plwFTD)
Individual decline in sustained attention/response inhibition as measured by Cumulus Double Take task (A) and CWIT Inhibition task (B). PlwFTD (purple) is compared with a gender, age and education matched control (blue).
*Higher scores on CWIT indicate poorer performance.

Conclusions

Effect sizes of cross-sectional comparisons were similar between Cumulus and benchmark neuropsychological tests and there was some evidence that the platform can capture speech fluency and emotion recognition decline in plwALS, offering potential utility as a digital biomarker of cognitive decline.

Overall, these findings provide proof-of-concept that the Cumulus Neuroscience platform can capture meaningful neuropsychological data, relevant to the heterogeneity of the ALS-FTSD phenotype.

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