Association of British Neurologists

Clinical Research Training Fellowships

Dr Kerala Adams-Carr

Early Detection Of Frontotemporal Dementia Using Digital Biomarkers

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BACKGROUND

Frontotemporal dementia (FTD) is a common cause of early onset dementia, and approximately one third of cases are caused by genetic mutations. Studying this at-risk group allows us to characterise the earliest stages of the disease and identify the optimal treatment window.

With a number of clinical trials now underway in genetic FTD, there is a growing need for sensitive and accessible clinical outcome measures. 'Digital' approaches may offer a solution.

My ABN research fellowship investigates these possibilities within the Genetic FTD Initiative (GENFI) cohort. A combination of wearable devices, computerised testing, and portable investigations have been chosen to target the earliest features of FTD, capturing changes in cognition, behaviour, and motor function.

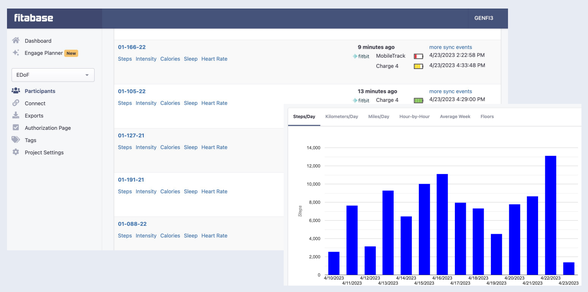
METHODS

WEARABLE DEVICES

1 Fitbit Charge 4 device

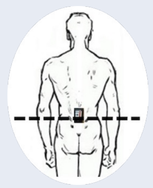


- Participants wear for 28 days
- Data accessed via platform Fitabase, and can be downloaded as csv files
- Step count - 1 minute epochs, HR - 5 second epochs

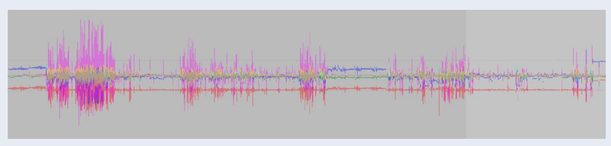


2 Axivity AX6 accelerometer





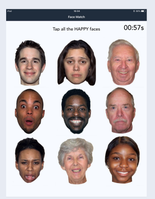
- Worn on the lower back for 7 days continuously
- Algorithm outputs 14 'micro-characteristics' of gait, which map to 5 domains (pace, rhythm, variability, postural control, symmetry)



COMPUTERISED TESTS

3 Ignite

- iPad based cognitive tests
- 20 mins to complete 12 tests
- Burst testing protocol – 4x over 4 weeks
- Targeted to test executive function, social cognition, naming and calculation
- Outputs include proportion correct, reaction time, and speed-accuracy trade off scores



4 BRAIN test



- Keyboard tapping task
- Designed to detect parkinsonism
- Outputs include:
  - Kinesia score (number of taps in 30s)
  - Incoordination score (variance of travelling time between keys)
  - Dysmetria score (accuracy of key taps)

PORTABLE INVESTIGATIONS

Muscle ultrasound & High Density Surface EMG

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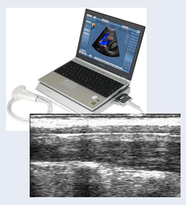

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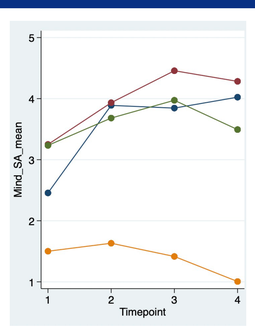
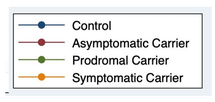
- Subclinical & clinical motor neurone disease is common in those with C9orf72 expansions
- Computerised analysis determines fasciculation frequency
- Both devices are more sensitive for fasciculation detection than needle EMG
- They are portable and non-invasive

IGNITE PRELIMINARY RESULTS

1a





1b

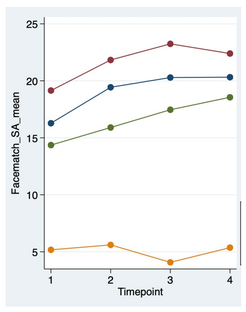


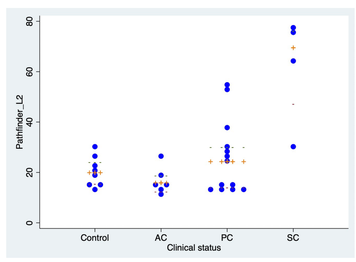
Figure 1 (left) – Change in mean scores over 4 timepoints (0 weeks, 1 week, 2 weeks and 4 weeks) by clinical status (n=37)

- 1a – Mind Reading speed accuracy trade-off – task based on 'Reading the Mind in the Eyes Test'
- 1b – Face Match speed accuracy trade-off score – based on the Ekman 60 Faces emotion recognition task

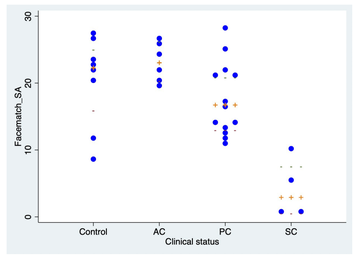
Figure 2 (right) – Comparison of scores between controls, asymptomatic mutation carriers (AC), prodromal carriers (PC) and symptomatic carriers (SC) at timepoint 3

- Dotplots show median (+) and IQR (---), n=31
- Majority of the tests showed a plateau in practice effect by timepoint 3 (2 weeks)
- 2a – Path Finder level 2, based on Trail Making Test Part B
- 2b – Face Match speed accuracy trade-off score

2a



2b



SUMMARY

- Digital tools enable remote assessment, are sensitive to small changes, and can measure a variety of clinical features
- Their deployment in the 'real world' improves 'ecological validity' as well as making them accessible and cost effective
- Data collection can be passive or active, or a combination of the two
- Computerised neuropsychological testing allows for 'burst testing' where practice effects can be studied
- This set of tests has been selected to detect the earliest features of FTD including changes in:
  - Activity, which may negatively correlate with apathy
  - Cognition - particularly executive function, social cognition and naming
  - Motor function – early parkinsonism and subclinical motor neurone disease

BLUEFIELD PROJECT Curing FTD

Patrick Berthoud Charitable Trust

GENFI GENETIC FTD INITIATIVE

DRC DEMENTIA RESEARCH CENTRE

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