Early Detection of FTD & MND (EDoF):

A Digital Biomarker Study

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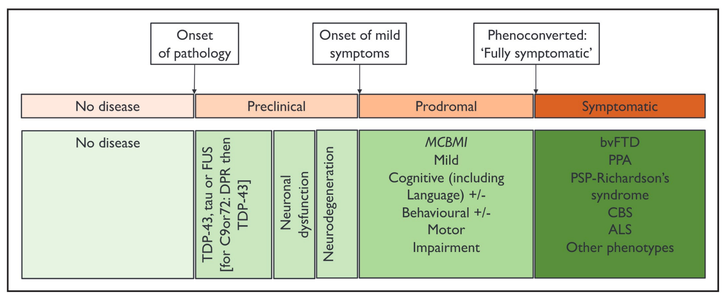
Background

The subtle and heterogeneous changes that emerge in the prodromal stages of FTD and MND are encompassed by the label **'Mild Cognitive, Behaviour and Motor Impairment' (MCBMI)**. This disease stage is of increasing interest as trials look to enrol participants earlier. Genetic FTD Initiative (GENFI) UCL participants are using digital technologies alongside traditional assessments. We aim to use these to sensitively detect and quantify changes across the MCBMI domains.

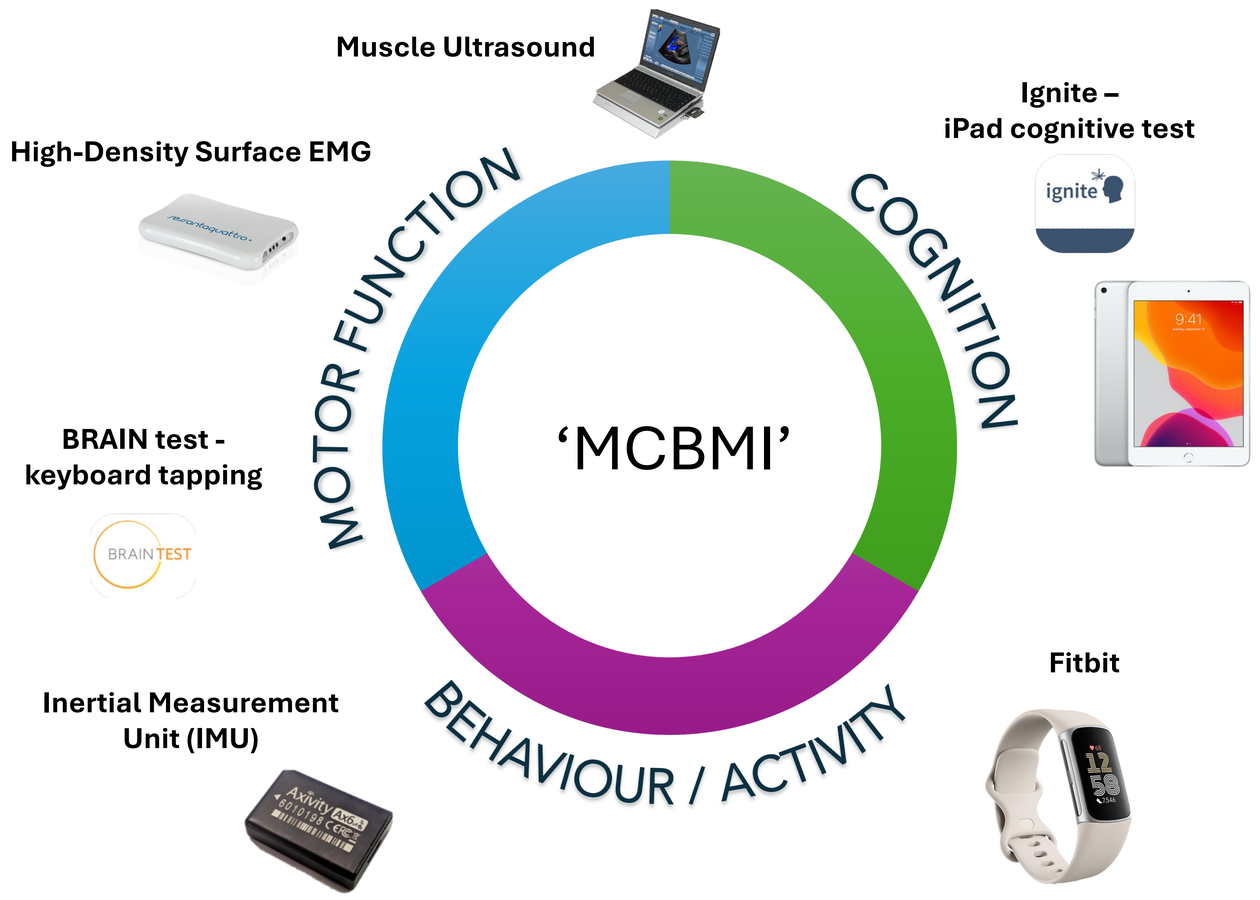


Three cohorts are being studied:

1) **EDoF-N**: a normative control cohort of 120 participants from the general population aged 20-80 years
2) **EDoF-P**: a predominantly presymptomatic cohort of C9orf72, GRN and MAPT mutation carriers from the UCL GENFI site
3) **EDoF-S**: a symptomatic cohort including those with behavioural variant FTD (bvFTD) and MND (ALS)

Participants complete the EDoF protocol consisting of 4 weeks of testing using 2 wearable devices, 2 computerised tests, and 2 non-invasive muscle tests.

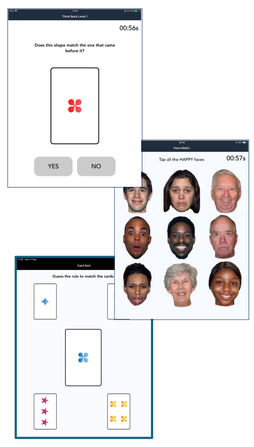
The EDoF Protocol



Computerised Tests

Ignite, an iPad based cognitive app

- 20-25 min test of cognitive function
- Repeated 4 x over 4 weeks to examine practice effects
- Speed-accuracy trade off scores are calculated (correct but slow responses are penalised)
- Outcomes are converted to z-scores using normative data from >2000 individuals, adjusting for age, sex and gender



BRAIN keyboard tapping

- Performed 4 x over 4 weeks
- Measures speed of tapping, decrement and accuracy of key presses with the aim of detecting early parkinsonism or pyramidal dysfunction



Muscle Investigations

High-Density Surface EMG

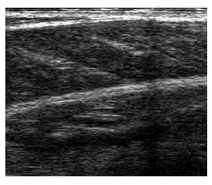
- 5 min rest and 1 min contraction recordings taken from biceps brachii, first dorsal interosseous and tibialis anterior, on dominant side
- Outcomes include fasciculation frequency and amplitude, and estimated motor unit number index



Muscle Ultrasound

- 60 second recordings of the tongue and bilateral T5 paraspinals, biceps brachii, first dorsal interosseous, tibialis anterior and medial gastrocnemius muscles
- Outcome measures include fasciculation frequency, size and depth
- Other measures include echointensity and echovariance





Wearable Devices

Inertial Measurement Unit (IMU)

- Axivity AX6 IMU device (triaxial gyroscope and triaxial accelerometer)
- Worn for 7 days on the lower back
- Outputs include:
  - Macro gait characteristics
    - Volume, pattern and variability e.g. total walking time per day, mean walking bout length, variability of bout length
  - Micro gait characteristics
    - Measures of rhythm, asymmetry, pace, variability, and postural control

Fitbit Charge

- Worn for 28 days
- Outputs include:
  - Mean and standard deviation of total daily step count
  - Peak 30 min cadence
  - Measures of circadian rhythm e.g. interdaily stability and intraday variability





Conclusions

- Early data from the EDoF-P (GENFI) cohort demonstrates significant differences in cognition in presymptomatic FTD mutation carriers compared to controls, detected using the iPad test *Ignite (see Ignite posters P013, P263, P264 and P194)*.
- Analysis of IMU and Fitbit data is underway to explore gait and activity, including circadian rhythm and sleep.
- Additional studies of speech and language measures, phone metadata, and mobile eyetracking will enhance data from *Ignite* on cognition and language.
- Outcomes will be correlated with clinical scales, imaging, and fluid biomarkers, with results contributing to a multi-stage and subtype-specific model of genetic FTD/MND.
- These digital biomarkers may be used in clinical trials: as screening criteria to identify prodromal participants, and as outcome measures that are sensitive to early clinical change.

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