

App-based cognitive assessment and monitoring: a feasibility study in patients with immune-mediated inflammatory and neurodegenerative disorders.

F. Cormack¹, V. Ticcinelli², N. Taptiklis¹, J. Kudelka³, K. Emmert³, W. Maetzler³, R. Reilmann⁴, R.D. Lutzman⁵, W.F. Ng^{6,7}, V. McRae⁷, K. Davies⁷, J. van der Woude⁸, J. Fierrez⁹, T. Ahmaniemi⁸, M. Chatterjee¹⁰

¹Cambridge Cognition, Research and Development, Cambridge, United Kingdom. ²UCB, pharma, Braine-l'Alleud, Belgium. ³University Hospital Schleswig-Holstein- Kiel University, Department of Neurology, Kiel, Germany; ⁴George Huntington Institute, n/a, George Huntington Institute: Muenster, Germany; ⁵Takeda, Quantitative Sciences - Digital and Translational, Cambridge, United States.; ⁶Newcastle University, Translational and Clinical Research Institute-, Newcastle upon Tyne, United Kingdom.; ⁷Newcastle Hospitals NHS Foundation Trust, NIHR Newcastle Biomedical Research Centre and NIHR Newcastle Clinical Research Facility, Newcastle upon Tyne, United Kingdom.; ⁸Universidad Autonoma de Madrid, Spain.; Erasmus University Rotterdam; ⁹VTT Technical Research Centre of Finland Ltd., n/a, Espoo, Finland.; ¹⁰Johnson & Johnson, Research & Development, Cambridge, United States.

Background

Fatigue is a transdiagnostic symptom that has a profound impact on quality of life and activities of daily living, resulting in high economic costs. The availability of objective, reliable and sensitive measures would help to better understand the entity of this unmet need and possibly facilitate the discovery of new drugs.

The IDEA-FAST consortium aims to further the measurement of fatigue by capturing multiple physiological and behavioural measures from patients in their free-living setting using digital technology. Here we describe the performance of three brief cognitive assessments, which have been previously shown to be sensitive to fatigue, sleep or daily activities, deployed as part of the IDEA-FAST feasibility study (Figure 1), with a focus on data coverage and psychometric properties.

Aims

This analysis focuses on 1) Coverage - defined as participant adherence with the scheduled testing sessions 2) Stability over time, assessed through reliability and linear regression 3) associations with pencil and paper neuropsychological tests.

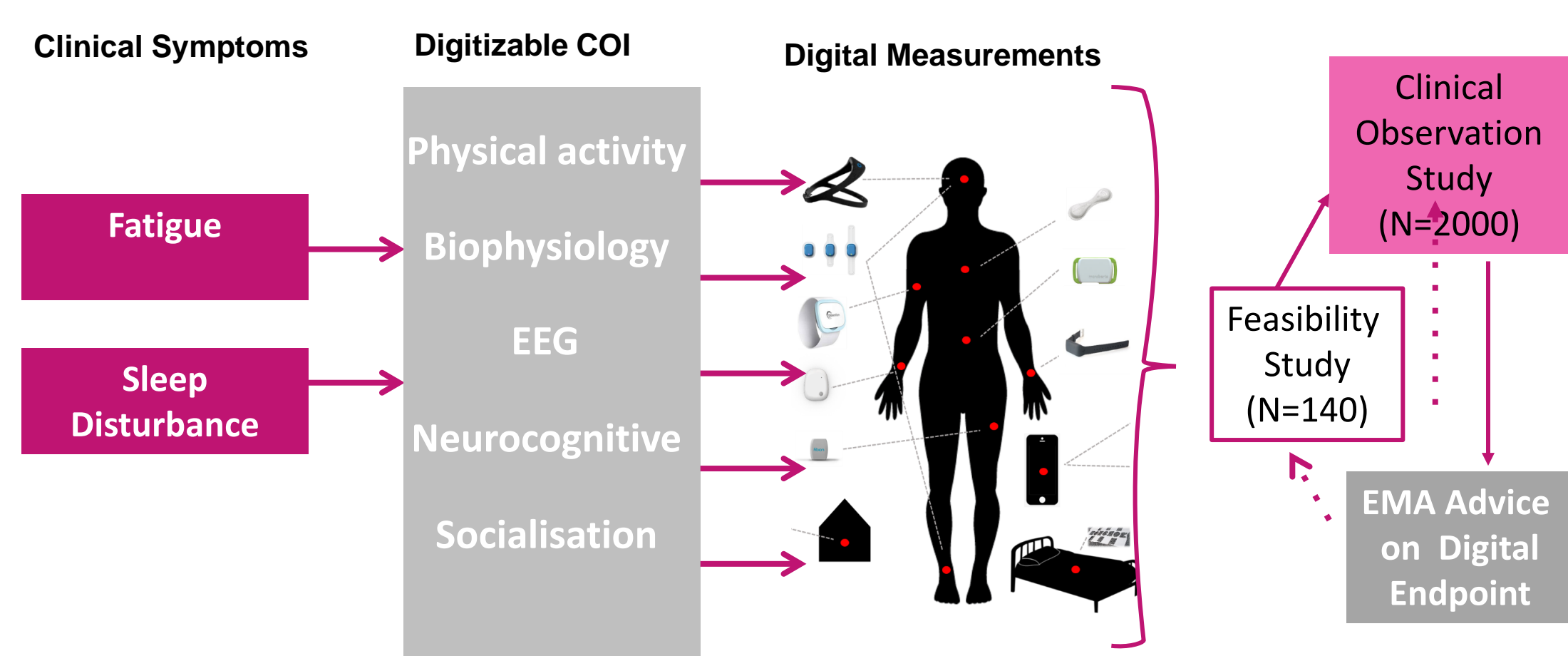


Figure 1: Schematic of the IDEA-FAST project. Data here are presented from the Neurocognitive COI acquired during the feasibility study.

Methods

These data were collected as part of the IDEA-FAST feasibility study, which aimed at selecting wearable technologies (e.g., activity tracking, EEG) and digital tools for a larger-scale observational study. This poster focuses on the neurocognitive data collected through the CANTAB™ App.

Study participants

Inclusion criteria were age over 18 years, consent to participate in the study; use of a smartphone in the past three months; ability to follow written and oral instructions in the local language, to walk, sit, and stand independently and to socialize and communicate; a Montreal Cognitive Assessment (MoCA) score of over 15.

Exclusion criteria were comorbid major sleep disorders, chronic fatigue syndrome, respiratory, cardiovascular or metabolic disorders or physical traumas with hospitalization in the past three months, diagnosis of cancer in the past three years, major psychiatric disorders, suicidal attempt in the past five years or suicidal ideation in the past six months, substance or ethanol abuse or severe visual impairment.

The participants were either healthy or suffered from neurodegenerative diseases (NDD - n=33 - Huntington's disease (HD) and Parkinson's disease (PD)) or and immune-mediated inflammatory diseases (IMID - n=63 - inflammatory bowel disease, primary Sjögren's syndrome, rheumatoid arthritis, and systemic lupus erythematosus). Data were also collected from 38 Healthy Participants.

Cognitive Tasks

Three tests were deployed via the CANTAB™ App from Cambridge Cognition: the Cognition Kit Digit Symbol Substitution test (DST), the Psychomotor Vigilance Test (PVT) and the Cognition Kit N-back test (NBX) (Figure 2). These assessments assess global cognition, attention and working memory, respectively.

Study Design

Participants were enrolled in the study for up to 60 days. The DST and PVT were administered twice a day for a device-use period of 5 days each, whereas the NBX tasks were administered over two device-use periods. Use periods were interspersed with weekend rest periods. A total of 5333 observations were collected across all participants over the three cognitive assessments.

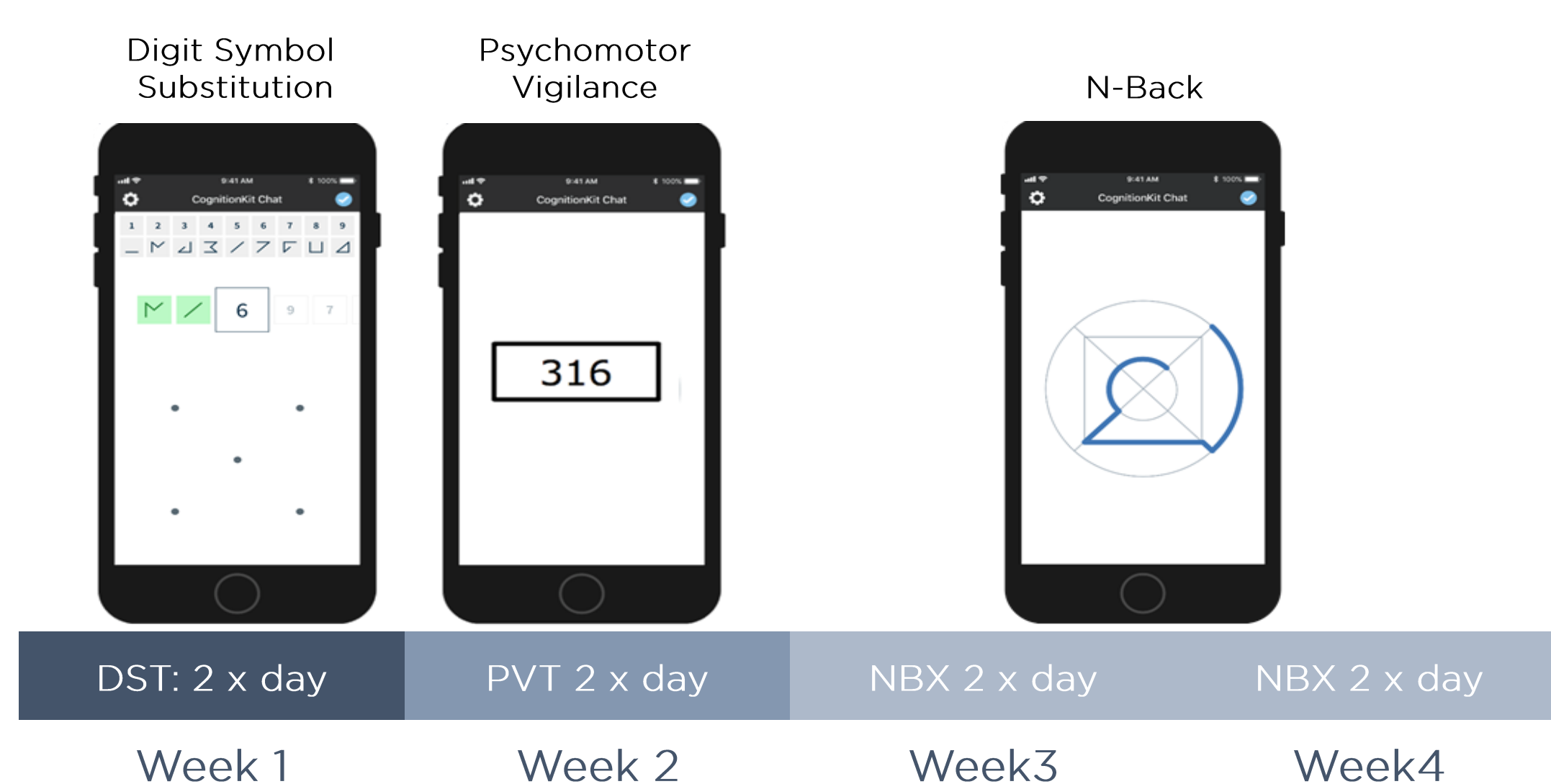


Figure 2: Schematic of tasks and data collection schedule

Results

Coverage

- Coverage was calculated as the ratio of scheduled to completed sessions. Participants frequently completed assessments outside of the use period, hence coverage could exceed 100%
- PVT had the highest coverage (110%), with 75.9% completing 100% or more of the required assessments and NBX the lowest coverage (90%, with 61.5% completing 100% or more) Figure 3.
- Poor compliance, classified as coverage of <50% was observed in 9% of participants for PVT, 12.3% on DST and 22% on NBX.
- Compliance was highest for participants in the IMID (mean of 77.14% with 100% compliance, and mean of 9.69% with poor compliance (<50% coverage), and lowest in the NDD group (53.8% with 100% compliance, 21.93% with poor compliance.)

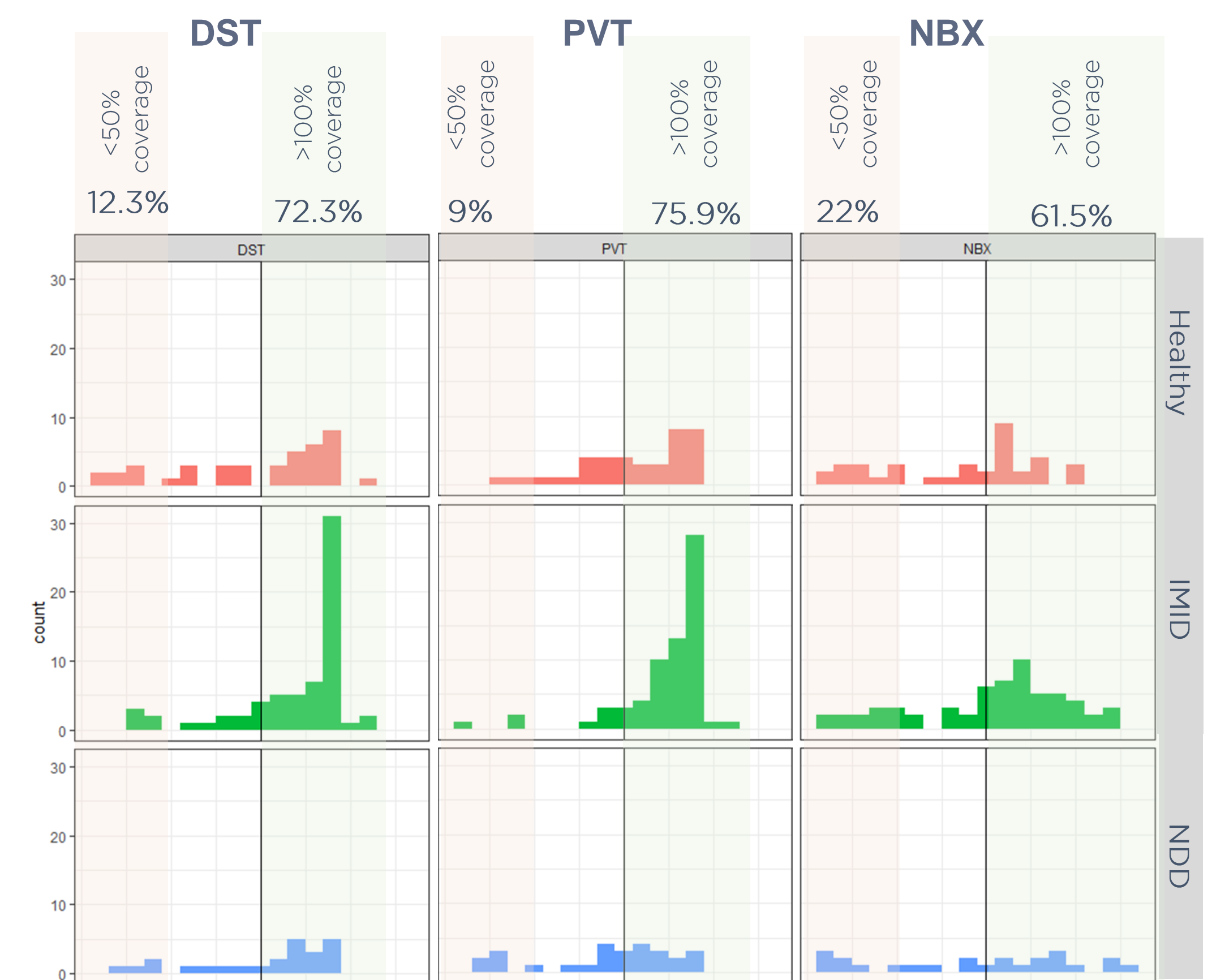


Figure 3: Histograms of percent coverage by task and by cohort. Shaded areas represent high and low compliance

Reliability

- Reliability was measured under two scenarios:
 - Performance was averaged across first and second halves of testing days for each participant, and correlations were computed across first and second halves.
 - Single random attempts were selected for each participant from the first and second half of testing.
- Plots of correlation between firsts and second half scores are shown in Figure 4.
- Good to excellent correlations were observed for all measures with highest values for DST.
- Aggregation over multiple sessions increased test-retest reliability for these brief tests

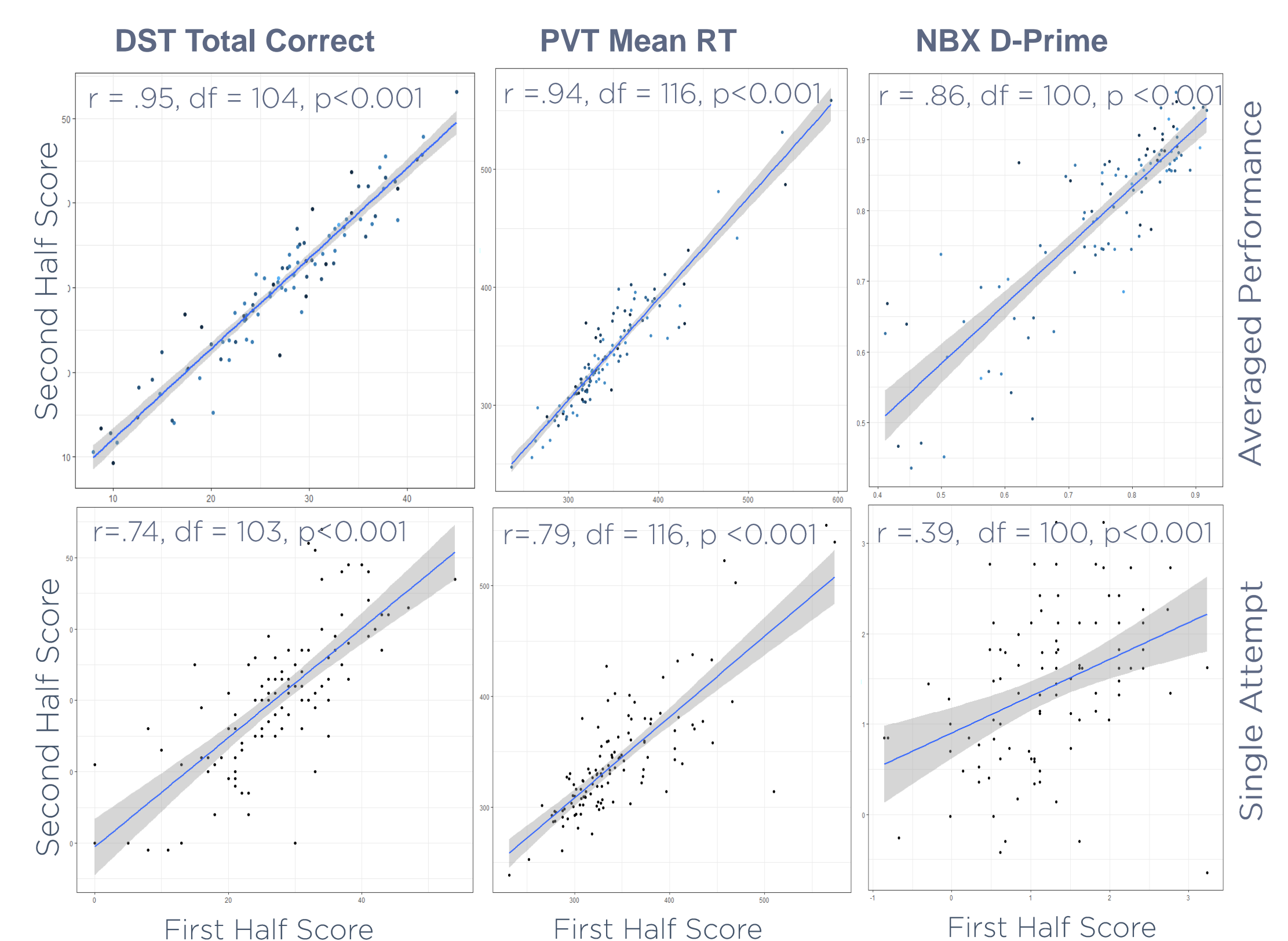


Figure 4: Correlations of scores from first and second halves by task, and aggregation.

Mixed-effects Modelling

- Mixed effects modelling, with a random intercept for participant, was carried out to explore the main effect of session and cohort on performance, adjusting for Age and baseline cognitive function measured through the MoCA. Trends over time in for the three tasks, in the different cohorts are shown in Figure 4.
- For DST, significant effects of session ($F(1,1111.77) = 170.78, p < 2.2e-16$) and cohort ($F(2, 105.44) = 8.56, p = 0.0003$), adjusting for age ($F(1, 104.94) = 106.52, p < 2.2e-16$) and MoCA ($F(1, 104.59) = 16.85, p = 8.025e-05$). With poorer performance in the NDD group ($df = 105.47, t = -3.49, p = 0.00071$).
- For PVT, no significant effect of Age or MoCA were observed. There was, however, a significant effect of cohort, $F(2, 117.2) = 3.96, p = 0.022$. Session did not reach the threshold for statistical significance ($F(1, 1191.47) = 3.68, p = 0.055$).
- For NBX, significant effects of Age ($F(1, 101.54) = 70.08, p = 3.268e-13$) and MoCA ($F(1, 99.77) = 22.5, p = 7.020e-06$) were observed. There was, however, a significant effect of session ($F(1, 2162.11) = 52.27, 6.664e-13$), but cohort did not reach the threshold for statistical significance ($F(2, 100.73) = 2.92, p = 0.058$).

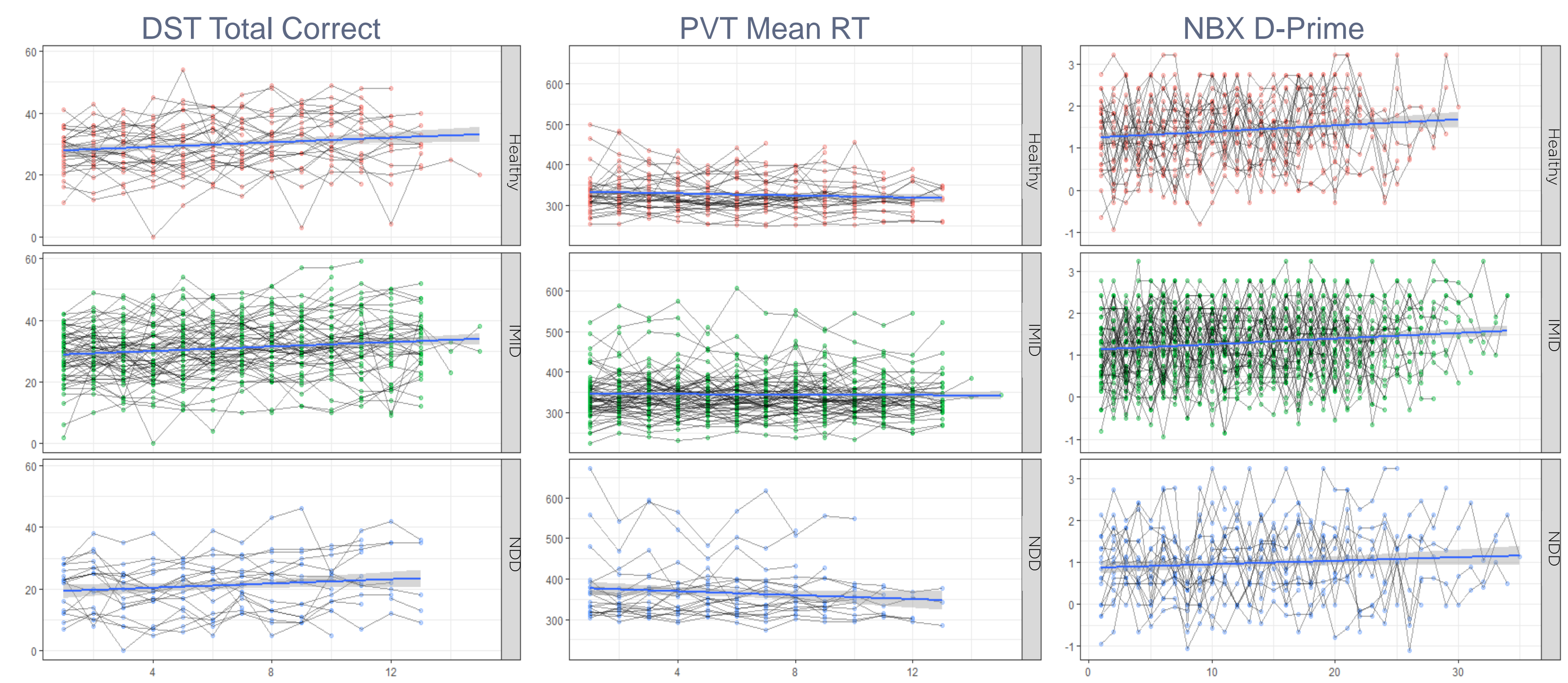


Figure 5: Time series plots of individual participant performance and trends over time for the three tasks, by patient group

Conclusion

These preliminary data suggest that brief measures of cognition can be reliably captured from patients across a range of neurological and IMI disorders in a free-living environment.

Acknowledgements

The project leading to this application has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under Grant Agreement No. 853981 (IDEA-FAST). This Joint Undertaking receives the support from the European Union's Horizon 2020 research and innovation programme and EFPIA.