High compliance to remote, high-frequency cognitive testing across immune-mediated inflammatory disease and neurodegenerative disease patients

The methodological question: Is it feasible to collect high quality, high-frequency cognitive and patient reported outcome data remotely in transdiagnostic studies?

Background

In recognition of the frequency of specific symptoms across disorders, there has been an increase in transdiagnostic approaches to digital biomarker discovery. Cognitive impairment, as a core pillar of the National Institute of Mental Health Research Domain Criteria, is a key target for transdiagnostic drug development.

Cognition can be measured briefly and repeatedly in decentralised clinical trials and has known associations with other transdiagnostic symptoms such as sleep disruption and fatigue. Adherence to high-frequency testing is important for reliable data capture and biomarker discovery.

We investigated adherence to high-frequency testing across six patient groups: Huntington's and Parkinson`s disease (neurodegenerative disease, NDD) as well as primary Sjogren's syndrome, rheumatoid arthritis and systemic lupus erythematosus (immune-mediate inflammatory disease, IMID) as part of the IDEA-FAST consortium that is investigating objective digital biomarkers of fatigue and sleep disturbance.

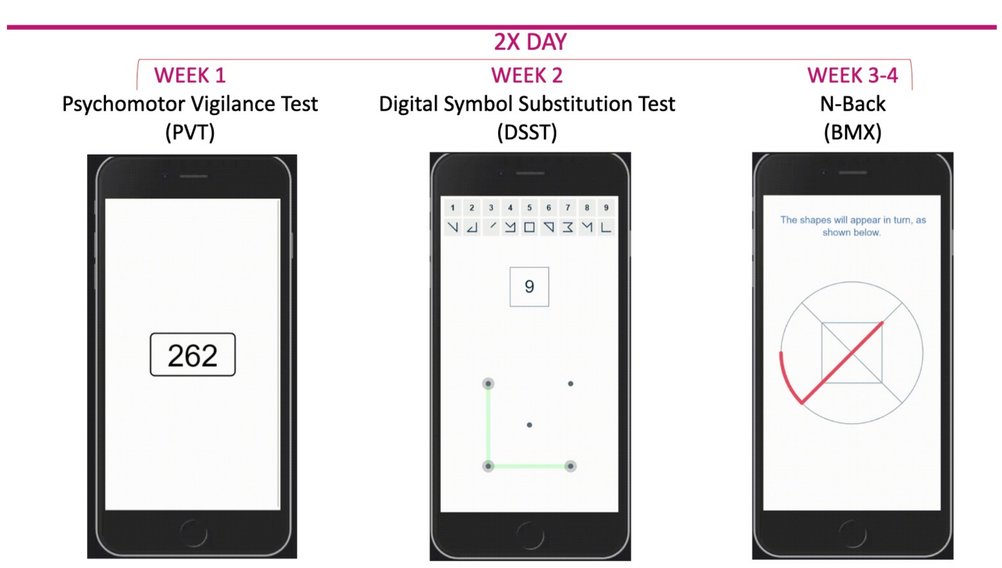


Figure 1: Cognitive tasks delivered via smartphone app. Cognitive tasks were delivered twice a day for five days across a total of 4 weeks.

Methods

In the IDEA-FAST feasibility study, participants completed cognitive tests and questionnaires via smartphone twice a day for five days, in their own homes. Cognitive tests included the psychomotor vigilance test (PVT) of attention, the digit substitution test (DST) assessing global cognition, and N-back task (NBx) of working memory. Patients also completed standardised assessments and measures of sleep, fatigue and activities of daily living.

Compliance was calculated as the proportion of completed, to expected, cognitive tasks. We explored whether clinical features were related to compliance, to determine what might be a barrier to adherence in decentralised clinical trials. High compliance across diagnostic groups, would indicate feasibility for, not only individual patient clinical trials, but also for transdiagnostic studies.

136 individuals were followed for 1297 days, with each participant enrolled for a duration of 60 days. Participants were identified through routine clinical appointments, public outreach efforts or support groups.

Results

	NDD			IMI			
	Healthy Controls	PD	HD	IBD	SLE	PSS	RA
N (M)	31	21	4	14	14	17	19
Mean Age (SD)	44 (11)	63 (10)	52(6)	36 (12)	49 (15)	59 (14)	64 (13)
MOCA	28(1)	27(3)	NA	28(2)	29(2)	28(2)	28(2)
Mean MFI total score (SD)	64(1)	58(5.5)	NA	59(5.5)	63(5.3)	60(4)	60(5)
Mean ESS (IQR)	3.8(3)	10.6(4.8)	NA	6.8(5.5)	9.4(4)	7.8(6.8)	7.2(7)
Mean PSQI (IQR)	3.9(2)	7.3(4)	NA		10.2(4)	7.6(3.5)	7.3(6.3)
Mean Godin Score (IQR)	50(4.5)	48(13)	32(1.5)	36(20.3)	25(26.3)	32(27)	35(27.3)

Table 1: Demographics across cohorts. MOCA – Montreal Cognitive Assessment; ESS – Epworth Sleepiness Scale; PSQI- Pittsburgh Sleep Quality Index; Godin-Shephard Leisure-Time Physical Activity Questionnaire. NA indicated missing data

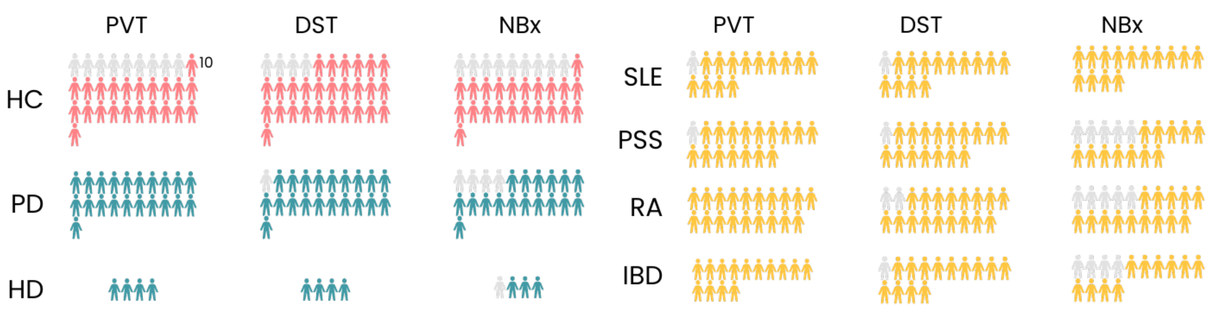
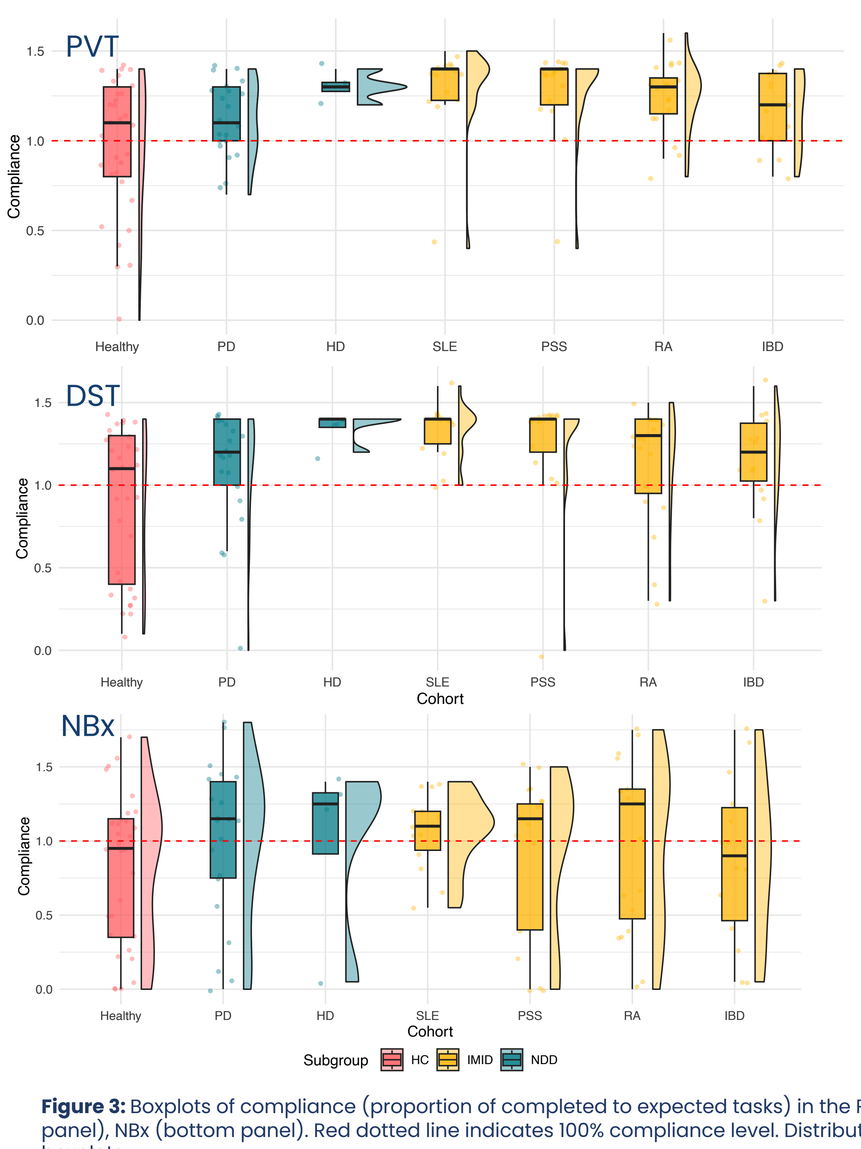


Figure 2: Representation of compliance across tasks (PVT – psychomotor vigilance task; DST – digit symbol substitution, NBX, - nback task. Each row is 10 participants. Greyed out symbols represent compliance under 50%. HC- healthy controls, PD- Parkinson's Disease, HD – Huntington's Disease, PSS- primary Sjogren's syndrome, RA- rheumatoid arthritis and SLE- systemic lupus erythematosus

Compliance was very high (median >100%, indicating patients did *more* than necessary) across all patient groups and cognitive tasks. Non-parametric Kruskal-Wallis ANOVA tested whether coverage differed between patient cohorts, and subgroups. Post-hoc comparisons (FWE-corrected) of PVT and DST coverage across patient cohorts and subgroups, showed significantly *higher* coverage in PSS ($p<0.005$), RA($p<0.05$) and SLE ($p<0.01$) compared to healthy controls for PVT.

Results



For the DST, coverage was significantly lower in the healthy controls compared to PSS ($P<0.05$) and SLE ($p<0.01$). Linear regression with age, general cognition (MOCA score) and baseline fatigue and sleepiness as covariates, showed no significant predictors of coverage in the DST or NBX task, and only baseline sleepiness as a significant predictor of PVT coverage.

Figure 3: Boxplots of compliance (proportion of completed to expected tasks) in the PVT (top panel), DST (middle panel), NBx (bottom panel). Red dotted line indicates 100% compliance level. Distributions displaced alongside boxplots.

In the PD cohort, there was no significant correlation between disease severity (as measured by the MDS-UPDRS) and adherence to testing (PVT: $r(19)=-.31$, $p=0.26$; DST: $r(18)=-.21$, $p=0.47$; NBX: $r(18)=-.39$, $p=0.17$;) despite, a wide range of disease severities across patients (see figure 4). Given the relatively high level of compliance, and relatively low number of patients (n=19), we cannot rule out this being due to ceiling effects or low power

Figure 4: Representation of compliance across tasks (PVT – psychomotor vigilance task; DST – digit symbol substitution, NBX, - nback task.

Conclusion: Brief, repeated, measures of cognition can be captured remotely from patients in a free-living environment. Compliance was high across different patient groups, with varying motor and cognitive abilities, indicating that digital high-frequency cognitive and patient reported outcome data can be reliably collected for transdiagnostic decentralised clinical trials.

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