Remote assessment of cognition with the unsupervised version of the Cogstate Brief Battery: Association of composite endpoints with Alzheimer's disease biomarkers.

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Background

In people at risk of Alzheimer's disease (AD), access to cognitive assessment can be increased through application internet-based registries. While cognitive data collected remotely from registries provides only limited information to support clinical decision making, it can be linked to specialist management clinics which allow for analyses and more comprehensive follow-up. The Cogstate Brief Battery (CBB) has been optimized for unsupervised remote use in registries with CBB outcomes sensitive to dementia risk factors such as carriage of the Apoe4 allele, higher levels of cerebral vascular risk factors, and sleep disorders. To determine the utility of validity of data collected from remote administration of the CBB, data from adults with various AD risk factors who are enrolled in a registry were investigated for its relationships with in-clinic performance on standardized neuropsychological assessments and with AD biomakers obtained from cerebral spinal fluid (CSF) sampling.

Method

Adults (40-70years) enrolled in The Healthy Brain Project https://www.healthybrainproject.org.au, (HBP) were invited to participate in biomarker assessments if they had completed 80% of HBP assessments, provided a saliva sample, indicated they were able to attend a major metropolitan hospital. Interested participants underwent comprehensive medical screening on the phone with a member of the research team to determine safety and eligibility. Exclusion criteria were active infection/skin rash, uncontrolled headaches, immunodeficiency, uncontrolled epilepsy or blood clotting abnormalities. Initially, 331 participants expressed interest and of these, 82 completed an in-clinic assessment that included biomarker and neuropsychological testing. APOE ε4 carriers were given the first opportunity for participation, resulting the proportion of ε4 carriers (38%) being greater than in the general population (~15%). Participants and raters were unaware of APOE status. Table 1 summarises the demographic and clinical characteristics of the sample.

Table 1: Demographic and clinical characteristics of the study sample

Demographic and clinical characteristic	Mean (SD)
Age *(Mean SD)*	58.36 (6.74)
Female *(n, %)*	N= 51 (67%)
Family History of Dementia *(n, %)*	60 (79%)
Education *(Mean, SD)*	16.45 (3.50)
Difference in time between online and biomarker assessments (years)	0.36 (0.86)
IQ *(Mean, SD)*	114.29 (5.53)
MMSE *(Mean, SD)*	28.84 (1.17)
CDR Sum of Boxes *(Mean, SD)*	0.04 (0.16)
HADS Depression *(Mean, SD)*	2.24 (2.41)
HADS Anxiety *(Mean, SD)*	4.25 (2.84)
ISLT Total Recall *(Mean, SD)*	24.89 (3.67)
ISLT Delayed Recall *(Mean, SD)*	8.90 (2.05)

Remote cognitive assessment was conducted in the HBP using the Cogstate Brief Battery (CBB) (www.cogstate.com) optimized for self-administration through inclusion of Learn tests. CBB test include the Detection (DET) to measure psychomotor function, the Identification (IDN) to measure Attention, the One Card Learning Test (OCL) to measure Learning and Memory and One Back (OBK) to measure working memory. Performance on the DET and IDN was defined using speed (msec) of correct answer. Performance on the OCL and OBK tests was measured using speed and the accuracy (proportion of correct responses). Scores were standardised using mean and SD of the HBP sample. Composite scores were computed by averaging scores of the component tests to provide the Cognigram Learning/Working Memory, Cognigram Psychomotor/Attention composites as well as the OCL composite (OCL speed and OCL accuracy) and OCL/OBK speed & accuracy composite.

CSF samples stored in polypropylene tubes were transferred for processing on wet ice following guidelines. Samples were spun at 2000 x g at +4 ◦C for 10 minutes. Supernatant was pipetted to new polypropylene tubes and gently inverted to avoid gradient effects. Samples were 0.5mL aliquots into screw-cap polypropylene tubes, stored at −80 ◦C. CSF concentrations of amyloid beta 42 (Aβ1-42), total tau (t-tau), and tau phosphorylated at threonine 181 (p-tau181) were measured by immunoassay (Roche Elecsys®) and CSF concentrations of neurofilament light chain protein (NfL) were measured using ELISA (UmanDiagnostics, Umeå, Sweden). Analyses were conducted at the National Dementia Diagnostics Laboratory, Melbourne, Australia. 25 participants had Aβ42 levels above maximum limits of detection so were assigned the top range score (1700 pg/mL). Aβ+ was classified when CSF Aβ42 levels < 1000, in accord with standardised cut-scores provided by Roche.

In-clinic cognitive assessment consisted of the Mini-Mental State Examination (MMSE), the National Adult Reading Test (NART) and the Preclinical Alzheimer's Cognitive Composite (PACC). PACC was computed by averaging the standardized values of the Logical Memory delayed recall, the International Shopping List Test delayed recall, the WAIS Digit Symbol Coding test, and the D-KEFS FAS test (Lim et al., 2016).

Results

Multiple regression analyses assessed the relationship between the composite scores from the remote CBB and the in-clinic PACC and CSF biomakers (Table 2).

Table 2: Magnitude and statistical significance of relationships between remote CBB performance, PACC (in- clinic) and CSF AD biomarkers

	Learning/Working Memory *(OCL & OBK Acc)*		Psychomotor/ Attention *(DET & IDN Spd)*		OCL composite *(OCL Spd/Acc)*		OCL/OBK speed and accuracy composite *(OCL & OBK Spd/Acc)*	
	β(SE)	p	β(SE)	p	β(SE)	p	β(SE)	p
Aβ42	-0.09 (0.12)	.493	-0.15 (0.11)	.175	-0.12 (0.12)	.297	-0.10 (0.12)	.420
t-tau	-0.25 (0.13)	.051	0.00 (0.12)	.999	**-0.27 (0.12)**	**.028**	**-0.27 (0.13)**	**.036**
p-tau181	-0.24 (0.13)	.069	0.02 (0.12)	.851	**-0.25 (0.12)**	**.047**	-0.24 (0.13)	.061
NfL	**-0.33 (0.14)**	**.022**	0.11 (0.14)	.439	**-0.31 (0.14)**	**.027**	-0.26 (0.14)	.072
PACC	**0.38 (0.14)**	**.006**	0.10 (0.13)	.473	**0.31 (0.13)**	**.022**	**0.39 (0.14)**	**.005**

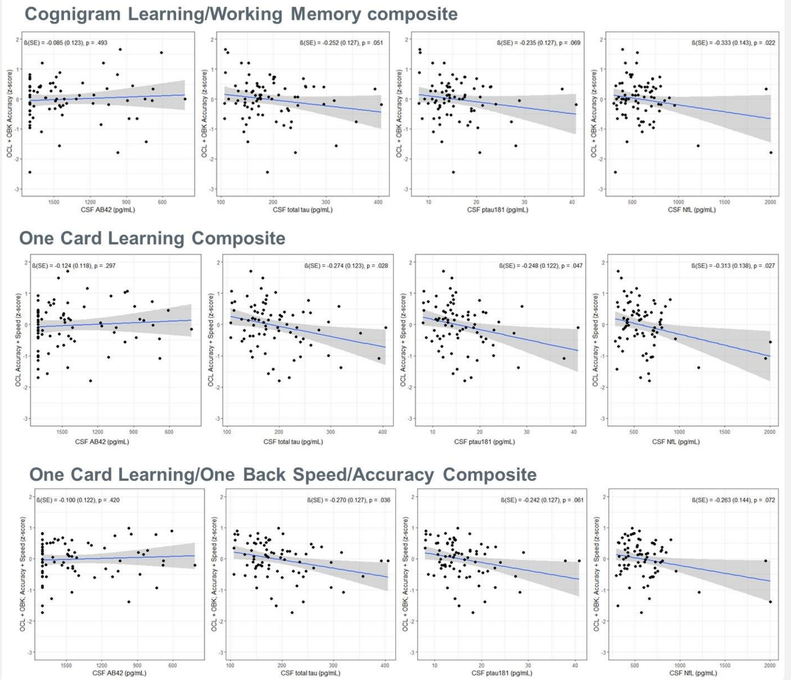

Figure 1: Nature and strength of relationships between each CBB composite score and AD biomakers

Relationships between the CBB composite scores collected remotely and the CSF AD biomakers are summarised on Table 2 and shown graphically on Figure 1. First performance on each of the CBB composites that included the OCL showed significant relationships with the PACC. Those same composite scores showed relationships with CSF t-tau, p-Tau181 and NFL but not with AB42.

Conclusion

In non-demented adults enrolled in AD registries, performance from remote assessment of cognition is associated with AD disease markers and with in-clinic cognitive status. Remote assessment could therefore provide a valuable tool for managing AD in the community.