# A cross-sectional and longitudinal investigation of the Cambridge Behavioural Inventory – Revised (CBI-R) in behavioural variant frontotemporal dementia (bvFTD)

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## BACKGROUND

Changes in behavioural and neuropsychiatric profiles are hallmark features of behavioural variant frontotemporal dementia (bvFTD)[1]. Informant based questionnaires that reliably capture these deficits in bvFTD, such as the Cambridge Behavioural Inventory-Revised (CBI-R)[2], are commonly used in clinical research and increasingly considered for therapeutic trials.

Whilst studies have investigated the cross-sectional validity of the CBI-R in bvFTD, little is known about how bvFTD compares with the primary progressive aphasia (PPA) variants of FTD. In addition, the longitudinal feasibility of these scales is currently lacking.

The current study therefore investigated the cross-sectional CBI-R profiles in the three canonical variants (bvFTD, semantic variant PPA (svPPA) and non-fluent PPA (nfvPPA)) and assessed its utility as a longitudinal biomarker of disease progression.

## METHODS

The CBI-R was completed by primary caregivers for 63 FTD patients (Table 1). For each of the 10 CBI domains (see Figure 2) scores were converted to percentage of maximum score. Total CBI-R is scored out of 180 with higher numbers indicating greater deficits. 29 FTD patients returned for longitudinal investigations (Table 1).

| BASELINE: Diagnosis | N | Age | Gender (M:F) | Disease duration |
|---|---|---|---|---|
| bvFTD | 32 | 63.8 (8.2) | 26 : 5 | 6.6 (4.6) |
| svPPA | 16 | 63. 2 (6.0) | 7 : 9 | 6.5 (2.4) |
| nfvPPA | 15 | 70.6 (6.7) | 6 : 9 | 3.2 (1.3) |
| **REPEAT: Diagnosis** | **N** | **Age** | **Gender (M:F)** | **Interval (years)** |
| bvFTD | 18 | 65.4 (7.2) | 16 : 2 | 1.2 (0.4) |
| svPPA | 7 | 66.4 (3.7) | 4 : 3 | 1.1 (0.6) |
| nfvPPA | 4 | 67.1 (5.4) | 2 : 2 | 1.3 (0.9) |

Table 1. Patient demographics for the cross-sectional and longitudinal analyses. Age, Disease duration and Interval are expressed as mean (standard deviation).

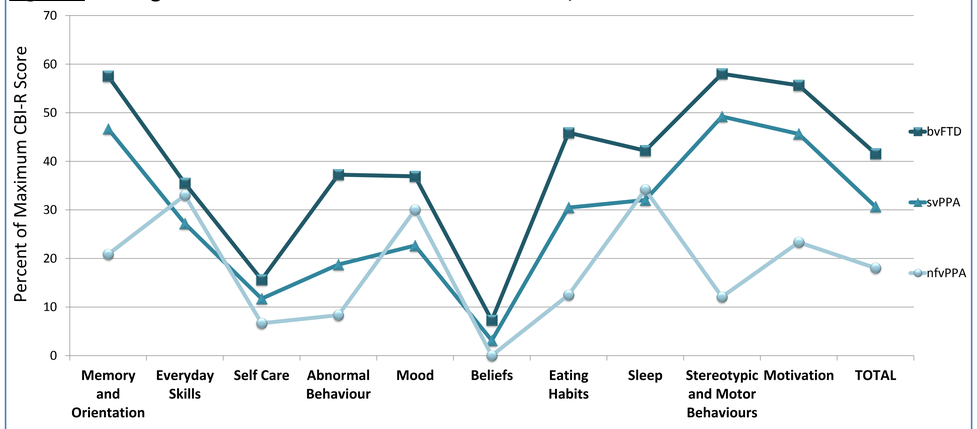
## METHODS

To investigate symptomatic profiles, baseline CBI-R scores were compared between diagnoses using linear regression, correcting for age, gender and disease duration. To assess its longitudinal feasibility, annualised rates of change for all CBI-R subscales were calculated and compared using linear regression within each diagnosis group.

## RESULTS: CROSS-SECTIONAL ANALYSIS

Across all 10 CBI-R domains bvFTD demonstrated the greatest deficits (Figure 1). The most severely affected domains were '*Stereotypic and Motor Behaviours*', '*Memory and Orientation*', '*Motivation*' and '*Eating Habits*' *at 58.0%, 57.5%, 55.6%* and *45.9%* of maximum possible score respectively. The least affected domains were *'Beliefs'* and *'Self Care'* at 7.3% and 15.6%. The svPPA group also showed significant deficits in multiple domains. Although scores were lower than the bvFTD group, they were not significantly different. nfvPPA demonstrated fewer deficits with significantly lower scores in multiple domains (Table 2).

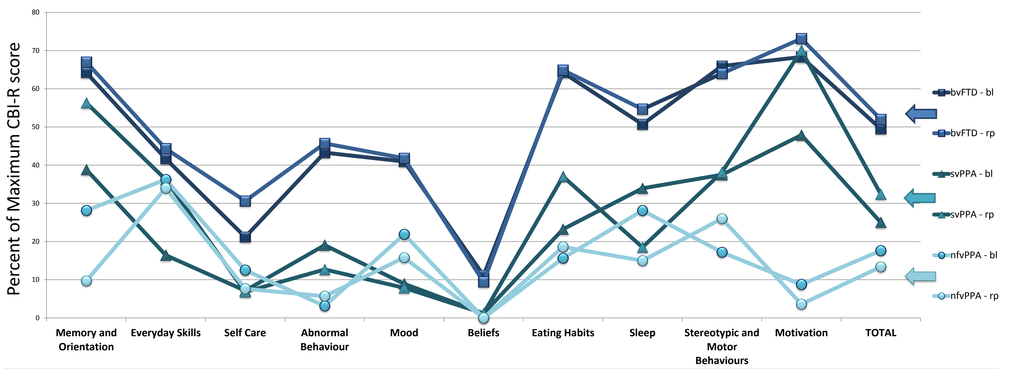
**Figure 1. Average CBI-R subscale and Total scores for bvFTD, svPPA and nfvPPA at baseline**




| | Memory and Orientation | Everyday Skills | Self Care | Abnormal Behaviour | Mood | Beliefs | Eating Habits | Sleep | Stereotypic and Motor Behaviours | Motivation | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| bvFTD vs svPPA | −2.5, [−8.5, 3.5] | −1.7, [−5.6, 2.1] | −0.5 [−2.9, 2.6] | −3.5, [−8.1, 1.1] | −2.3, [−4.9, 0.3] | −0.6, [−1.3, 0.1] | −2.4, [−5.3, 0.4] | −0.2, [−1.7, 1.2] | −0.4, [−3.86, 3.15] | 0.0, [−4.0, 4.0] | −13.8, [−36.7, 9.2] |
| bvFTD vs nfvPPA | **−12.5, [−19.1, −5.9] *** | −0.3, [−4.9, 4.3] | −0.7, [−3.2, 1.7] | **−7.5, [−11.1, −3.9] *** | −1.0, [−4.2, 2.1] | **−0.9 [−1.7, −0.1]*** | **−3.8, [−7.1, −0.6] *** | −0.2, [−2.2, 1.9] | **−5.9, [−9.5, −2.4] *** | −5.2, [−11.1, 0.7] | **−38.1, [−63.2, −13.0] *** |
| nfvPPA vs svPPA | 1.2 [−8.3, 10.7] | −2.2, [−9.7, 5.3] | −1.3, [−4.9, 2.3] | −0.0, [−4.4, 4.3] | −2.0, [−5.8, 1.9] | 0.3, [−0.3, 1.0] | **5.7, [0.8, 10.5] *** | 1.5, [−1.2, 4.2] | **5.5, [0.2, 10.9] *** | 4.0, [−4.5, 12.5] | 12.6, [−20.8, 46.1] |

Table 2. Mean group difference and 95% confidence intervals derived from the linear regression analysis comparing each CBI-R subscale score across each diagnostic group combination. * = $p < 0.05$

**Figure 2. Average baseline (bl) and annualised repeat (rp) CBI-R scores for bvFTD, svPPA and nfvPPA**



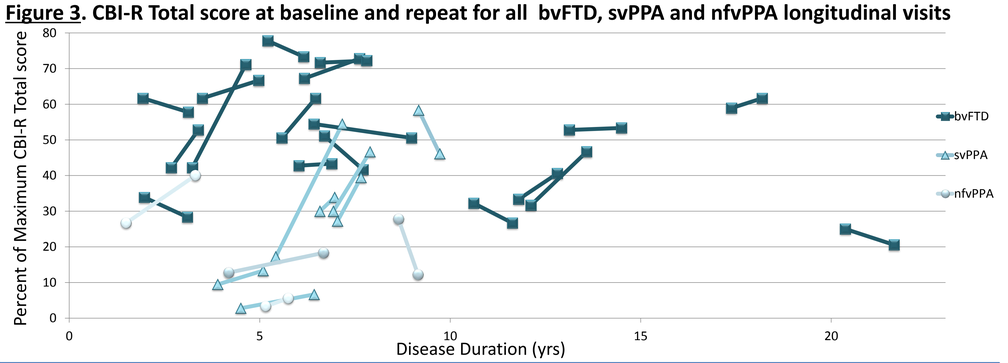

## RESULTS: LONGITUDINAL ANALYSIS

Mean (sd) annual percentage change in CBI-R scores are shown in Table 3. The domains which exhibited the greatest annualised change were *'Self Care'* for bvFTD, *'Motivation', 'Memory and Orientation', 'Everyday Skills'* and *'Eating Habits'* for svPPA and *'Stereotypic and Motor Behaviours'* for nfvPPA, although the large variability in each domain resulting in a non-significant difference (Figure 2). Total CBI-R score was also variable, demonstrating an overall increase in only 9/18 bvFTD, 6/7 svPPA and 3/4 nfvPPA patients (Figure 3).

| | Memory and Orientation | Everyday Skills | Self Care | Abnormal Behaviour | Mood | Beliefs | Eating Habits | Sleep | Stereotypic and Motor Behaviours | Motivation | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| bvFTD - % annual change | 2.7 (11.8) | 2.6 (23.3) | 9.4 (17.7) | 2.5 (15.3) | 1.0 (21.1) | −1.6 (15.7) | 0.7 (12.8) | 3.9 (11.9) | −2.0 (20.3) | 4.8 (12.7) | 2.5 (8.0) |
| svPPA - % annual change | 17.5 (23.7) | 19.8 (14.6) | −0.4 (13.0) | −6.3 (22.3) | −1.0 (17.8) | 0 (0) | 13.8 (28.4) | −15.4 (29.6) | 0.6 (21.0) | 22.2 (50.2) | 7.4 (15) |
| nfvPPA - % annual change | −18.5 (49.0) | −2.25 (19.0) | −4.8 (22.7) | 2.6 (3.3) | −6.1 (12.2) | 0 (0) | 3.0 (3.5) | −13.2 (25.7) | 8.8 (22.4) | −5.2 (23.8) | −4.3 (17.5) |

Table 3. Mean (sd) Annual percentage change in CBI-R score for bvFTD, svPPA and nfvPPA.

**Figure 3. CBI-R Total score at baseline and repeat for all bvFTD, svPPA and nfvPPA longitudinal visits**




## CONCLUSIONS

CBI-R proved useful as a cross-sectional marker in multiple symptomatic domains across the FTD spectrum. bvFTD demonstrated the greatest deficits across all domains, although there were also significant deficits within the svPPA group. The longitudinal variability of CBI-R scores undermines it as a marker of disease progression. This highlights the importance of validating biomarkers longitudinally for clinical research and prior to inclusion as outcomes in putative therapeutic trials.

1. Rascovsky K, Hodges JR, Knopman D, *et al*. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain* 2011;**134**:2456–77
2. Wear HJ, Wedderburn CJ, Mioshi E, et al. The Cambridge Behavioural Inventory Revised, *Dementia &Neuropsychologia* 2008; **2(2)**:102 – 7

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