

Supplementary Material. Binary reversals: a diagnostic sign in primary progressive aphasia, by Eoin Mulroy et al

Table S1. Clinical survey of binary reversals and other behavioural symptoms

Symptom	Explanation	Yes	No	Please give examples:
Binary reversals	Tends to reverse opposites (e.g. Yes/No, Up/Down, etc) when speaking or otherwise communicating (e.g. head nod / shake, etc)			
Disinhibition	Socially inappropriate behaviour, lack of adherence to social norms, loss of manners or decorum			
Apathy	Loss of interest, drive and motivation, decreased initiation of activities			
Obsessiveness	Activities or ideas which s/he engages in or expresses obsessively, e.g. repetitive or ritualistic routines that s/he seems compelled to perform			
Aberrant motor	Paces without purpose, repeatedly dresses or undresses, excessively fidgety			

The survey was completed by each patient's primary caregiver (or equivalent close informant), following an initial explanation by the researcher. For this first study we simply recorded whether or not the symptom had definitely been noted since the onset of the illness. For each item the caregiver was invited to give examples from the patient's daily life.

Table S2. Complete test statistics and sample sizes comparing phenotypic associations in bvFTD patients with and without binary reversals

Characteristic	Absent: n ^a	Present: n ^a	Test Statistic	Degrees of freedom	P value
General					
Sex	15	12	X ² = 0.01 (Fisher exact sig. = 1)	1	0.92
Age at assessment (years)	15	12	t = 2.85	25	<0.01
Symptom duration (years)	15	12	U = 46.00	NA	0.03
MMSE	15	12	t = 1.83	25	0.08
Neuropsychology					
<i>Executive functions</i>					
TMT A	14	12	t = -0.97	24	0.34
TMT B	14	12	t = -1.35	24	0.19
Phonological fluency	14	12	t = 2.22	24	0.04
Category fluency	14	12	t = 0.99	24	0.33
Stroop: Colour	14	12	t = -1.82	24	0.08
Stroop: Word	14	12	U = 126.50	NA	0.03
Stroop: Ink	14	12	t = -1.18	24	0.25
<i>Working memory</i>					
Digit span forward	15	12	U = 55.50	NA	0.09
Digit span reverse	15	12	t = 2.10	25	0.046
<i>Language functions</i>					
GNT	15	12	U = 68.50	NA	0.30
BPVS	14	12	U = 43.50	NA	0.04
NART	14	12	t = 3.10	24	<0.01
<i>Episodic memory</i>					
RMT Faces	15	12	t = 0.37	25	0.72
RMT Words	14	11	t = 0.20	23	0.84
<i>Other skills</i>					
GDA	13	11	t = 1.70	22	0.10
VOSP	13	12	t = 0.76	23	0.45
Behavioural changes					
Disinhibition	15	12	X ² = 0.17 (Fisher exact sig. = 1)	1	0.68
Apathy	15	12	X ² = 0.06 (Fisher exact sig. = 1)	1	0.81
Obsessiveness	15	12	X ² = 0.10 (Fisher exact sig. = 1)	1	0.76
Aberrant motor	15	12	X ² = 0.14 (Fisher exact sig. = 1)	1	0.71
Parkinsonism					
Present	15	12	X ² = 0.68 (Fisher exact sig. = 0.57)	1	0.41

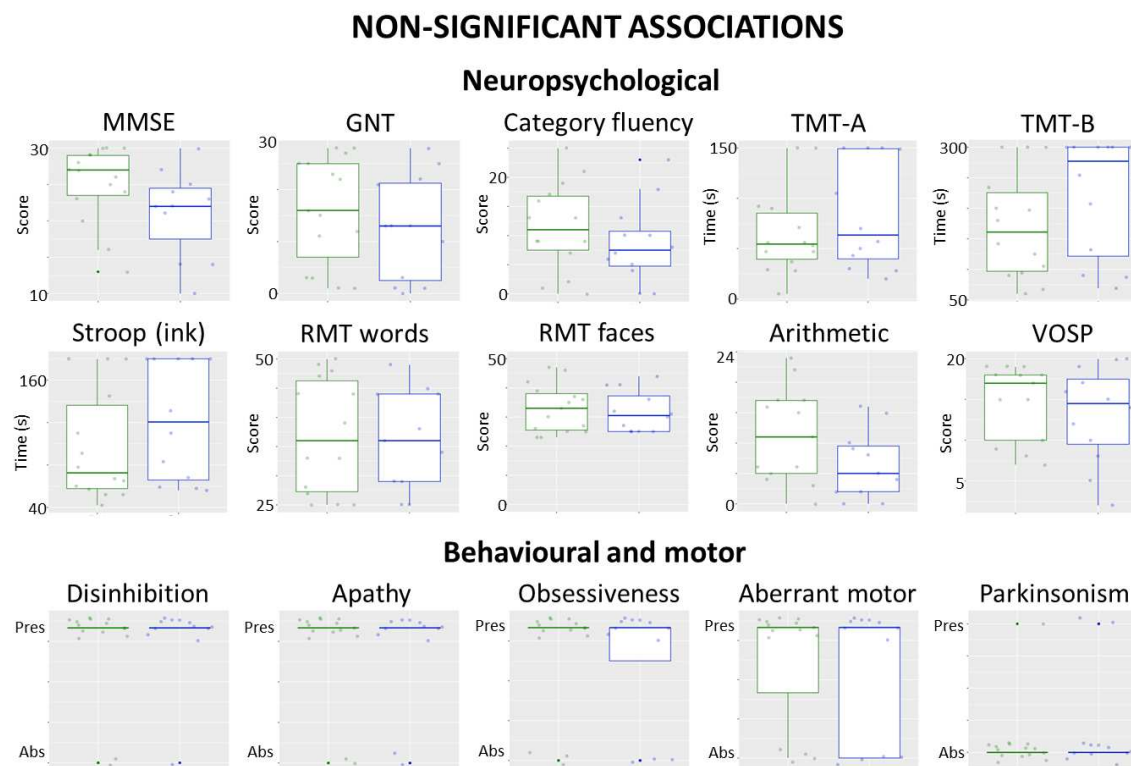
The Table presents results for all comparisons of clinical, neuropsychological and behavioural characteristics between subgroups of behavioural variant frontotemporal dementia (bvFTD) patients with (Present) and without (Absent) binary reversals. Between-group differences were assessed as follows. Mann-Whitney U tests were used to compare Stroop Word, Digit Span forward, GNT, and BPVS scores, due to violations of the normality assumption. Chi² and Fisher's exact tests were used to assess presence of behavioural changes and parkinsonism. Independent sample t-tests were used for all other measures. Significant comparisons (p < 0.05) are in bold. ^aSome patients did not

complete all tests. BPVS, British Picture Vocabulary Scale; GDA, Graded Difficulty Arithmetic Test; GNT, Graded Naming Test; MMSE, Mini-Mental State Examination score; n, number; NA, not applicable; NART, National Adult Reading Test; RMT, Recognition Memory Test; TMT, Trail Making Test Parts A / B; VOSP, Visual Object and Space Perception Battery.

Table S3. Results of binomial logistic regression analysis on the diagnostic predictive value of binary reversals, with and without correcting for covariates.

Comparison	OR	95% CI	p-value
<i>Including covariates</i>			
nfvPPA vs all other syndromes	5.07	2.74, 10.04	<0.001
nfvPPA vs other PPA	5.07	2.74, 10.01	<0.001
nfvPPA vs lvPPA	3.87	1.41, 8.84	<0.001
nfvPPA vs svPPA	5.39	2.94, 11.25	<0.001
nfvPPA vs bvFTD	5.30	2.46, 10.73	<0.001
<i>Without covariates</i>			
nfvPPA vs all other syndromes	4.42	2.35, 9.28	<0.001
nfvPPA vs other PPA	4.79	2.64, 9.67	<0.001
nfvPPA vs lvPPA	3.62	1.30, 8.53	<0.001
nfvPPA vs svPPA	5.87	3.47, 10.83	<0.001
nfvPPA vs bvFTD	3.98	1.82, 8.86	<0.001

This analysis examined the effect of binary reversals on the likelihood of having a diagnosis of nfvPPA versus other syndromes, with (above) and without (below) adjusting for age, symptom duration and MMSE score (see main text). Firth's bias reduction method was applied. bvFTD = behavioural variant frontotemporal dementia; CI = confidence interval; lvPPA = logopenic variant PPA; nfvPPA = non-fluent/agrammatic variant PPA; OR = odds ratio; PPA = primary progressive aphasia; svPPA = semantic variant PPA.

Figure S1. Plots of non-significant phenotypic associations of binary reversals in the behavioural variant frontotemporal dementia group

This Figure is a companion to Figure 1. It shows box-and-whisker plots of other associations (clinical, neuropsychological and behavioural characteristics) assessed in comparisons of patients with and without binary reversals, across individual patients with behavioural variant frontotemporal dementia (the patient group in which associations could be most reliably assessed; see main text). Associations shown here were all non-significant at the prescribed threshold ($p > 0.05$) (significant associations are plotted in Figure 1; see also Table S2). Boxes represent the interquartile range, and whiskers indicate the overall range of values in each group; the horizontal line in each box represents the median; in each panel, data for patients who exhibited binary reversals at the time of assessment are presented on the right (in blue) and data for patients who did not exhibit reversals on the left (in green). **GNT**, Graded Naming Test; **MMSE**, Mini-Mental State Examination score; **RMT**, Recognition Memory Test; s, seconds; **TMT**, Trail Making Test Parts A / B; **VOSP**, Visual Object and Space Perception Battery.