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Interpersonal traits change as a function of disease type and severity in degenerative brain diseases

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Abstract

Background—Different degenerative brain diseases result in distinct personality changes as a result of divergent patterns of brain damage, however, little is known about the natural history of these personality changes throughout the course of each disease.

Objective—To investigate how interpersonal traits change as a function of degenerative brain disease type and severity.

Methods—Using the Interpersonal Adjective Scales, informant ratings of retrospective premorbid and current scores for dominance, extraversion, warmth, and ingenuousness were collected annually for one to four years on 188 patients [67 behavioural variant frontotemporal dementia (bvFTD), 40 semantic dementia (SemD), 81 Alzheimer's disease (AD)] and 65 older healthy controls. Using random coefficient models, interpersonal behaviour scores at very mild, mild, or moderate-to-severe disease stages were compared within and between patient groups.

Results—Group-level changes from premorbid personality occurred as a function of disease type and severity, and were apparent even at a very mild disease stage (Clinical Dementia Rating=0.5) for all three diseases. Decreases in interpersonal traits associated with emotional affiliation (i.e., extraversion, warmth, and ingenuousness) and more rigid interpersonal behaviour differentiated bvFTD and SemD patients from AD patients.

Conclusions—Specific changes in affiliative interpersonal traits differentiate degenerative brain diseases even at a very mild disease stage, and patterns of personality change differ across bvFTD, SemD, and AD with advancing disease. This study describes the typical progression of change of interpersonal traits in each disease, improving the ability of clinicians and caregivers to predict and plan for symptom progression.

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Keywords

neurodegenerative diseases; dementia; personality; affiliation; mixed effects model

INTRODUCTION

Personality - an individual's habitual pattern of cognition, emotion, and behaviour - can change dramatically in people with traumatic brain injury or degenerative brain disease.^{1, 2} Depending on the neuroanatomic localization of brain damage, personality changes differ in degree and direction, allowing differentiation among various degenerative brain diseases^{2, 3} and between degenerative and non-degenerative brain diseases.^{4, 5} Recently, disease-specific personality changes have been associated with degenerative lesions to specific brain structures.⁶

Given these brain structure-personality relationships, it seems likely that personality changes not only as a function of disease type but also of disease severity. Indeed, personality changes such as decrease in extraversion and increase in neuroticism occur in the early stages of Alzheimer's disease (AD),⁷ and behavioural changes such as passivity and self-centred, agitated behaviour increase as the disease progresses.^{8, 9} Two longitudinal studies have suggested that personality change may precede the clinical diagnosis of AD.^{10, 11} In contrast, little is known about personality changes as a function of disease severity in other degenerative brain diseases such as behavioural variant frontotemporal dementia (bvFTD) or semantic dementia (SemD). Thus far, studies measuring personality in these diseases have grouped together patients at different disease stages,^{2, 3} presumably to compensate for small sample sizes. This approach has prohibited direct comparison of personality changes across diseases at a similar disease stage, an important step towards improved differential diagnosis of these diseases.

In this study, we hypothesized that changes in specific interpersonal traits would be apparent at a very mild disease stage in bvFTD, SemD, and AD, and that these traits would change as a function of disease type and severity. To test these hypotheses, we collected premorbid and current quantitative scores for four interpersonal traits at yearly intervals for bvFTD, SemD, and AD patients at very mild, mild, or moderate-to-severe disease stages. Using random coefficient models, interpersonal trait scores were then compared within and between patient groups.

METHODS

Subjects

A total of 188 patients, of whom 67 were diagnosed with behavioural variant frontotemporal dementia (bvFTD),¹² 40 with semantic dementia (SemD),¹² and 81 with Alzheimer's disease (AD),¹³ were recruited into the study, along with 65 older normal controls (NC) (table 1). 117 (62%) of the 188 patients and 42 (65%) of the 65 NCs were previously included in a recent neuroimaging study of interpersonal traits.⁶ Older NCs were included to create a gender-specific normative dataset of interpersonal T-scores based on informant ratings and to compare their interpersonal traits scores with those of the patients at their premorbid stage.

Procedures

Patients were identified from the clinic subject pool by diagnosis and were then recruited as potential study participants. Informants/Caregivers filled out the Interpersonal Adjective

Scales (IAS) questionnaire¹⁴ describing the subjects' current interpersonal traits, and the Clinical Dementia Rating (CDR) Scale¹⁵ was completed via family interview with clinicians. Informants also provided a retrospective description of the patients' premorbid personality for 83% of the patients. Additional IAS and CDR measures were collected longitudinally in 30% of the patients (ranging from one to four follow-ups) and in 17% of the NCs (ranging from one to three follow-ups). Retrospective and repeated assessments totalled 567 observations (425 for patients, 142 for NCs). At each assessment, a patient's disease stage was classified as very mild (CDR=0.5), mild (CDR=1.0), or moderate-to-severe (CDR $\geq$ 2). Notably, the distribution of patients with a CDR of 2 or 3 was similar in the three diagnostic groups (bvFTD: mean CDR = 2.3 $\pm$ 0.5; SemD: mean CDR = 2.2 $\pm$ 0.4; AD: mean CDR = 2.0 $\pm$ 0.2).

Measures

The IAS is a well-validated self- or other-report questionnaire based on the circumplex model of personality, which aims to measure individual differences in interpersonal traits (fig 1).¹⁴ The instrument and the rationale for using informant rather than self-reports have been detailed elsewhere.¹⁶ Patients' T-scores were generated based on our sample of 65 older NCs, which was rigorously screened to exclude early neurologic or psychiatric disease, and on whom informant data was collected, making this a more appropriate standardization sample for our patients than the community-based, self-rated normative sample collected by the IAS developers.¹⁷ Separate T-scores for men and women were generated.

Based on recent neuroimaging findings for IAS interpersonal traits,⁶ we derived four interpersonal composite trait scores from the eight IAS trait scores (i.e., dominance, submissiveness, extraversion, introversion, warmth, coldness, ingenuousness, and arrogance) and labelled them as Dominance, Extraversion, Warmth, and Ingenuousness. (For more details on subjects and measures, see the supplementary data).

Data Analyses

General linear models were used to compare diagnostic groups for age, education, CDR sum of box scores, Mini-Mental State Examination (MMSE), Neuropsychiatric Inventory (NPI) Total Score,¹⁸ and Geriatric Depression Scale (GDS)¹⁹ at time of initial presentation. Chi-square tests were used to assess for group differences in gender distribution. Interpersonal trait and vector length T-scores were considered clinically abnormal if they fell more than 1.5 SD from the mean, i.e., scores below 35 or above 65. Statistical differences are reported whether or not clinical differences are seen.

To appropriately handle the semi-longitudinal nature of the data, random coefficient models using SAS Proc Mixed²⁰ were used to generate estimates of interpersonal trait and vector length T-scores for patient groups at four clinical stages (premorbid stage, very mild (CDR=0.5), mild (CDR=1.0), and moderate-to-severe (CDR $\geq$ 2.0) disease stages) and for the NC group (CDR=0). Patients' CDR scores did not necessarily change year to year, so patients with repeated measurements could be classified into the same CDR group more than once. We created two types of random coefficient models, described below, adjusting for age and gender in both (see the syntax in the supplementary data).

Univariate Model—To examine group differences for each interpersonal trait (Dominance, Extraversion, Warmth, and Ingenuousness) and the vector length (measure of an individual's flexibility in social interactions) separately, estimates of trait and vector length T-scores were generated for NCs and each patient group at each clinical stage and were compared: First, each patient group's premorbid scores were compared with NCs (e.g.,

premorbid Extraversion score of bvFTDs vs. Extraversion score of NCs). Second, scores at two different clinical stages were compared within a patient group (e.g., premorbid Extraversion score of bvFTDs vs. Extraversion score of bvFTDs with a CDR of ≥ 2.0). Third, scores at the same disease stage were compared between two patient groups (e.g., Extraversion score of bvFTDs with a CDR of 1.0 vs. Extraversion score of ADs with a CDR of 1.0).

Multivariate Model—To directly compare patterns of change of each trait against the other traits, estimates of interpersonal trait T-scores (Dominance, Extraversion, Warmth, and Ingenuousness) for each patient group were compared at the same clinical stage (e.g., Extraversion vs. Dominance scores of bvFTDs with a CDR of 1.0).

To correct for multiple comparisons, Fisher's least significant difference (LSD) was used to test the global hypothesis of each statistical model at $p < .05$. In the univariate analyses, a deviation statistic was calculated between the conditional means model, consisting of the covariates age and gender, and the overall model, consisting of CDR, diagnostic group, CDR*diagnostic group, age, and gender. In the multivariate analyses, a deviation statistic was calculated between the conditional means model, consisting of the covariates age and gender, and the overall model, consisting of CDR, interpersonal traits, CDR*interpersonal traits, age, and gender. Pair-wise comparisons were carried out at the same level of significance ($p < .05$) only when the deviation statistic was statistically significant.

RESULTS

Average patient age was 64 years old (range 42–86), and mean education level was 16 years (range 8–24). Patients in all three disease groups initially presented to clinic a median of 4 years after symptom onset, with interquartile ranges of 2–6 years for all three groups regardless of CDR score, suggesting that duration of clinical symptoms was not an appropriate proxy for disease severity.

The global hypothesis of each statistical model in the univariate and multivariate analyses was statistically significant ($p < .05$); thus all planned pair-wise comparisons could be performed at the same level of significance.

Normal Control and Premorbid Scores

No significant differences were found between interpersonal trait and vector length scores of NCs and premorbid scores of the bvFTD, SemD, or AD group ($p < .05$), suggesting there were no pre-existing personality differences across diagnostic groups.

Comparison of trait and vector length scores within patient groups (tables 2–4, fig 2)

In the bvFTD group, Dominance and Extraversion scores were significantly lower at all disease stages than at the premorbid stage ($p < .05$). In addition, both scores were abnormally low (< 35) at all disease stages. Warmth score showed a significant drop at the very mild stage of disease (CDR=0.5), but did not drop to a clinically abnormal level until the mild disease stage (CDR=1.0). Ingenuousness score was not clinically abnormal or significantly different from the premorbid level at any disease stage. The vector length (representing rigidity of interpersonal behaviour) was abnormally high (> 65) at the mild and moderate-to-severe disease stages. Extraversion, Warmth, and vector length scores changed significantly as a function of disease severity, whereas Dominance and Ingenuousness scores did not.

In the SemD group, Dominance and Warmth scores became abnormally low only at the moderate-to-severe disease stage (CDR ≥ 2.0), though both showed an early (CDR=0.5)

significant drop from premorbid levels. Extraversion score already showed a significant drop to an abnormally low level at the very mild disease stage. The vector length score became abnormally high only at the moderate-to-severe disease stage ($CDR \geq 2.0$). Extraversion, Warmth, Ingenuosness, and vector length scores changed significantly as a function of disease severity, whereas Dominance score did not.

In the AD group, Dominance score became abnormally low at the mild disease stage ($CDR=1.0$) and decreased significantly as a function of disease severity ($p < .05$). Though Extraversion score showed a significant drop at the very mild disease stage ($CDR=0.5$), it did not decrease significantly as a function of disease severity and never decreased to a clinically abnormal level. Warmth, Ingenuosness, and vector length scores were not abnormal or significantly different from premorbid levels at any disease stage.

Comparison of trait and vector length scores between patient groups (table 5, fig 3)

Comparison of the bvFTD and SemD groups with the AD group: All trait scores except Dominance score were significantly lower in bvFTD than AD patients beginning at the very mild disease stage ($CDR=0.5$) and the vector length score was significantly higher beginning at the mild disease stage ($CDR=1.0$). A similar pattern of contrast was seen with the SemD group, except Ingenuosness score became significantly lower in SemD than AD patients at the mild disease stage, and the vector length became significantly higher at the moderate-to-severe disease stage ($CDR \geq 2.0$).

Comparison of the bvFTD group with the SemD group: The bvFTD group became significantly less extraverted and less warm than the SemD group by the time their disease was at the mild level of severity ($CDR=1.0$), and their vector length score was significantly higher at this time. By contrast, at the time the diseases reached the moderate-to-severe stage ($CDR \geq 2$), these differences had evened out and the SemD patients were no longer significantly different from the bvFTD patients on any interpersonal factor.

Comparisons between trait scores within patient groups at the same clinical stage (fig 2)

In the bvFTD group, the four interpersonal trait scores did not differ significantly from each other at the premorbid stage ($p < .05$). At all three disease stages Dominance, Extraversion, and Warmth scores were significantly lower than Ingenuosness score. In addition, at the mild disease stage Extraversion score was significantly lower than Dominance score, and at the moderate-to-severe disease stage Extraversion score was significantly lower than Dominance and Warmth scores.

The four interpersonal trait scores did not differ significantly in the SemD group at the premorbid stage ($p < .05$), however, as in the bvFTD group, Dominance, Extraversion, and Warmth scores dropped significantly lower than Ingenuosness score at all three disease stages. In addition, at the very mild disease stage Extraversion score was significantly lower than Warmth score, and at the moderate-to-severe disease stage Extraversion score was significantly lower than Dominance score.

In the AD group, the four interpersonal trait scores did not differ significantly from each other at the premorbid stage ($p < .05$). At all three disease stages Dominance score was significantly lower than Extraversion, Warmth, and Ingenuosness scores, and Extraversion score was significantly lower than Warmth and Ingenuosness scores.

DISCUSSION

This is the first study to systematically measure the progression of change of interpersonal traits in different degenerative brain diseases, as well as to directly compare these patterns of

change across diseases. bvFTD, SemD, and AD patients showed changes in specific personality traits at a very mild stage of disease, and these traits changed with disease progression. bvFTD and SemD patients could be differentiated from AD patients based on their progressively decreasing extraversion, warmth, and ingenuousness (i.e., interpersonal traits associated with emotional affiliation) and their increasing interpersonal rigidity. Among these behaviours, lack of warmth best differentiated bvFTD and SemD patients from AD patients at all disease stages.

An important methodological advantage of this study was the use of random coefficient (mixed) models for estimating group values of interpersonal traits and vector length over disease stages. These models allowed us to analyze repeated measures, collected in a subset of patients, providing more statistical power than a cross-sectional approach. Another advantage of using random coefficient modelling is that group means are not simply averaged, but the reliability of measures and the number of observations in a group are taken into account.²¹ Because of the procedural difficulties involved in collecting longitudinal data in neurodegenerative disease patients, and the high prevalence of missing data points in real-world datasets, this analytic method provides a distinct advantage for analysis of symptom progression.

Progression of change of interpersonal traits in bvFTD

Compared to retrospective accounts of their premorbid personality, dominance, extraversion, and warmth were significantly decreased in bvFTD patients at all disease stages, whereas ingenuousness did not change during the disease. These findings are consistent with the reported neural substrates of these interpersonal traits, as well as with the known course of regional atrophy in bvFTD. A neuroimaging study of interpersonal traits in patients with degenerative brain diseases showed that affiliative traits, including warmth and extraversion, relate primarily to right>left ventromedial frontal, anterior insular, and anterior temporal structures.⁶ These structures, in particular the frontoinsula paralimbic circuit, are part of the earliest and most strongly affected structures in bvFTD patients.^{22, 23} Traits involving interpersonal agency, such as dominance and extraversion, correspond primarily to dorsolateral prefrontal and lateral frontopolar structures,⁶ which sustain mild atrophy in bvFTD patients at the earliest phase of the disease (CDR=0.5), but which sustain more extensive atrophy with disease progression.²² In contrast, neural substrates of ingenuousness, involving more posterior right temporal structures,⁶ are affected later and less severely than prefrontal structures in bvFTD patients.^{22, 23}

Given the predominance of frontoinsula paralimbic over dorsolateral frontal damage in early bvFTD, the finding that dominance, extraversion, and warmth were decreased to a similar degree in very mild bvFTD patients was unexpected. Also, unlike extraversion and warmth, dominance did not decrease as a function of disease severity in bvFTD patients, despite evidence that dorsolateral prefrontal structures associated with dominance do show progressive damage across disease stages.²² This finding is consistent with another study which found dominance similarly decreased across brain diseases with divergent patterns of focal atrophy such as bvFTD, SemD, corticobasal syndrome, and progressive supranuclear palsy.⁶ Thus, dominance seems influenced by factors that are unrelated to dorsolateral prefrontal and frontopolar structures. In bvFTD patients, clinical factors such as apathy, disinhibition, and cognitive deficits²⁴ and/or biochemical factors such as the serotonin imbalance²⁵ might play an important role.

As a sign of inflexible and rigid interpersonal behaviour, the vector length was significantly increased in bvFTD patients at all disease stages and increased as a function of disease severity, consistent with the increasingly stereotyped and dysfunctional interpersonal behaviour observed in bvFTD patients.²⁴

Progression of change of interpersonal traits in SemD

Like bvFTD patients, SemD patients became less dominant, less extraverted, and less warm in interpersonal interactions even at the very mild disease stage (CDR=0.5). Extraversion and warmth decreased significantly as a function of disease severity, consistent with studies showing that SemD progressively involves the frontoinsula paralimbic regions²⁶ that overlap considerably with neural substrates of extraversion and warmth.⁶ SemD patients differed most substantially from bvFTD patients at the moderate stage (CDR=1.0) of disease, when these two personality traits plateaued temporarily before again dropping to bvFTD levels at the moderate-to-severe disease stage. As in bvFTD patients, dominance showed a non-specific pattern that did not change significantly as a function of disease severity and was largely unrelated to known patterns of SemD atrophy,²⁶ highlighting the complex and non-specific characteristics of this trait as measured by the IAS.

SemD has traditionally been conceptualized as a primary aphasia, thus these significant early personality changes may seem unexpected. However, because the Nears research criteria for SemD focus on language rather than behavioural symptoms, patients meeting criteria for the disease are likely to have left temporal pathology, yet may have highly divergent degrees of concomitant right temporal pathology, even early in the disease.²⁷ Thus, many of the socioemotional changes seen in bvFTD patients that originate in right temporal pathology may also be seen in SemD patients, which is consistent with our data. However, our data also suggest that personality is the most clinically heterogeneous in the SemD group, thus these results should only be applied to individual patients with caution. In particular, patients with predominantly left-sided disease are less likely to show these significant bvFTD-like personality change at early stages.

SemD patients were rated as less ingenuous (more arrogant) in the mild (CDR=1.0) and moderate-to-severe (CDR $\geq$ 2.0) disease stages, and became significantly more arrogant with disease progression, a pattern not observed in either bvFTD or AD groups. This finding is consistent with the primarily right temporal neural substrate of ingenuousness,⁶ and with studies suggesting that SemD patients with right temporal damage are more likely to engage in antisocial behaviours.^{26, 28, 29}

Patients' level of rigidity in interpersonal behaviours did not become pathologically elevated until the moderate-to-severe stage (CDR $\geq$ 2.0). As noted above, though patients who met diagnostic criteria for SemD in this study were clinically heterogeneous, and only the subset with predominantly right-temporal involvement^{28, 30} would be expected to show rigid and dysfunctional interpersonal behaviour at a very mild disease stage.

Progression of change of interpersonal traits in AD

AD patients already showed significantly decreased dominance and extraversion at the very mild stage of disease (CDR=0.5). Previous studies have reported similar decreases in traits involving high levels of interpersonal agency. Using the Blessed Dementia Scale (BDS),³¹ Balsis and colleagues found that individuals who later converted to AD were more apathetic (24% vs. 8%) and more egocentric (21% vs. 4%) than healthy older people.¹⁰ Similarly, using the five-factor model of personality,³² Duchek and colleagues found less extraversion in very mild AD patients than in healthy older people.⁷ The development of increased apathy and decreased dominance and extraversion is consistent with greater interpersonal passivity beginning early in AD.

In contrast to bvFTD and SemD, dorsal prefrontal brain regions are more affected in AD than frontoinsula paralimbic structures, which remain relatively intact even at an advanced stage.^{33–35} This may explain the absence of significant changes in warmth and, to a lesser degree, in ingenuousness in AD patients at any point of the disease. Given the lack of

apparent correlation between loss of dominance and dorsolateral atrophy pattern in bvFTD and SemD patients, however, the fact that dominance does decrease with disease progression in AD patients can only be cautiously attributed to their progressive dorsolateral atrophy, and other biochemical and cognitive factors must also be considered.

The fact that frontoinsula regions which are crucial for emotion processing^{36, 37} are minimally affected in most AD patients^{33–35} might explain why inflexible interpersonal behaviour was not observed at any disease stage. This finding supports the clinical observation that AD patients behave socially appropriately throughout most of the disease course, although in very severe (MMSE<10) patients social inappropriateness tends to emerge.⁹

Implications of disease-specific patterns of change in interpersonal traits

bvFTD patients are well-known to experience early and drastic changes in their capacity for affectionate, affiliative behaviours³⁸, but our results suggest that as a group, SemD patients experience a similar initial loss of warmth, extraversion, and ingenueness, and show increasingly pathological interpersonal behaviour with disease progression. SemD was the only group rated as becoming progressively more socially calculating (e.g., described as “crafty”, “wily”, “sly”) at the moderate-to-severe disease stage, likely due to their increasing right-temporal pathology in the context of largely preserved frontal structures. The overlap in loss of capacity for affiliative interpersonal behaviour between bvFTD and SemD groups likely occurs because both diseases damage brain regions associated with emotion processing such as the orbitofrontal cortex, the insula, and the temporal poles, albeit at different rates and times.^{36, 37, 39} These same affiliative behaviours remain unchanged in AD patients even at the moderate-to-severe stage of their disease, likely because these same emotion-related regions are preserved.^{33–35}

While another study suggests that loss of dominance is associated with loss of grey matter volume in left>right dorsolateral prefrontal and lateral frontopolar structures,⁶ the loss of dominance seen in this study in all three diseases was likely multifactorial. Factors potentially include changes in patients’ biochemical, cognitive, and social-environmental status, in addition to focal atrophy. Additional investigation into the relative contributions of these factors to patients’ loss of social dominance is warranted.

Limitations

CDR, an instrument developed for staging AD clinically, is limited for staging bvFTD and SemD because it lacks domains specifically affected in these brain diseases, in particular changes in behaviour and personality (bvFTD and SemD with predominantly right-temporal involvement) and changes in language (SemD with predominantly left-temporal involvement). New staging tools for frontotemporal lobar degeneration (FTLD) (i.e., bvFTD, SemD, and progressive non-fluent aphasia) such as the FTLD-modified CDR⁴⁰ and the Frontotemporal Dementia Rating Scale (FRS),⁴¹ have been developed recently, and would be recommended for future studies. Another limitation of this study is that despite using random coefficient modelling, statistical power was limited by the modest number of observations in few groups, especially in the very mild stage of bvFTD (11 observations) and in the moderate-to-severe stage of SemD (15 observations), suggesting that only moderate to large effects would reach statistical significance in these groups. Finally, the current research criteria defining the clinical syndromes for all three of these diseases allows patients with heterogeneous neuroanatomy and even neuropathology to be classified in the same diagnostic group. This results in substantial within-group heterogeneity, as well as between-group overlap in behavioural symptoms, particularly between SemD and bvFTD syndromes.⁴² This is certainly true of our study, in which patients have not undergone

additional subgroup classification based on anatomic markers (e.g., further dividing SemD patients based on degree of right temporal pathology). Until more precise clinical diagnostic categories are defined which delineate clinical syndromes with better sensitivity and specificity, findings on a disease-group level need to be interpreted cautiously at an individual patient-level.

Conclusions

Changes of interpersonal traits in bvFTD, SemD, and AD patients occur as a function of disease type and severity, providing further evidence of direct brain-behaviour relationships for some aspects of personality. While patients with all three diseases experienced loss of social dominance early, only bvFTD and SemD patients showed progressive alterations in their capacity for affiliative social behaviour, consistent with the severity of damage known to occur in emotion-related frontoinsula and anterior temporal cortex. While these changes occur on a disease group level and many individual patients will diverge from these patterns, this study provides information about the typical progression of change of interpersonal traits in each disease that may improve the ability of clinicians and caregivers to predict the patient's symptom progression.

The analytic design of this study maximized the use of partial longitudinal data points to obtain more accurate estimates than a cross-sectional design would permit. Given the difficulty of obtaining many time-points of longitudinal data on a complete cohort of neurodegenerative disease patients, mixed modelling is an effective alternative to throwing out "extra" longitudinal data points to perform a cross-sectional analysis.

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Figure 1.
The Interpersonal Circumplex of the Interpersonal Adjective Scales: Eight interpersonal traits, derived from two orthogonal dimensions, agency and affiliation, are evenly distributed around the circumference.

Figure 2. Comparison of the four interpersonal trait T-scores within each patient group (bvFTD, SemD, and AD) as a function of clinical stages. A random coefficient model (univariate model) using SAS Proc Mixed was used to estimate the group's values at the different clinical stages, controlling for age and gender. Values are estimates and standard errors. For abbreviations see table 1.

Figure 3.

Comparison of the four interpersonal trait and vector length T-scores between the bvFTD, SemD, and AD groups as a function of clinical stages. A random coefficient model (univariate model) using SAS Proc Mixed was used to estimate the group's values at the different clinical stages, controlling for age and gender. Values are estimates and standard errors. For abbreviations see table 1.

Table 1

Subject characteristics at first presentation classified by diagnostic group. The *F*-ratio is for overall diagnostic group differences in age, gender, and education and for overall patient group differences in CDR box score sum, MMSE, NPI total, and GDS. Values are listed as mean (standard deviation).

	NC n = 65	bvFTD n = 67	SemD n = 40	AD n = 81	F-ratio(df)
Age, y	66.8 (8.8)	61.4 (8.2)	63.7 (7.8)	65.6 (10.6)	$F_{(3, 249)} = 4.44^*$
Gender (M/F)	22/43	39/28	25/15	41/40	$\chi^2_{(3, N=253)} = 11.09^*$
Education, y	17.2 (2.5)	15.7 (2.6)	16.2 (2.9)	15.6 (3.1)	$F_{(3, 239)} = 4.74^*$
CDR box score sum	NA	7.7 (3.7)	4.8 (3.0)	5.1 (2.9)	$F_{(4, 183)} = 13.73^*$
MMSE	29.7 (0.6)	21.3 (8.9)	20.6 (8.3)	19.8 (5.8)	$F_{(4, 174)} = 0.96^*$
NPI total	NA	36.0 (19.6)	30.3 (21.7)	8.6 (12.5)	$F_{(4, 150)} = 37.34^*$
GDS	2.4 (2.7)	7.4 (6.4)	7.5 (5.1)	6.7 (5.7)	$F_{(4, 118)} = 0.24$

Abbreviations: NC, Normal Controls; bvFTD, Behavioural Variant Frontotemporal Dementia; SemD, Semantic Dementia; AD, Alzheimer's Disease; CDR, Clinical Dementia Rating [0.5 (very mild), 1.0 (mild), and ≥ 2 (moderate-to-severe disease stage)], box score sum: 0–18]; MMSE, Mini-Mental State Examination (0–30); NPI, Neuropsychiatric Inventory (0–144); GDS, Geriatric Depression Score (0–30)

* $p < .05$ between groups

Table 2

Comparison of interpersonal trait and vector length T-scores between different clinical stages in the bvFTD group. A random coefficient model (univariate model) using SAS Proc Mixed was used to generate estimates of interpersonal trait and vector length T-scores at different clinical stages, adjusting for age and gender. Values are listed as estimates (standard error).

	Behavioural Variant Frontotemporal Dementia (bvFTD)			
	premorbid	CDR 0.5	CDR 1.0	CDR ≥2.0
	obs. = 57	obs. = 11	obs. = 41	obs. = 40
Dominance	46.8 (1.5)	30.4 (3.0) *	31.0 (1.7) *	31.6 (1.7) *
Extraversion	50.3 (1.8)	33.3 (3.6) *	26.6 (2.0) *	22.7 (2.0) *†
Warmth	48.7 (1.6)	37.6 (2.9) *‡	30.6 (1.7) *†	28.6 (1.7) *†
Ingenuousness	49.2 (1.2)	45.4 (2.3)	46.8 (1.3)	46.6 (1.4)
Vector length	51.3 (1.6)	59.2 (3.5) *	66.5 (1.9) *	69.7 (1.9) *†

CDR 0.5 (very mild), 1.0 (mild), and ≥2 (moderate-to-severe disease stage); for other abbreviations see table 1.

* $p < .05$ vs. premorbid;

† $p < .05$ vs. CDR 0.5;

‡ $p < .05$ vs. CDR 1.0

Bold type signifies a score which fell more than 1.5 SD from the mean, i.e., scores below 35 or above 65.

Table 3

Comparison of interpersonal trait and vector length T-scores between different clinical stages in the SemD group. A random coefficient model (univariate model) using SAS Proc Mixed was used to generate estimates of interpersonal trait and vector length T-scores at different clinical stages, adjusting for age and gender. Values are listed as estimates (standard error).

	Semantic Dementia (SemD)			
	premorbid	CDR 0.5	CDR 1.0	CDR ≥2.0
	obs. = 36	obs. = 25	obs. = 20	obs. = 15
Dominance	49.6 (1.8)	37.4 (2.2) *	36.6 (2.3) *	33.0 (2.6) *
Extraversion	49.0 (2.2)	32.3 (2.6) *	34.5 (2.8) *	27.0 (3.1) *†
Warmth	47.4 (1.9)	37.7 (2.3) *	38.0 (2.4) *	29.1 (2.6) *†‡
Ingenuousness	50.0 (1.5)	50.9 (1.8) ‡	44.9 (1.8) *†	42.8 (2.0) *†
Vector length	52.4 (2.0)	59.9 (2.5) *	56.8 (2.7)	66.9 (3.0) *‡

CDR 0.5 (very mild), 1.0 (mild), and ≥2 (moderate-to-severe disease stage); for other abbreviations see table 1.

* $p < .05$ vs. premorbid;

† $p < .05$ vs. CDR 0.5;

‡ $p < .05$ vs. CDR 1.0

Bold type signifies a score which fell more than 1.5 SD from the mean, i.e., scores below 35 or above 65.

Table 4

Comparison of interpersonal trait and vector length T-scores between different clinical stages in the AD group. A random coefficient model (univariate model) using SAS Proc Mixed was used to generate estimates of interpersonal trait and vector length T-scores at different clinical stages, adjusting for age and gender. Values are listed as estimates (standard error).

	Alzheimer's Disease (AD)			
	premorbid	CDR 0.5	CDR 1.0	CDR ≥2.0
	obs. = 63	obs. = 35	obs. = 56	obs. = 25
Dominance	47.9 (1.3)	35.6 (1.8) *	33.0 (1.5) *	26.9 (2.2) * ^{†‡}
Extraversion	51.5 (1.6)	42.6 (2.1) *	41.4 (1.7) *	37.3 (2.6) *
Warmth	52.3 (1.4)	49.9 (1.8)	49.3 (1.5)	48.5 (2.2)
Ingenuousness	51.1 (1.1)	51.0 (1.4)	51.3 (1.2)	51.3 (1.7)
Vector length	52.6 (1.5)	54.1 (2.0)	54.9 (1.6)	57.1 (2.4)

CDR 0.5 (very mild), 1.0 (mild), and ≥2 (moderate-to-severe disease stage); for other abbreviations see table 1.

* $p < .05$ vs. premorbid;

[†] $p < .05$ vs. CDR 0.5;

[‡] $p < .05$ vs. CDR 1.0

Bold type signifies a score which fell more than 1.5 SD from the mean, i.e., scores below 35 or above 65.

Table 5

Comparison of interpersonal trait and vector length T-scores between patient groups at the same disease stage. A random coefficient model (univariate model) using SAS Proc Mixed was used to estimate the group's values of interpersonal trait and vector length T-scores at the same disease stage, adjusting for age and gender. Values are listed as estimates (standard error).

	Dominance	Extraversion	Warmth	Ingenueness	Vector length
bvFTD - AD					
CDR 0.5	-5.2 (3.5)	-9.3 (4.2)*	-12.4 (3.5) [†]	-5.6 (2.7)*	5.1 (4.1)
CDR 1.0	-2.0 (2.3)	-14.7 (2.7) [‡]	-18.7 (2.3) [‡]	-4.5 (1.8)*	11.6 (2.5) [‡]
CDR ≥2.0	4.7 (2.8)	-14.6 (3.3) [‡]	-19.9 (2.8) [‡]	-4.7 (2.2)*	12.5 (3.1) [‡]
ScmD - AD					
CDR 0.5	1.8 (2.8)	-10.3 (3.4)*	-12.2 (2.9) [‡]	-0.1 (2.2)	5.8 (3.2)
CDR 1.0	3.6 (2.8)	-6.8 (3.3)*	-11.2 (2.8) [‡]	-6.3 (2.2)*	1.8 (3.1)
CDR ≥2.0	6.1 (3.4)	-10.3 (4.0)*	-19.4 (3.4) [‡]	-8.5 (2.6)*	9.7 (3.9)*
bvFTD - ScmD					
CDR 0.5	-6.9 (3.7)	1.0 (4.4)	-0.2 (3.7)	-5.5 (2.9)	-0.7 (4.3)
CDR 1.0	-5.7 (2.9)	-8.0 (3.4)*	-7.5 (2.9)*	1.9 (2.3)	9.8 (3.2)*
CDR ≥2.0	-1.3 (3.1)	-4.4 (3.7)	-0.5 (3.1)	3.8 (2.4)	2.8 (3.6)

CDR 0.5 (very mild), 1.0 (mild), and ≥2 (moderate-to-severe disease stage); for other abbreviations see table 1.

* $p < .05$;

[†] $p < .001$;

[‡] $p < .0001$ between the two diagnostic groups