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Language and Behavior Domains Enhance the Value of the Clinical Dementia Rating Scale

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Abstract

Background—The standard 6 domain Clinical Dementia Rating Scale (CDRstd) scale has been successful for staging patients with the clinical syndrome of probable Alzheimer's disease (AD). The CDRstd does not specifically address language dysfunction or alteration in personality and social behaviors which are prominent in behavioral variant frontotemporal dementia (bvFTD) and Primary Progressive Aphasia (PPA).

Objective—To determine the value of adding domains of Language (LANG) and Behavior, Comportment and Personality (BEHAV) to the CDRstd for the evaluation of patients with bvFTD and PPA.

Methods—Two new domains, LANG and BEHAV, were constructed to parallel the 6 domains sampled in the CDRstd. Clinical and neuropsychological test data were obtained from the National Alzheimer's Coordinating Center. The data set contained information on 2550 probable AD, 88 Vascular Dementia, 281 Dementia with Lewy Body, 234 bvFTD and 137 PPA patients.

Results—There were 76.5% of bvFTD and 99.3% of PPA patients with abnormal ratings (>0) on the LANG domain; 90.2% of bvFTD and 63.5% of PPA had abnormal ratings on the BEHAV domain. In patients with a CDRstd sum of boxes score <4, 53.7% of bvFTD had BEHAV domain and 78.6% of PPA patients had LANG domain scores >1. Among probable AD patients, 3.7% had scores in LANG that were ≥ 1 and 3.8% had scores in BEHAV that were ≥ 1. Logistic regression analyses showed that adding either the LANG or BEHAV domains to the CDRstd sum of boxes score significantly improved the discrimination between probable AD, bvFTD and PPA.

Conclusions—The new LANG and BEHAV domains add value to the CDRstd for the characterization of the non-amnesic symptoms that are prominent in patients with bvFTD and PPA but that also occur in those with probable AD.

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Keywords

Alzheimer disease; frontotemporal dementia; primary progressive aphasia; rating scales

Rating scales that depend upon clinical judgment are important tools for the characterization and longitudinal evaluation of patients with neurodegenerative diseases. One such scale is the Clinical Dementia Rating Scale (CDR)¹. The 6 domains of cognitive and functional levels that comprise the standard CDR (CDRstd) capture a substantial portion of the clinical symptoms in probable Alzheimer's disease (AD) across the spectrum of disease severity. A unique strength of the CDRstd is that clinicians are able to integrate structured information from a knowledgeable informant and from the patient in order to arrive at a global rating for each domain. That integration by a skilled clinician is what makes the CDRstd a favored rating scale for a wide variety of applications from clinical trials (eg,²) to clinical-biological correlation studies (eg,³).

The CDRstd was developed to sample symptoms and signs in six distinctive domains associated with probable AD. Three domains that query level of ability in Episodic Memory, Orientation and Judgment and Problem Solving involve both assessments of the patient as well as information from an informant. The remaining 3 domains, Community Activities, Hobbies, and Personal Care, are evaluated based on information from the informant. Missing from the CDRstd are domains of Language and aspects of Social Cognition/Behavior that are less common as early symptoms of probable AD and more often the presenting symptoms of dementia not commonly associated with Alzheimer pathology. Thus, there are patients with Primary Progressive Aphasia (PPA) who might be rated as "unimpaired=0" or "questionably impaired=0.5" on all CDRstd domains and yet be severely impaired in speech output or level of semantic knowledge. Similarly, patients with behavioral variant- frontotemporal dementia (bvFTD) often have relatively preserved memory and orientation and may perform only slightly worse than normal on the tests of mental agility that are part of the CDRstd interview. Yet, their behavior, personality and comportment (social behavior and interpersonal relationships) may be severely compromised⁴. Although the "Judgment and Problem Solving" domain of the CDRstd might capture some elements of impaired social judgment, it has more of a focus on executive cognitive function and problem solving.

In order to enable the CDR instrument to reflect more accurately the clinical status of a broad spectrum of patients with dementia, additional scales for language and behavior-comportment-personality were needed. These new domains were developed and incorporated into the CDR used in the Uniform Data Set (UDS)⁵ of the National Institute on Aging (NIA)-funded Alzheimer's Disease Centers in February 2008. We examined the performance characteristics of the two new domains of the augmented CDR in a large, diagnostically diverse group of subjects.

Methods

Subjects

This cross-sectional analysis used data in the Uniform Data Sets (UDS) maintained in a database of the National Alzheimer Coordinating Center (NACC)⁶ from initial clinic visits collected by the 30 NIA-funded Alzheimer's Disease Centers from February 2008 to September, 2009. Subjects were selected if they received a final clinical diagnosis that was one of the following – probable AD, vascular dementia (VaD), Dementia with Lewy Bodies (DLB), bvFTD or one of the several subtypes of PPA. Only subjects in whom the evaluations were carried out in English were considered. The diagnoses of probable AD⁷,

DLB⁸, VaD⁹, as well as the diagnosis of PPA^{10, 11} or bvFTD¹² were made based on published criteria incorporated into the UDS procedures (<https://www.alz.washington.edu/NONMEMBER/UDS/DOCS/VER2/ivpfillable.pdf>). Neither the CDRstd nor the new domains are part of any diagnostic algorithm in the UDS.

CDRstd evaluation

The CDRstd was completed by clinicians using published procedures for rating the standard 6 domains¹. Five domains of the CDRstd are rated along a scale with 5 choices, ranging from 0 (normal), 0.5 (very mildly impaired), 1 (mildly impaired), 2 (moderately impaired) and 3 (severely impaired). The sixth domain, personal care, is scored on a four point 0 – 3 scale. The CDRstd yields a global rating that was not used in the current analyses. The CDRstd ratings are commonly presented as the sum of the ratings for each of the 6 standard domains, a value known as the “CDR Sum Of Boxes score (CDR6SB)”.

The formats of the rating systems for the new Language (LANG) and Behavior/Comportment/Personality (BEHAV)¹³ domains, were identical to the standard 6 domains (Figure). For the LANG domain, for example, a rating of “1” indicated that patients had “moderate word finding difficulty....reduced phrase length...or reduced comprehension.” For the BEHAV domain, a rating of “1” indicated that patients had “mild but definite changes in behavior.” In the manual of the UDS, the basis for rating each domain is described (Figure). Before the new domains were used by Alzheimer Center clinicians, a training session focussed on the new domains was held for the clinicians.

Other covariates

Each subject underwent a neuropsychological assessment as part of the UDS described previously⁶, and an informant for each subject was interviewed by research coordinators in order to complete an assessment of function in daily activities, the Functional Activities Questionnaire¹⁴ (FAQ) and the Neuropsychiatric Inventory Questionnaire (NPI-Q)¹⁵.

Analyses

The demographic features of the study subjects were summarized and compared across study groups. Kruskal-Wallis tests were performed to detect differences in neuropsychological scores among all dementia types. For scales where differences were identified, pair-wise Mann-Whitney tests were carried out to test for differences among the three dementia types of primary interest here: AD, PPA and bvFTD. The frequency of non-zero (abnormal) ratings on the Language Domain (LANG) and the behavior-comportment and personality Domain (BEHAV) as a function of primary diagnosis among all subjects was calculated. A series of analyses were performed to determine whether LANG and BEHAV provided unique information. First, the number of subjects per primary diagnosis with LANG or BEHAV scores ≥ 1 , among cognitively impaired and demented participants who scored < 4 on the standard CDR6SB was tabulated. The designation of CDR6SB < 4 was an arbitrary choice that identifies persons who were highly likely to have no individual domain ratings > 1 . A CDR6SB < 4 thus represented a mildly affected group of individuals. Spearman correlation coefficients were then computed to assess how ratings on LANG and BEHAV correlated with items in the neuropsychological test battery and the other rating instruments. Finally, a series of logistic regression analyses were performed to determine how well the CDR6SB and the ratings on the LANG and BEHAV domains discriminated among probable AD, bvFTD and PPA. We computed odds ratios (OR) and their 95% confidence intervals to summarize these associations. Concordance statistics (c-statistics, or area under the ROC curve) were calculated to further compare the ability of the various scores to discriminate among different types of dementia. A c-statistic of 0.5 suggests the

model is no better than chance alone in discriminating among study groups, while a c-statistic of 1.0 indicates that the model is a perfect discriminator¹⁶.

Results

The demographic features of the study subjects (2550 probable AD, 281 DLB, 88 VaD, 234 bvFTD and 137 PPA patients) are given in Table 1. There was a wide range of severity, as reflected in the mental status examination scores, the CDR6SB, and the FAQ. As expected, scores on most of the neuropsychological measures differed among groups.

As anticipated, patients with bvFTD and PPA had a high frequency of non-zero ratings on both LANG and BEHAV domains (Table 2). In contrast, fewer probable AD, DLB and VaD patients had abnormal LANG or BEHAV domain ratings. Examination of PPA syndromes (Table 2) showed that, as expected, the semantic PPA subjects were more likely to have abnormal ratings in the BEHAV domain than the non-fluent PPA subjects.

Because patients who are globally impaired in cognition and behavior would be expected to have abnormal scores in all domains, we examined the two new domains in patients with CDR6SB <4 (Table 2), representing a group of mildly impaired individuals. In this group of patients, 53.7% of bvFTD had BEHAV domain rating of > 1. Among PPA patients, 78.6% had LANG domain scores >1. In contrast, only 3.7% of probable AD patients with a CDR6SB <4 were rated as > 1 on LANG and only 3.8% on BEHAV. Few patients with DLB or VaD had ratings > 1 on either LANG or BEHAV.

Correlation analyses (Table 3) in patients with bvFTD or PPA demonstrated that ratings of the LANG domain were moderately correlated with most of the psychometric battery except for Trail Making. Ratings of the BEHAV domain also correlated with most of the battery as well, with the exception again of Trail Making and digit span. Visual inspection of scatterplots of the bivariate distributions confirmed that there was no relationship between time to complete the Trail Making part B and ratings on either LANG or BEHAV. Both the LANG and BEHAV domain ratings were correlated with the FAQ and the CDR6SB. In the bvFTD patients, the BEHAV domain rating was moderately correlated with the total score on the NPI-Q, but the amount of shared variance was low ($R^2 = .12$). In contrast, the CDR6SB was correlated with all the tests in the psychometric battery, the FAQ and the NPI-Q.

Logistic regression analyses (Table 4) using the CDR6SB showed that it did not discriminate well between probable AD and bvFTD or PPA. In contrast, higher ratings on the LANG domain were associated with lower odds of probable AD, and higher odds of bvFTD and PPA. In fact, an increase in one point on the LANG domain was associated with a 3-fold increase in the odds of PPA, with a c-statistic (a measure of concordance) of 0.845. When the LANG domain was simultaneously modeled with the CDR6SB, both added significant information towards discriminating among different dementia types. When used to discriminate between PPA and probable AD, the combination of both the CDR6SB and LANG resulted in a c-statistic of 0.931, which was significantly higher than the c-statistic of 0.660 for CDR6SB alone ($p < 0.001$). Similarly, when both CDR6SB and BEHAV were simultaneously included in individual logistic regression models, they each provided independent information towards discriminating between different dementia types. When used to discriminate among bvFTD and probable AD, the combination of CDR6SB and BEHAV resulted in a c-statistic of 0.862, which was significantly higher than the c-statistic of 0.605 for CDR6SB alone ($p < 0.001$).

Discussion

Structured rating scales such as the CDRstd allow clinicians to integrate information from the history and examination in order to make a judgment severity of functional impairment, or the “stage” of the illness, and about the clinical salience of symptoms. The present study explored the utility of two new domains that had been added to broaden the reach of the CDRstd. Using data collected by the NIA-Alzheimer's Disease Centers, analyses showed that the addition of LANG and BEHAV domains aided in the characterization of patients with PPA and bvFTD. PPA and bvFTD patients were almost always rated as having abnormalities in the new domains even when their CDR6SB score was in the very mild range. While the LANG and BEHAV domains were occasionally rated as abnormal in patients with other dementias, ratings for LANG and BEHAV in non-PPA and non-bvFTD patients were largely at the questionable abnormality level, that is, a rating of 0.5.

The new domains were designed to capture the key manifestations of PPA and bvFTD for clinical trials and other longitudinal investigations, and to increase the breadth of the CDR instrument for characterizing patients with prominent deficits in language or social behavior in longitudinal studies. In showing that abnormal ratings on the LANG or BEHAV domains distinguished patients with PPA and bvFTD from patients with the syndrome of probable AD, the new domains also provide unique information about the cognitive disorders in bvFTD and PPA that was not represented in the 6-domain CDRstd. Although the new domains were used in a distinctly different manner in the more mildly affected patients, the new domains should be equally valuable in characterizing patients with more advanced impairment. The value of the new domains lies primarily in their ability to characterize patients with PPA or bvFTD, and not in differential diagnosis.

The LANG and BEHAV ratings were modestly, but significantly, correlated with most of the neuropsychological tests, as well as a measure of daily functioning, the FAQ. The LANG domain ratings were no more strongly correlated with either the Boston Naming Test or the two verbal fluency measures than the other tests in the battery. Performance on the one measure in the brief neuropsychological battery of the UDS that was intended to assess executive mental functioning, the Trail Making test, had no relationship to the two new domains. Furthermore, the shared variance between the BEHAV domain ratings and the NPI-Q was low, particularly in bvFTD patients. Thus, the new domains added information about the PPA and bvFTD patients that was not contained in the neuropsychological test results or in the questionnaires for neuropsychiatric symptoms and activities of daily functioning.

The analyses reported here are entirely cross-sectional. However, prior studies with the augmented CDR that included the BEHAV domain and a LANG domain item that was similar though not identical to the one used here, showed that the new domains detected change over one year in patients with bvFTD and PPA¹³. In addition, change on the augmented CDR that included the new domains correlated with worsening of whole brain volume and ventricular volume¹⁷. A study of SPECT imaging in a series of 99 patients with frontotemporal lobar degeneration showed that the augmented CDR¹⁷ correlated with perfusion abnormalities in the frontal and temporal lobes¹⁸.

Patients with probable AD, DLB and VaD sometimes have linguistic or behavioral abnormalities that are clinically relevant. On average, changes in speech, language and behavior occur later in the course of probable AD than in PPA or bvFTD¹⁹, although there are many exceptions as our data show. Indeed, some patients in these dementia categories had abnormal ratings on either the LANG or BEHAV domains. For those individuals, the new domains may be useful for cross-sectional and longitudinal analyses as well.

Neither of the new domains represents homogeneous constructs. The LANG domain combines analysis of verbal expression, lexical knowledge and auditory comprehension, each of which can be independently affected or spared in neurodegenerative diseases. There are many circumstances where more detailed characterization of disease features is required. For example, the Progressive Aphasia Severity Scale, a new clinical aphasia rating scale developed specifically for the characterization and severity staging of PPA divides language into its different components²⁰. The BEHAV domain similarly includes aspects of social conduct and personality that may be differentially impaired with brain pathology in diverse regions. The BEHAV domain could also be broken down into subcategories of apathy, empathy, disinhibition, and several other constructs. Use of the augmented CDR is not intended to replace the use of detailed scales such as the NPI, the Frontal Behavioral Inventory²¹, the Cambridge Behavioral Inventory²² the Middelheim Frontality Score²³ for assessment of changes in behavior or personality, or the Primary Progressive Aphasia Scale (PASS)²⁰, an instrument designed to capture very detailed information about functional language impairment for the assessment of changes in behavior and personality. Instead, global ratings such as the CDR serve a purpose when a single rating can condense clinical judgment about disease severity.

At this time we do not have information on the test-retest reliability of these two scales, as we have used them. However, a FTLT data module is being added to the UDS and a test-retest reliability study is planned for the LANG and BEH scales.

Strengths of this analysis include the prospective nature of the collection of the data, and the very large number of subjects available for analysis. The limitations of this study, however, must be considered. The ratings were completed by clinicians at federally-funded Alzheimer Disease Centers, whereas the expertise in the diagnosis and characterization of dementing illness is not typical in the general primary care setting. There was no imaging or pathological confirmation of syndromic diagnoses. The neuropsychological battery was limited to domains most often associated with dementia of the Alzheimer type; more detailed assessments of executive and linguistic functions might have shown more overlap with the new domain ratings. Finally, as the new domains were being used for the first time at most centers, it is likely that they will undergo change on the basis of data derived from their use. This could alter the relationships between diagnosis and ratings reported here. Nonetheless, this study emphasizes the importance of capturing the functional manifestations of neurocognitive deficits primarily associated with non-Alzheimer type dementia.

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Figure. The BEHAV and LANG domains of the augmented CDR and their descriptions in the Manual. From Uniform Data Set, NACC

Behavior, Comportment and Personality Domain: This item should be completed by a clinician or other trained health professional who is skilled in the assessment of FTLD, based on informant report and a review of the subject's cognitive functional and behavioral status. This domain is intended to assess changes in personality, aberrant behaviors and changes in interpersonal relationships from a prior customary level. The kinds of specific issues that might fall under these rubrics include: loss of insight, disinhibition, apathy, social withdrawal and disengagement, emotional lability, easy distractability, reduced empathy for the feelings of others, impulsivity and changes in eating habits and table manners. A key element of each of these is the degree to which these behaviors affect interpersonal relationships.

Language Domain: This item should be completed by a clinician well versed in aphasia and aphasic disorders, based on information derived from the informant and also from clinical assessment of the patient's language functions in the course of the clinical interview and the mental status examination. This domain is intended to assess changes in language from a prior level of skill. The components of language that are primarily of interest include: spontaneous speech, auditory comprehension, object naming, reading and writing. Semantic, grammatical, and phonemic components should be reviewed. Using these in combination, the goal is to assess the subject's ability to generate and comprehend various forms of communication. The rate of speech output, also known as "fluency", is also taken into account.

Table 1

Demographic, neuropsychological and clinical features of patients, by diagnostic group

	Probable AD	DLB	Vascular	bvFTD	PPA	p-value ^{***}
N	2550	281	88	234	137	
Age	77.2 (9.5)	74.7 (8.7)	79.6 (9.2)	64.8 (9.7)	67.0 (9.0)	<0.0001 ^{abc}
Sex (% Female)	52.3	33.1	50.0	38.5	54.7	<0.0001 ^{ac}
Education (yrs)	14.7 (3.2)	14.9 (3.5)	13.9 (3.7)	15.2 (2.9)	15.4 (3.0)	0.001 ^{ab}
MMSE [†]	19.6 (7.0)	19.5 (7.7)	20.3 (7.9)	20.6 (8.1)	19.6 (8.3)	<0.0001 ^{ab}
LM immediate recall	4.4 (4.1)	5.6 (4.4)	6.4 (5.0)	6.5 (5.1)	4.5 (4.5)	<0.0001 ^{ab}
LM delayed recall	2.3 (3.6)	4.4 (4.5)	4.9 (5.0)	5.3 (5.3)	4.0 (4.0)	<0.0001 ^{abc}
Digit span forward	5.8 (1.5)	5.6 (1.5)	5.7 (1.5)	5.5 (1.7)	4.7 (1.9)	0.485
Digit span backward	3.6 (1.4)	3.3 (1.4)	3.3 (1.5)	3.3 (1.7)	3.1 (1.7)	0.208
Animal Fluency	10.3 (5.5)	10.0 (5.5)	9.6 (5.1)	10.1 (6.9)	7.4 (5.7)	0.922
Vegetable Fluency	6.7 (4.2)	6.2 (3.8)	7.2 (3.9)	6.2 (4.6)	4.8 (4.3)	0.215
Digit symbol subst	26.0 (14.7)	20.7 (14.3)	22.2 (16.0)	30.9 (16.1)	33.3 (16.4)	<0.0001 ^{ab}
Trailmaking A (sec)	70.9 (42.0)	89.9 (44.3)	89.9 (44.7)	64.1 (42.1)	56.8 (36.6)	<0.0001
Trailmaking B (sec)	204.0 (89.4)	232.9 (86.1)	218.7 (89.9)	157.0 (88.9)	170.9 (89.6)	0.001
BNT (30 item version)	19.3 (7.8)	21.4 (7.4)	19.7 (7.8)	19.6 (9.3)	13.8 (10.2)	<0.0001
FAQ total score [‡]	18.9 (9.6)	21.9 (8.4)	17.4 (10.1)	20.7 (8.4)	13.7 (10.4)	<0.0001 ^{abc}
NPI total score [‡]	4.6 (4.6)	6.9 (5.3)	4.4 (3.9)	9.0 (5.5)	5.6 (5.1)	<0.0001 ^{ac}
CDR6SB [‡]	6.9 (4.7)	7.5 (5.0)	7.2 (5.1)	7.8 (5.0)	5.0 (4.7)	<0.0001 ^{abc}

NOTE: Values in table are mean (standard deviation) unless noted.

^{***} Comparisons simultaneously made among all dementia types using the Kruskal-Wallis test for all patient features but sex (Chi-Square test). For features with significant differences, pair-wise comparisons were made among subjects with AD, bvFTD and PPA dementias using Mann-Whitney rank sum tests for all features but sex (Chi-Square tests).

^a AD significantly different from bvFTD.

^b AD significantly different from PPA.

^c bvFTD significantly different from PPA.

[†]MMSE=Mini-Mental State Examination (higher score=less impairment); FAQ=Functional Activity Questionnaire (higher score=more impairment); CDR6SB= sum of domain scores for the 6 items of the CDRsd. LM=Logical Memory Scale-Revised; Digit Symbol Subst=Digit Symbol substitution subtest (Wechsler Adult Intelligence Scale-Revised); BNT=Boston Naming Test, 30 item; NPI-Q =Neuropsychiatric Inventory Questionnaire (higher score=more impairment).

Table 2

Percent of subjects in each diagnostic group with abnormal ratings on the LANG and BEHAV scales

	Probable AD N=2550	DLB N=281	Vascular N=88	bvFTD* N=234	PPA* N=137	Non-Fluent PPA N=60	Semantic PPA N=48	Other PPA** N=29
	Percent subjects with Ratings > 0							
LANG	50.7	66.6	62.5	76.5	99.3	98.3	100	100
BEHAV	39.4	52.3	47.7	90.2	63.5	50.0	85.4	55.2
	Percent subjects with Ratings ≥ 1							
LANG	26.0	36.3	28.4	50.0	86.9	83.3	93.8	82.8
BEHAV	25.8	35.2	30.7	81.6	46.0	35.0	70.9	27.6
	In patients with CDR6SB <4, Percent subjects with ratings ≥ 1							
	N=653	N=71	N=30	N=54	N=70	N=37	N=14	N=19
LANG	3.7	7.0	6.7	24.1	78.6	75.7	92.9	73.7
BEHAV	3.8	11.3	6.7	53.7	24.3	16.2	50.0	21.1

* Proportions with abnormal ratings for both bvFTD and PPA groups differ from other three groups combined, p<0.001 for all comparisons

** Other PPA = logopenic PPA and PPA not otherwise specified

Table 3

Spearman Correlation coefficients for CDR6SB, LANG and BEHAV domains and neuropsychological tests and informant-based assessments, in patients with bvFTD or PPA

	bvFTD			PPA		
	LANG domain	BEHAV domain	CDR6SB	LANG domain	BEHAV domain	CDR6SB
MMSE [†]	-0.54****	-0.40****	-0.71****	-0.48****	-0.34***	-0.72****
Logical memory immediate recall	-0.40****	-0.32****	-0.55****	-0.27**	-0.36***	-0.61****
Logical memory delayed recall	-0.35****	-0.29****	-0.53****	-0.26*	-0.42****	-0.59****
Digit span forward	-0.37****	-0.21	-0.29****	-0.37****	0.03	-0.35****
Digit span backwards	-0.38****	-0.28	-0.44****	-0.40****	-0.18	-0.49****
Animal Fluency	-0.58****	-0.39****	-0.60****	-0.37****	-0.45****	-0.64****
Vegetable Fluency	-0.47****	-0.39****	-0.54****	-0.29**	-0.36***	-0.62****
Digit symbol substitution	-0.25***	-0.25***	-0.46****	-0.05	-0.14	-0.42****
Trail Making part A	0.16*	0.10	0.43****	0.01	0.12	0.38****
Trail Making part B	0.15	0.03	0.25****	0.31**	0.02	0.19*
Boston Naming Test score	-0.44****	-0.24***	-0.39****	-0.26**	-0.48****	-0.58****
FAQ total score [†]	0.47****	0.62****	0.86****	0.48****	0.50****	0.89****
NPI-Q total score [†]	0.03	0.34****	0.26****	0.29****	0.67****	0.52****
CDR6SB [†]	0.52****	0.69****	1.00	0.44****	0.60****	1.00

[†] MMSE=Mini-Mental State Examination; FAQ=Functional Activity Questionnaire; NPI-Q =Neuropsychiatric Inventory Questionnaire; CDR6SB= sum of domain scores for the 6 items of the CDRsid

* p<0.05

** p<0.01

*** p<0.001

**** p<0.0001

Table 4
Discrimination among Probable AD, bvFTD and PPA for the CDR6SB and for the CDR6SB with the added domains*

	Probable AD		bvFTD		PPA	
	OR (95% CI)	c-statistic	OR (95% CI)	c-statistic	OR (95% CI)	c-statistic
CDR6SB ¹	1.00 (0.98–1.02)	0.584	1.05 (1.02–1.08)	0.605	0.89 (0.85–0.94)	0.660
LANG domain ¹	0.53 (0.48–0.59)	0.688	1.79 (1.55–2.06)	0.675	3.00 (2.54–3.56)	0.850
BEHAV domain ¹	0.50 (0.45–0.55)	0.693	3.29 (2.86–3.78)	0.826	1.49 (1.25–1.78)	0.645
CDR6SB ² plus LANG						
CDR6SB	1.13 (1.10–1.16)	0.701	0.97 (0.93–1.00)	0.677	0.60 (0.56–0.65)	0.931
LANG domain	0.33 (0.28–0.38)		2.04 (1.68–2.47)		25.0 (16.7–37.3)	
CDR6SB ² plus BEHAV						
CDR6SB	1.15 (1.12–1.19)	0.723	0.78 (0.75–0.82)	0.862	0.75 (0.71–0.80)	0.775
BEHAV domain	0.30 (0.26–0.35)		8.51 (6.64–10.9)		3.77 (2.88–4.95)	

* All analyses were performed via logistic regression and included sex and education as covariates. In the analyses, comparison groups consisted of all other individuals with at least probable evidence of dementia who did not carry the diagnosis being examined.

¹ Analysis included only the noted component(s) of the CDR.

² Analyses included both the CDR6SB and the additional domain, as noted