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A Scale of Socioemotional Dysfunction in Frontotemporal Dementia

Joseph P. Barsuglia[1,2,*], Natalie C. Kaiser[1,2], Stacy Schantz Wilkins[1,4], Aditi Joshi[1,2], Robin J. Barrows[1,2], Pongsatorn Paholpak[1,2], Hemali Vijay Panchal[1], Elvira E. Jimenez[1,2], Michelle J. Mather[1,2], Mario F. Mendez[1,2,3]

[1]*V.A. Greater Los Angeles Healthcare System, Los Angeles, CA, USA*
[2]*Department of Neurology, University of California at Los Angeles, Los Angeles, CA, USA*
[3]*Department of Psychiatry & Biobehavioral Sciences, University of California at Los Angeles, Los Angeles, CA, USA*
[4]*Department of Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA*

*Corresponding author at: Neurobehavior Service (116AF), West Los Angeles VA Healthcare Center, 11301 Wilshire Boulevard, Los Angeles, CA 90073, USA. Tel.: 1-310-478-3711; fax: 1-310-268-4181.
E-mail address: joseph.barsuglia@va.gov; joseph.barsuglia@gmail.com.

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Abstract

Early social dysfunction is a hallmark symptom of behavioral variant frontotemporal dementia (bvFTD); however, validated measures for assessing social deficits in dementia are needed. The purpose of the current study was to examine the utility of a novel informant-based measure of social impairment, the Socioemotional Dysfunction Scale (SDS) in early-onset dementia. Sixteen bvFTD and 18 early-onset Alzheimer's disease (EOAD) participants received standard clinical neuropsychological measures and neuroimaging. Caregiver informants were administered the SDS. Individuals with bvFTD exhibited greater social dysfunction on the SDS compared with the EOAD group; $t(32) = 6.32$, $p < .001$. The scale demonstrated preliminary evidence for discriminating these frequently misdiagnosed groups (area under the curve = 0.920, $p = <.001$) and internal consistency $\alpha = 0.977$. The SDS demonstrated initial evidence as an effective measure for detecting abnormal social behavior and discriminating bvFTD from EOAD. Future validation is recommended in larger and more diverse patient groups.

Keywords: Dementia; Neurodegenerative diseases; Social behavior; Behavioral assessment; Semantic dementia; Presenile dementia

Introduction

Early acquired social dysfunction is a hallmark sign of incipient behavioral variant frontotemporal dementia (bvFTD) (Edwards-Lee et al., 1997; Lindau et al., 2000; Neary, Snowden, & Mann, 2005; Pardini et al., 2013). Central facets of the current international consensus criteria for bvFTD include disinhibition, manifesting as socially inappropriate behavior, lack of social graces, and impulsive acts (Neary et al., 1998; Rascovsky et al., 2011). Particular characteristic signs include poor social tact and manners (Mathias & Morphett, 2010; Mendez, Fong, et al., 2014), interpersonal boundary infringements (Rankin et al., 2008), unsolicited affiliative contact with strangers (Mendez, Chen, Shapira, Lu, & Miller, 2006), and criminal acts (Diehl et al., 2006; Mendez & Shapira, 2009; Mendez, Shapira, & Saul, 2011). Symptoms related to socioemotional dysfunction are prominent in bvFTD and include relational detachment and interpersonal disinterest (Rankin, Kramer, Mychack, & Miller, 2003), poor insight regarding self and others (Mendez & Shapira, 2005, 2011), loss of empathy (Hsieh, Irish, Daveson, Hodges, & Piguet, 2013), and impaired sarcasm detection (Kumfor et al., 2014) and theory of mind (Irish, Piguet, & Hodges, 2011). These socioemotional changes are associated with structural atrophy and functional hypometabolism in the orbitofrontal, ventromedial prefrontal, anterior cingulate, insular and anterior and lateral temporal regions, often with a right hemispheric prominence (Borroni et al., 2012; Chiong et al., 2013; Couto et al., 2013).

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Individuals with other forms of early-onset neurodegenerative disease exhibit social and personality changes, thus complicating the diagnosis of bvFTD. Alzheimer's disease is the most prevalent early-onset neurodegenerative disease (Picard, Pasquier, Martinaud, Hannequin, & Godefroy, 2011; Vieira et al., 2013) and these patients often exhibit early personality changes prior to dementia onset which include increased rigidity, self-preoccupation, and impaired emotional control (Balsis, Carpenter, & Storandt, 2005). Patients with AD also display social deficits, specifically, impaired recognition of the emotional expressions of others (Bediou et al., 2009). In a comparison study of bvFTD and AD groups, both groups had loss of social insight on a patient and caregiver-informant-based questionnaire, which corresponded to ventromedial and frontopolar atrophy (Hornberger et al., 2014). Individuals with bvFTD, however, exhibited impaired social and emotional insight to a greater degree than those with AD.

Clinicians frequently misdiagnose dementias when they are of early onset (<65 years) (Mendez, 2006; van Vliet et al., 2013). Several neuropathology studies demonstrate that individuals clinically diagnosed with bvFTD exhibited primary Alzheimer's pathology postmortem (Alladi et al., 2007; Mendez, Joshi, Tassniyom, Teng, & Shapira, 2013). In a cohort of 156 patients with early-onset dementia, revised FTD diagnostic criteria were effective in diagnosing patients with bvFTD; however, the most common false-positive diagnosis was AD (Harris et al., 2013). Despite the frequent misdiagnoses of bvFTD, more careful clinical phenotyping demonstrates reliable correlations with histopathologic findings (Snowden et al., 2011). Yet, it remains important to distinguish bvFTD from "frontal variant AD," two diseases with somewhat different alterations in behavior as well as distinct neuropathologies. In particular, careful analysis of social behavior appears most sensitive in making accurate clinical distinction, as socioemotional symptoms are more severe in bvFTD in comparison with typical or frontal variants of AD (Leger & Banks, 2013; Mendez, Joshi, et al., 2013).

The misdiagnosis of bvFTD and early-onset dementias requires effective diagnostic tools that focus on socioemotional changes. In consensus diagnostic consensus criteria for bvFTD, two of the six core diagnostic features involve social or emotional changes that may be difficult for clinicians to directly assess as they are dependent on relationship or situation (i.e., criterion A—behavioral disinhibition including socially inappropriate behavior and criterion C—early loss of sympathy or empathy) (Rascovsky et al., 2011). Numerous sources have confirmed the complexity of diagnosing early bvFTD and the need for effective tools for assessing social change early in the disease (Pasquier, 2013; Rosness, Haugen, Passant, & Engedal, 2008; Vleugel, Chong, & van der Mast, 2006). Several tasks assessing aspects of socioemotional behavior have demonstrated efficacy in the diagnosis of bvFTD (Narme, Mouras, Roussel, Devendeville, & Godefroy, 2013). These tasks are associated with medial prefrontal and orbitofrontal dysfunction on neuroimaging (Bertoux et al. 2012, 2014; Funkiewiez, Bertoux, de Souza, Levy, & Dubois 2012).

The most documented similar informant-based measures in the literature are the Frontal Behavior Inventory (FBI), the Neuropsychiatric Inventory (NPI), and Frontal Behavior Rating Scale (FrSBe). The FBI (Kertesz, Davidson, & Fox, 1997) includes a variety of frontally mediated symptoms (e.g., apathy, disorganization, and alien hand); however, only a few of the 24 items specifically assess interpersonal behaviors (i.e., social inappropriateness). The NPI (Cummings et al., 1994), which was developed to assess neuropsychiatric symptoms in AD and other dementias, has been utilized to measure symptoms in bvFTD (Leger & Banks, 2014); however, no items pertain to pathognomonic social/emotional FTD symptoms such as reduced empathy, embarrassability, and guilt. The FrSBe (Grace & Malloy, 2001) is perhaps the most widely utilized informant-based measure of frontal-executive functions in the literature. The authors identified three subscale factors: apathy, disinhibition, and dysexecutive symptoms; however, these subscales contain items pertaining to both social and non-social items which are collapsed in the FrSBe subscales mentioned previously. In sum, the assessment of social dysfunction in bvFTD and other dementias would benefit from an instrument that is more comprehensive, focused, and specific to disturbances in social behavior in bvFTD.

In the assessment of social change, a close confidant, caregiver, and/or spouse may be the best source of clinical data regarding early changes in a patient's socioemotional functioning. Informants well known to a patient have likely observed their behavior across various settings and times, and may be better situated to compare behaviors and change from baseline (Gifford et al., 2014; Naglie et al., 2011). Previous literature suggests that informant-based measures of behavioral change in bvFTD are effective in discriminating bvFTD patients from those with AD (Hooten & Lyketsos, 1998; Joshi et al., 2014; Pijnenburg et al., 2008). However, at present, there are no informant-based measures specifically developed to assess socioemotional dysfunction in early-onset dementia patients.

Thus, the focus of the present study is to evaluate the diagnostic utility and psychometric properties of a novel informant-based measure of socioemotional dysfunction in bvFTD, in comparison with early-onset Alzheimer's disease (EOAD). Our primary aims are to compare these groups on the Socioemotional Dysfunction Scale (SDS), a caregiver-rating scale of social dysfunction, and examine preliminary evidence for the validity of the scale. We hypothesized that the SDS would effectively discriminate groups and demonstrate acceptable psychometric properties. We posited that our scale would exhibit convergent validity with relevant subscales of widely used informant-based clinical rating scales and divergent validity from measures of neuropsychological and psychiatric functioning.

Method

Participants

A total of 34 participants, 16 with bvFTD and 18 with EOAD, were recruited from an outpatient behavioral neurology clinic in an academic university medical center. BvFTD participants met criteria for "probable" bvFTD based on revised International Consensus Criteria (Rascovsky et al., 2011) including clinical features of disinhibition, apathy/inertia, loss of sympathy or empathy, perseverative, stereotyped or compulsive-like behaviors, hyperorality or dietary changes, and disproportionate executive dysfunction on neurocognitive testing. The bvFTD patients also had impairments in daily functioning as reported by caregivers and characteristic frontotemporal changes on magnetic resonance imaging (MRI) of the brain. Participants with EOAD were diagnosed according to the National Institute of Communicable Diseases and Stroke-Alzheimer's Disease and Related Disorders Association for clinically probable AD (McKhann et al., 1984). In order to provide a matched cohort with the bvFTD group, the EOAD patients were comparable in current age, age at initial clinical symptom onset, time since symptom onset, years of education, ethnicity, gender, and global cognitive functioning on the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) (see Tables 1 and 2). The diagnoses of bvFTD and EOAD were made before and independent from knowledge of the results of the SDS or the informant-based scales.

The study was reviewed and approved by the local Institutional Review Board (IRB) and study participants were enrolled according to IRB guidelines. None of the participants had histories of psychiatric or neurological disease, other than related to bvFTD or EOAD, or were currently taking medications that could impact performance on the neurological examination. Across both groups, individuals with major medical illnesses (except well-controlled hypertension or diabetes) were excluded. All patients had clinical MRI of the brain, and no participant had significant cerebrovascular changes on MRI (greater than minor white matter capping or ventricular lining) or other focal lesions. A caregiver accompanied all participants, and data were collected across two to three study visits. Caregivers were also matched between groups in age, gender, relationship status to the patient, cohabitation status with the patient, ethnicity, and education. The patient was not present in the room when the caregiver completed the informant rating scales. The majority of caregivers were spouses who were currently living with the patient and similar to the patient in age, education, and ethnicity, as identified in Table 1.

Procedures

All participants completed a neurological examination with a neurologist and neuropsychological testing with a neuropsychologist researcher. Caregivers attended all research visits with the participants and completed behavioral rating scales.

Socioemotional Dysfunction Scale. The measure is a 40-item informant-based rating scale, which is completed by a spouse, family member, caregiver, or other informant who resides with the patient, or knows the patient well. Thirty-one items of the scale were modified from the Social Competency Questionnaire (SCQ) (Schneider, Ackerman, & Kanfer, 1996). The SCQ is a

Table 1. Participant and caregiver demographics

	BvFTD ($n = 16$)	EOAD ($n = 18$)	t or χ^2	p
Participant				
Age (years)	61.06 ± 10.55	59.17 ± 4.97	0.66	.52
Estimated age at Initial onset	57.13 ± 10.23	55.16 ± 6.15	0.66	.51
Estimated time since onset	3.94 ± 3.19	4.00 ± 2.22	−0.07	.95
Gender (male/female)	8/8	6/12	0.97	.32
Education (years)	15.56 ± 2.25	16.17 ± 2.26	−0.78	.44
White (%)	15 (94%)	18 (100%)	1.16	.28
Caregiver				
Age (years)	59.60 ± 14.48	61.67 ± 13.45	−0.43	.67
Gender (male/female)	7/9	9/9	0.13	.72
Relationship spouse (%)	15 (94%)	15 (83%)	1.89	.39
Lives with patient (%)	14 (88%)	17 (94%)	0.51	.48
White (%)	15 (94%)	18 (100%)	1.16	.28
Education (years)	16.14 ± 2.14	16.29 ± 1.86	−0.21	.84

Notes: BvFTD = behavioral variant frontotemporal dementia; EOAD = early-onset Alzheimer's disease. Independent samples t-test for demographic variables and χ^2 analysis on gender and ethnicity. Means ± *SD*.

Table 2. Measures of dementia severity—independent samples *t*-test

	BvFTD ($n = 16$) $M \pm SD$	EOAD ($n = 18$) $M \pm SD$	t	p
CDR Memory	0.81 ± 0.25	0.94 ± 0.24	−1.58	.12
CDR Orientation	0.63 ± 0.53	0.63 ± 0.53	0.09	.93
CDR Judgment	1.59 ± 0.55[a]	0.83 ± 0.24	5.07	<.001
CDR Community Affairs	1.50 ± 0.71[a]	0.69 ± 0.35	4.13	<.001
CDR Home & Hobbies	1.44 ± 0.60[a]	0.78 ± 0.49	3.47	.002
CDR Personal Care	1.00 ± 0.82[a]	0.11 ± 0.32	4.08	.001
CDR Global Score	1.13 ± 0.47[a]	0.75 ± 0.26	2.86	.01
CDR Sum of Boxes	6.97 ± 2.09[a]	3.97 ± 1.34	4.90	<.001
CDR BEHAV	1.88 ± 0.34[a]	0.39 ± 0.56	9.23	<.001
CDR LANG	0.28 ± 0.41	0.44 ± 0.42	−1.16	0.26
FAQ	17.80 ± 6.67[a]	12.00 ± 6.13	2.60	.01

Notes: BvFTD = behavioral variant frontotemporal dementia; EOAD = early-onset Alzheimer's disease; CDR = Clinical Dementia Rating Scale; FAQ = Functional Activities Questionnaire.
[a]Group Score significant in the direction of impairment. On the FAQ, one case is missing in the bvFTD group ($n = 15$).

self-report measure of adaptive social behaviors validated in typical, healthy adults and measures constructs including extraversion, warmth, social influence, insight, openness, appropriateness, and maladjustment. The remaining nine items of the SDS were added via a deductive process based upon bvFTD research literature and select facets of the International consensus bvFTD diagnostic guidelines (Rascovsky et al., 2011). Written instructions are "For each item, base ratings on a comparison with typical behavior before disease symptoms emerged." Informants rate items regarding the participant's social behavior on a five-point Likert scale (1–5) as follows: 1 = Very Inaccurate; 2 = Somewhat Inaccurate; 3 = Neither Accurate Nor Inaccurate; 4 = Somewhat Accurate; 5 = Very Accurate. The 40 items are summed, yielding a total raw score with higher scores suggestive of greater social dysfunction. Potential scores on the measure range from a low score of 40 (endorsing all items as "very inaccurate") to a maximum score of 200 (endorsing all items as "very accurate"). The SDS items are listed in Tables 5 and 6.

The following caregiver-rating scales were included to characterize the sample and establish preliminary convergent and divergent validity with the SDS

The Washington University Clinical Dementia Rating Scale. The Clinical Dementia Rating Scale (CDR) (Morris, 1993) is a scale designed to classify dementia severity into stages of "none," "very mild," "mild," "moderate," and "severe." The informant is interviewed and the patient is administered several brief cognitive examination questions. Six domains of functioning are assessed including memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Items are scored as decline from the prior level due to cognitive loss. Each domain yields a score of 0–3, with higher scores reflecting greater impairment. The sum of boxes includes the sum of scores in each domain, while the global score is calculated based on an algorithm (Morris, 1993). Recently developed Language (LANG) and Behavior Domains (BEHAV) from the CDR were included (Knopman, Weintraub, & Pankratz, 2011).

Functional Activity Questionnaire. Functional Activity Questionnaire (FAQ; Pfeffer, Kurosaki, Harrah, Chance, & Filos, 1982) is an informant-based measure which requires the respondent to rate the patient's ability to complete ten different instrumental activities of daily living tasks on a four-point rating scale with potential responses of 0 (Normal), 1 (Does by self, but has difficulty), 2 (Requires assistance), or 3 (Dependent). Scores on the ten items are summed, yielding a score from 0 to 30. A cutoff of 9, with dependence in three or more activities, suggests impaired function and possible cognitive impairment.

Neuropsychiatric Inventory. The NPI (Cummings et al., 1994) measures the frequency, severity, and degree of caregiver distress associated with 12 psychiatric and behavioral symptom domains on the basis of caregiver report. Each domain begins with a screening question ("yes" or "no") to identify the presence or absence of the symptom, followed by 7–8 additional questions to determine the corresponding symptoms endorsed (again, in "yes" or "no" format). The caregiver is then asked to rate the overall frequency (1–4) and severity (1–3) thus providing an overall index of severity. In this analysis, the presence of symptoms (yes or no) was utilized (Table 3) and frequency times symptom severity was utilized to examine correlations with the SDS.

Frontal Systems Behavior Scale Family Version. The FrSBe Family version (Grace & Malloy, 2001) is a 46-item family/caregiver-report questionnaire designed to identify behavioral changes following brain injury or disease. The scale comprises

Table 3. Neuropsychiatric inventory presence of symptom

NPI symptom	BvFTD ($n = 16$) # yes (%)	EOAD ($n = 18$) # yes (%)	χ^2	P
Delusions	2 (13%)	2 (11%)	0.02	.90
Hallucinations	2 (13%)	0 (0%)	2.39	.12
Agitation/aggression	8 (50%)	3 (17%)	4.30	.04
Depression/dysphoria	2 (13%)	9 (50%)	5.44	.02
Anxiety	3 (19%)	9 (50%)	3.62	.06
Elation/euphoria	6 (38%)	0 (0%)	7.79	.005
Apathy/indifference	15 (94%)	7 (39%)	11.16	.001
Disinhibition	14 (88%)	3 (17%)	17.00	.000
Irritability/lability	6 (38%)	6 (33%)	0.06	.80
Aberrant motor behavior	15 (94%)	4 (22%)	17.58	.000
Sleep/nighttime behavior	4 (25%)	5 (28%)	0.03	.86
Appetite/eating changes	15 (94%)	2 (11%)	23.14	.000

Notes: BvFTD = behavioral variant frontotemporal dementia; EOAD = early-onset Alzheimer's disease; χ^2 analysis between diagnostic groups.

three domains: apathy, disinhibition, and executive dysfunction. The family member or caregiver rates the patient's behavior at two points in time: premorbid behaviors (prior to dementia onset) and current behavior (after dementia onset).

Neurocognitive Measures

The Neuropsychological assessment battery included the following measures. MMSE (Folstein, Folstein, & McHugh, 1975), Digits Forward/Backwards (unstandardized version), Trail Making Test Part A and B (Spreen & Benton, 1969; Spreen & Strauss, 1990) with age and education norms (Tombaugh, 2004), Boston Naming Test (Kaplan, Gloodglass, & Weintraub, 1983), Semantic "Animals" Fluency—The Animals task (Newcombe, 1969), Rey Osterreith Complex Figure Test (Meyers & Meyers, 1996), Wechsler Memory Scale, Third Edition—Logical Memory (Wechsler, 1997), Controlled Word Association Test (Spreen & Strauss, 1990), DKEFS Design Fluency (Delis, Kaplan, & Kramer, 2001).

Statistical Analyses

All statistical analyses were carried out using SPSS v.21.0 (IBM, Inc.), with the exception of the power analysis which was calculated in G*Power v.3.1.

Descriptives

Descriptive statistics and frequencies for participant and caregiver demographics, caregiver-rating measures, and neurocognitive test characteristics were produced for each diagnostic group. Independent samples *t*-tests were utilized to determine group differences on demographic variables including age, estimated age at initial symptom onset, estimated time since onset, years of education, and caregiver age. Chi-squared analysis was utilized to analyze differences in gender, ethnicity, and relationship and cohabitation status of the informant (see Table 1). An independent samples *t*-test was utilized to examine caregiver-rating measures including the CDR and FAQ (Table 2). Chi-square analysis was utilized to examine group differences on the presence of neuropsychiatric symptoms on the NPI (Table 3). Neurocognitive measures were examined in an independent samples *t*-test, without correction for multiple comparisons as this information is presented only for descriptive purposes (Table 4).

SDS Scale Development

The SDS scale contents are presented at the item level using Mann–Whitney *U* tests for non-parametric data (see Table 5). In a secondary χ^2 analysis, items were reduced to a binary coding system in order to determine and compare base rates of the presence or absence of a symptom within each diagnostic group (responses from "1—Very Inaccurate" to "3—Neither Accurate/Nor Inaccurate" were coded as a "no" response or symptom not present, and responses from "4—Somewhat Accurate" to "5—Very Accurate" were coded as a "yes" response or symptom is present) (see Table 6).

Table 4. Cognitive measures—independent samples *t*-test

Neurocognitive tasks	*n*	BvFTD, $M \pm SD$	*N*	EOAD, $M \pm SD$	*p*
Gross cognitive functioning					
MMSE	*16*	24.56 ± 4.33	16	24.44 ± 4.60	.84
Attention					
Longest digits forward	*13*	5.69 ± 1.18	12	5.42 ± 1.44	.68
Longest digits backward	*13*	2.85 ± 1.57	12	3.25 ± 1.54	.61
Information processing speed					
Trails A (raw)	*13*	65.15 ± 48.28	12	63.25 ± 57.84	.93
Trails A (%ile)		25.31 ± 31.25		38.67 ± 41.27	.38
Trails A (errors)		1.62 ± 2.50		0.55 ± 0.52	.16
Language					
Boston Naming Test (60 item)	*13*	47.31 ± 10.79	11	51.0 ± 6.96	.34
Animals fluency (raw)	*13*	10.54 ± 6.50	11	12.54 ± 5.34	.42
Visuospatial skills					
Rey-O complex figure (raw)	*12*	24.83 ± 5.34	9	20.78 ± 13.15	.40
Verbal memory					
Logical memory immediate (%ile)	*13*	14.08 ± 18.77	11	5.54 ± 14.75	.24
Logical memory delay (%ile)	*13*	20.08 ± 25.00	11	6.00 ± 14.62	.10
Nonverbal memory					
Rey-O delay (raw)*	*12*	10.71 ± 4.04	9	6.33 ± 5.25	.04
Executive functioning					
Trail making Test B (raw)	*13*	224.23 ± 95.3	10	187.70 ± 91.7	.36
%ile		10.50 ± 24.72		10.80 ± 20.75	.97
Errors*		5.00 ± 3.77		1.56 ± 1.74	.02
FAS fluency (raw)**	*13*	13.85 ± 7.86	10	34.00 ± 19.92	.01
FAS fluency (%ile)*	*13*	2.62 ± 3.93	10	34.40 ± 38.89	.03
DKEFS design fluency	*12*		13		
Total correct		12.50 ± 11.09		13.29 ± 8.62	.84
Total repeats***		18.75 ± 7.26		3.57 ± 4.68	<.001
Total rule violations		3.67 ± 2.71		6.07 ± 3.73	.08

Notes: BvFTD = behavioral variant frontotemporal dementia; EOAD = early-onset Alzheimer's disease; MMSE = Mini-Mental State Examination; FAS = Controlled Oral Word Association Test.
*$p < .05$. **$p < .01$. ***$p < .001$.

SDS Preliminary Validity

SDS scores were examined for skewness and kurtosis and exhibited acceptable values in the total sample and in each group. Pearson correlations were computed to evaluate the relation of scores on the SDS with demographic variables (age, education, and gender) as well as neuropsychological tests. The difference in the SDS total score was examined using independent samples *t*-test between diagnostic groups (Fig. 1). Estimates of effect size were obtained by calculating Cohen's *d* and power using G*Power. Binary logistic regression was used to determine the ability of the SDS to discriminate the bvFTD from the EOAD group. In order to determine sensitivity and specificity of the SDS in discriminating groups, a receiver operating characteristic curve analysis was utilized, which yielded an area under the curve (AUC) value (Fig. 2). A Youden Index (J = sensitivity + specificity − 1) was used to determine an SDS cutoff score with the best combination of sensitivity and specificity. Pearson correlations of the SDS with the NPI, CDR, and the FrSBe were utilized to evaluate the preliminary convergent and divergent validity of SDS.

Results

Participant and caregiver descriptives

There were no significant group differences on the preponderance of demographic variables relevant to dementia including age, estimated age of onset, time since illness onset, gender, years of education, ethnicity, and gross cognitive functioning (MMSE). The groups were dissimilar on two ratings of dementia severity (CDR and FAQ) that reflect particular aspects of dysfunction that are impacted differently during the disease course in each dementia type (see Table 2). For example, individuals with bvFTD exhibit greater social and functional impairment early on in the disease course than EOAD (Chow et al., 2012;

Table 5. Socioemotional Dysfunction Scale Score between groups sorted by *Z*-score

	Socioemotional Dysfunctional Scale items	FTD ($n = 16$), *M*/(*SD*)	AD ($n = 18$), *M*/(*SD*)	Mann–Whitney *U* test, *Z*-score	Asymp Sig.
1.	Has decreased self-consciousness or embarrassability.	4.50 (0.63)	1.74 (0.99)	−4.98	<.001
2.	Does not establish rapport with small talk.	4.50 (0.82)	2.26 (1.15)	−4.49	<.001
3.	Does not anticipate people's reactions to his/her behavior.	4.69 (0.48)	2.55 (1.28)	−4.41	<.001
4.	Does not understand how people react to him/her.	4.38 (1.09)	2.00 (1.25)	−4.38	<.001
5.	Does not take responsibility for his/her actions and lacks self-criticism, guilt, or remorse.	4.00 (1.32)	1.79 (1.23)	−4.05	<.001
6.	Does not respond correctly in social situations or follow social "rules of conduct."	3.81 (1.43)	1.58 (0.96)	−4.00	<.001
7.	Is excessively trusting of people, particularly strangers.	3.69 (1.30)	1.58 (0.96)	−3.98	<.001
8.	Often makes people uncomfortable.	3.25 (1.29)	1.53 (1.02)	−3.83	<.001
9.	Violates personal boundaries, for example, standing too close, touching, personal comments.	3.69 (1.54)	1.53 (1.02)	−3.77	<.001
10.	Is not concerned with the displeasure or disapproval of others	3.63 (1.41)	1.75 (1.02)	−3.70	.01
11.	Does not pay attention to "common courtesies" (e.g., opening doors for others).	3.63 (1.59)	1.63 (0.96)	−3.51	<.001
12.	Is not concerned about his personal appearance, grooming and hygiene	3.31 (1.49)	1.49 (0.89)	−3.46	.001
13.	Cannot make fun of him/herself when appropriate.	3.81 (1.38)	1.90 (1.33)	−3.44	.001
14.	Does not go out of his/her way to help others.	3.25 (1.34)	1.68 (0.95)	−3.42	.001
15.	Is unable to detect the gist of conversation; irony, sarcasm, or metaphor	4.06 (1.34)	2.30 (1.38)	−3.40	.001
16.	Does not appear happy when others experience joy.	3.06 (1.39)	1.58 (1.02)	−3.33	.001
17.	Does not give positive feedback to others	3.50 (1.41)	1.90 (1.17)	−3.30	.001
18.	Does not recognize irony, sarcasm, or the message between words.	4.13 (1.26)	2.42 (1.47)	−3.30	.001
19.	Is not interested in and concerned about others.	3.00 (1.59)	1.40 (0.68)	−3.22	.001
20.	Smiles and laughs at inappropriate times	2.81 (1.72)	1.40 (1.10)	−3.15	.002
21.	Does not understand the points of view or motivations of others.	3.88 (1.31)	2.45 (1.28)	−3.06	.002
22.	Does not cooperate with others on goals and tasks.	3.13 (1.36)	1.75 (0.85)	−3.05	.002
23.	Does not correctly "read" people or social situations.	3.88 (1.50)	2.32 (1.29)	−3.01	.003
24.	Often makes social errors.	3.63 (1.54)	2.05 (1.00)	−3.00	.003
25.	Does not express concern or provide comfort when others experience sadness or loss.	3.31 (1.82)	1.55 (1.00)	−2.98	.003
26.	Cannot see through phony behavior.	3.81 (1.60)	2.21 (1.32)	−2.97	.003
27.	Does not reciprocate expressions of warmth after receiving the consideration of others.	2.75 (1.53)	1.40 (0.60)	−2.93	.003
28.	Does not seek to share feelings or experiences.	3.94 (1.39)	2.60 (1.47)	−2.85	.004
29.	Does not seek to be around others or to interact with people.	3.63 (1.45)	2.21 (1.27)	−2.85	.004
30.	Lacks social tact, decorum, graces, or manners (esp. table manners).	3.06 (1.61)	1.7 (1.03)	−2.65	<.001
31.	Does not stay in contact with friends.	3.50 (1.59)	2.16 (1.21)	−2.57	.010
32.	Approaches strangers or expresses excessive familiarity.	3.06 (1.73)	1.75 (1.25)	−2.55	.011
33.	Does not show a tendency to nurture and protect small children, babies, or pets.	2.13 (1.41)	1.20 (0.70)	−2.63	.009
34.	Makes inappropriate comments to others	3.00 (1.71)	1.65 (1.23)	−2.55	.011
35.	Does not actively participate in social situations	3.56 (1.36)	2.37 (1.42)	−2.47	.014
36.	Approaches people that he/she would not have approached before.	2.81 (1.91)	1.42 (0.84)	−2.27	.023
37.	Waits for others to take the initiative.	3.94 (1.34)	2.90 (1.56)	−2.03	.042
38.	Displays public affection inappropriately.	2.25 (1.48)	1.37 (0.83)	−1.98	.048
39.	Tends to be silly and immature and to joke or pun.	2.13 (1.26)	1.45 (0.89)	−1.89	.058
40	Has an uncomfortable gaze; maintains it too long, often with a fixed smile.	2.06 (1.57)	1.20 (0.52)	−1.78	.075

Rosen et al., 2004). The EOAD group exhibited greater depression and anxiety ($p = .06$, trend) on the NPI (Table 3). The bvFTD group exhibited greater agitation, euphoria, apathy, disinhibition, aberrant motor behaviors, and eating behaviors on the NPI (Table 3). The groups did not differ on the majority of neurocognitive tasks; however, differences were discerned on the Rey-O Copy Delay, Trail making Test B raw errors, FAS fluency percentile, and raw repetitions errors on DKEFS Design Fluency (see Table 4). Participant caregivers similarly did not differ in their age, gender, relational status to the participant, ethnicity, or years of education (see Table 1).

SDS Psychometrics and Diagnostic Utility

In a comparison between groups on the SDS, there was a significant effect for group, $t(32) = 6.32$, $p < .001$ with the bvFTD group exhibiting significantly greater socioemotional dysfunction ($M = 138.13$, $SD = 32.35$, range 74–177) than the EOAD group ($M = 72.94$, $SD = 27.82$, range 40–120) (Fig. 1). Estimates of effect size were large with Cohen's $d = 2.16$ with power $(1 - \beta) = 0.99$. SDS score was normally distributed in the total sample, with skewness of 0.18 (SE = 0.4) and kurtosis of

Table 6. Socioemotional dysfunction scale percent endorsed item positive between groups

	Socioemotional Dysfunctional Scale items	% FTD endorsed ($n = 16$) (%)	% AD endorsed ($n = 18$) (%)	χ^2 Sig.
1.	Has decreased self-consciousness or embarrassability.	94	6	<.001
2.	Does not establish rapport with small talk.	94	22	<.001
3.	Does not anticipate people's reactions to his/her behavior.	100	22	<.001
4.	Does not understand how people react to him/her.	88	17	<.001
5.	Does not take responsibility for his/her actions and lacks self-criticism, guilt, or remorse.	75	17	<.001
6.	Does not respond correctly in social situations or follow social "rules of conduct."	69	6	<.001
7.	Is excessively trusting of people, particularly strangers.	63	6	<.001
8.	Often makes people uncomfortable.	50	11	.010
9.	Violates personal boundaries, for example, standing too close, touching, and personal comments.	75	11	<.001
10.	Is not concerned with the displeasure or disapproval of others.	63	11	.001
11.	Does not pay attention to "common courtesies" (e.g., opening doors for others).	63	6	<.001
12.	Is not concerned about his personal appearance, grooming, and hygiene.	56	6	.001
13.	Cannot make fun of him/herself when appropriate.	69	11	<.001
14.	Does not go out of his/her way to help others.	56	6	.001
15.	Is unable to detect the gist of conversation; irony, sarcasm, or metaphor.	75	28	.003
16.	Does not appear happy when others experience joy.	44	11	.025
17.	Does not give positive feedback to others.	63	17	.013
18.	Does not recognize irony, sarcasm, or the message between words	75	33	.010
19.	Is not interested in and concerned about others.	44	0	.001
20.	Smiles and laughs at inappropriate times.	38	11	.049
21.	Does not understand the points of view or motivations of others.	75	33	.007
22.	Does not cooperate with others on goals and tasks.	44	0	.001
23.	Does not correctly "read" people or social situations.	63	28	.031
24.	Often makes social errors.	69	11	.<001
25.	Does not express concern or provide comfort when others experience sadness or loss.	56	11	.003
26.	Cannot see through phony behavior.	63	28	.031
27.	Does not reciprocate expressions of warmth after receiving the consideration of others.	38	0	.003
28.	Does not seek to share feelings or experiences.	81	44	.013
29.	Does not seek to be around others or to interact with people.	56	28	.072
30.	Lacks social tact, decorum, graces, or manners (esp. table manners).	50	11	.008
31.	Does not stay in contact with friends.	63	22	.013
32.	Approaches strangers or expresses excessive familiarity.	50	22	.058
33.	Does not show a tendency to nurture and protect small children, babies, or pets.	25	6	.085
34.	Makes inappropriate comments to others.	44	17	.056
35.	Does not actively participate in social situations.	63	28	.031
36.	Approaches people that he would not have approached before.	44	6	.007
37.	Waits for others to take the initiative.	69	44	.115
38	Displays public affection inappropriately.	31	6	.042
39.	Tends to be silly and immature and to joke or pun.	13	6	.418
40.	Has an uncomfortable gaze; maintains it too long, often with a fixed smile.	25	0	.018

Notes: Chi-square analysis between groups on percentage of informants that positively endorsed each item. Responses between "1—Very Inaccurate" and "3—Neither Accurate/Nor Inaccurate" were coded as a negative symptom endorsement, items from "4—Somewhat Accurate" to "5—Very Accurate" were coded as a positive symptom endorsement.

-1.22 (SE $= 0.79$). In the bvFTD group, skewness was -0.52 (SE $= 0.56$) and kurtosis was -1.01 (SE $= 1.09$); while skewness in the EOAD group was 0.52 (SE $= 0.54$) and kurtosis was -1.12 (SE $= 1.04$).

A reliability analysis was conducted using Cronbach's α to determine internal consistency of the 40 items on the SDS, $\alpha = 0.977$. The inter-item correlation was $r = .58$ (ranging from 0.14 to 0.92). Item-total correlations ranged from $r = .43$ to .85. Average item variance was $M = 2.30$, and ranged from 1.42 to 2.81.

Using a binary logistic regression of the SDS total score to discriminate between the bvFTD and EOAD groups, 83% of the sample was correctly classified, and the model gave a significant result ($\chi^2 = 24.16$, $p < .001$ with $df = 1$), explaining between 50.9% (Cox and Snell R^2) and 67.9% (Nagelkerke R^2) of the variance in diagnostic group. AUC was excellent $=$ 0.920, SE $= 0.044$, $p < .001$ (Fig. 2). In assessing coordinates of the curve, based upon the greatest Youden index value ($J = 0.71$), a total SDS score of >105 yielded sensitivity $= 0.88$ and specificity $= 0.83$. For contextual adjustment, in settings where sensitivity is preferred (lower likelihood of false positives), an SDS cutoff score of >89 yielded higher sensitivity $=$ 0.94, with lower specificity $= 0.72$.

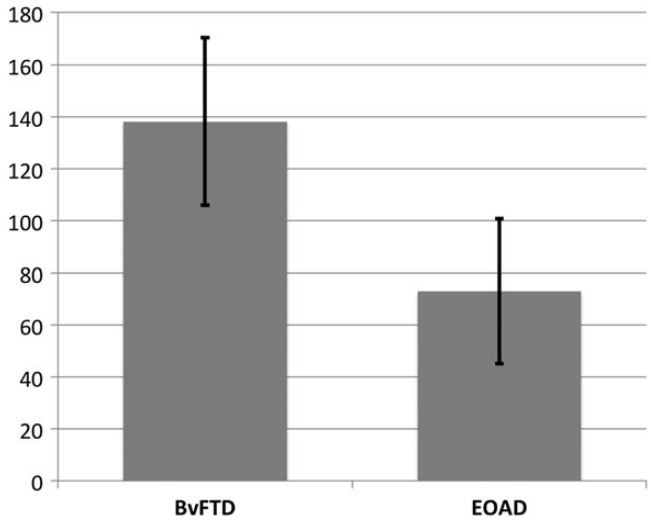

Fig. 1. Behavioral variant frontotemporal dementia (BvFTD) and early-onset Alzheimer's disease (EOAD) group means on the Socioemotional Dysfunction Scale (SDS) with bars for *SD*. Bar graph of SDS total mean score between groups.

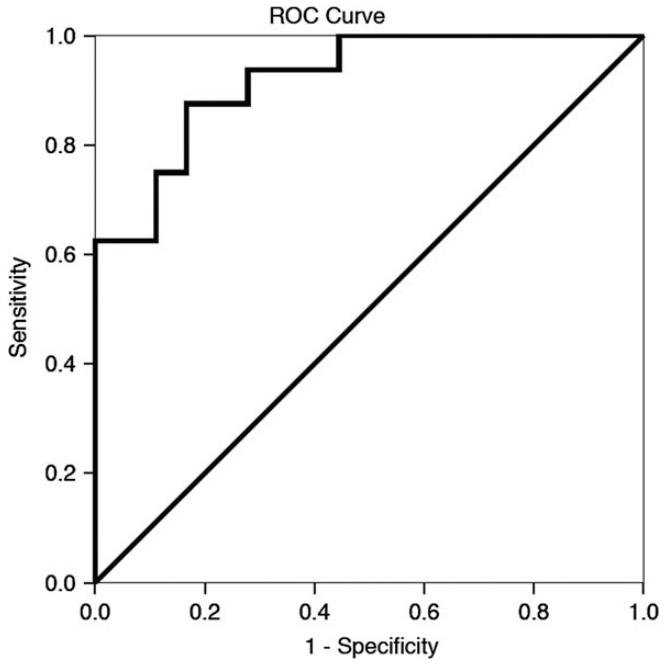

Fig. 2. Receiver operating curve statistic of the SDS discriminating BvFTD from EOAD. Area under the curve = 0.920, $p < .001$. Receiver operating curve statistic of the SDS discriminating BvFTD from EOAD.

SDS Relationship to Demographics and Preliminary Validity

The SDS did not significantly correlate with demographic variables (age, estimated age of onset, years since onset, education, or gender, all p's $> .20$). SDS scores were most strongly correlated with measures of conceptually similar constructs as follows in descending order (NPI scores are frequency times severity): CDR BEHAV ($r = .86$, $p = <.001$), NPI Disinhibition ($r = .82$, $p < .001$), FrSBe Disinhibition ($r = .77$, $p = .001$), FrSBe Executive Functioning ($r = .71$, $p = .001$), NPI Appetite/eating changes ($r = .71$, $p = <.001$), NPI Disinhibition ($r = .68$, $p = <.001$), CDR Community Affairs ($r = .67$, $p < .001$), NPI Agitation ($r = .65$, $p < .001$), CDR Judgment and Problem Solving ($r = .64$, $p < .001$), NPI aberrant motor behaviors ($r = .65$, $p = .000$), CDR Personal Care ($r = .63$, $p < .001$), NPI Elation ($r = .62$, $p < .001$), NPI elation/euphoria ($r = .60$,

$p = .000$), NPI Apathy ($r = .59, p < .001$), FrSBe Apathy ($r = .54, p = .02$), NPI agitation/aggression ($r = .55, p = .001$), CDR Home and Hobbies ($r = .50, p = .002$), and NPI Irritability ($r = .47, p = .004$). On neurocognitive measures, in the combined sample, greater scores on the SDS correlated positively with DKEFS Design Fluency repetitions ($r = .70, p = <.001$).

The SDS exhibited divergent validity compared with dissimilar subscales on symptom rating scales and neurocognitive measures. The SDS scores did not correlate with informant-report on the NPI of psychiatric symptoms of depression ($r = -.13, p = .45$), anxiety ($r = .07, p = .71$), and delusions ($r = .31, p = .07$). The SDS total score did not correlate with informant-based report of measures of memory ($r = .12, p = .51$) or orientation ($r = .18, p = .30$) on the CDR. Further, score on the SDS did not significantly correlate with the majority of the cognitive tasks (all p's $> .10$; Table 4) aside from one subscore of repetition errors on Design fluency.

Discussion

The current study compared differences on the SDS in bvFTD and early-onset Alzheimer's disease. The results showed significantly greater social dysfunction on the SDS among the bvFTD patients, compared with those with EOAD. The SDS demonstrated excellent utility in discriminating between these frequently misdiagnosed early-onset dementias. The established cutoff scores on the SDS are offered to aid in the differential diagnosis of bvFTD and EOAD. The SDS exhibited acceptable preliminary validity. The SDS demonstrated divergent validity from demographic, cognitive, and psychiatric constructs, as it was not correlated with age, education, or common measures of neurocognition (with the exception of repetition errors on the design fluency task), or psychiatric symptoms of depression and anxiety. The SDS exhibited convergent validity in strong correlations with conceptually related assessments of judgment, community involvement, personal care, behavior, and personality (on the CDR) in addition to relevant neuropsychiatric symptoms of apathy, disinhibition, elation (e.g., childish, abnormal humor), agitation and irritability (on the NPI). Moreover, the SDS demonstrated excellent internal consistency reliability.

The SDS is a relevant clinical assessment tool. The content in the revised International consensus diagnostic guidelines for bvFTD (Rascovsky et al., 2011) emphasize social interpersonal phenomena, which are reflected in the SDS. Specifically, behavioral disinhibition is defined in terms of interpersonal and social terms as "socially inappropriate behavior" and "loss of manners" in addition to "loss of empathy" with diminished "social interest, interrelatedness, or personal warmth." Similarly, the most promising discriminatory clinical markers of bvFTD include disinhibition, apathy, social disengagement, poor social awareness, and difficulty discerning negative feelings in others (Bozeat, Gregory, Ralph, & Hodges, 2000; Kipps, Mioshi, & Hodges, 2009; Lindau et al., 2000; Rankin et al., 2008). These collective clinical features are represented in the content of the SDS items, making the instrument especially relevant for clinicians.

The SDS may prove useful in facilitating the differential diagnosis of early-onset dementia and assessing for socioemotional changes in a brief format. In clinical settings, it is difficult to rapidly evaluate changes in social behavior and empathy, given interindividual and cultural variability, the need to establish change from baseline, and the lack of validated tools. Validated measures of social impairment are needed, since traditional neurocognitive testing has exhibited mixed utility in discriminating between AD and bvFTD (Graham et al., 2005). Moreover, although some variants of early-onset AD may have similar social and behavioral changes (Nygaard, Lippa, Mehdi, & Baehring, 2014), the documentation of a progressive social impairment should raise suspicion of bvFTD. The great majority of patients with bvFTD have social impairments early in their course, whereas few patients with EOAD have any early social impairments (Mendez, 2012). Several additional studies have demonstrated the utility of informant-based rating scales in differentiating between these groups (Barber, Snowden, & Craufurd, 1995; Hooten & Lyketsos, 1998; Pijnenburg et al., 2008). The SDS may be utilized to identify bvFTD patients for potential therapeutic interventions (Leger & Banks, 2013; Pasquier, 2013). Therefore, the SDS may assist in the process of developing disease-modifying interventions.

The current study has several limitations of note. First, the results of this study must be considered preliminary because of the relatively small sample size. This limits the generalizability of the results and indicates the need for further validation in larger and more diverse samples. This is particularly the case as the initial findings of this scale need validation in larger patient samples. Second, although the diagnostic groups were demographically matched and performed similarly on the majority of cognitive measures, they differed in the type and prevalence of neuropsychiatric symptoms and degree of functional impairment. The greater frequency of neuropsychiatric symptoms (i.e., eating changes, aberrant motor behaviors, disinhibition, apathy, etc.) and functional impairment in the bvFTD group is consistent with the well-documented differences between AD and bvFTD in rate of disease progression and behavioral change (Chow et al., 2012; Rosen et al., 2004). Third, although the SDS was effective in discriminating bvFTD from EOAD and demonstrated excellent internal consistency, the item content of the SDS is somewhat heterogeneous, spanning several facets of social behavior. Finally, the SDS may not be of value in cases of severe dementia or in the absence of a reliable caregiver informant. In sum, as this is the first study of the SDS, the measure requires additional validation in larger bvFTD and EOAD cohorts and in alternate patient populations where a diagnosis of bvFTD may not be diagnosed or be misdiagnosed.

Future examinations should include validation of the SDS in larger bvFTD and AD patient samples, as well as populations likely to be misdiagnosed with bvFTD, such as those with psychiatric disorders manifesting in mid-life (Panegyres, Graves, & Frencham, 2007; Rankin et al., 2008), or other FTLD disorders .The SDS should also be administered to groups with greater variation in education and ethnicity. A factor analytic study of SDS items would help determine if subscales could be established. Future studies may also identify non-discriminative items and reduce the scale length based upon clinical characteristics of larger samples.

In conclusion, the current study presents evidence for the utility of the SDS, an informant-based measure of socioemotional dysfunction, in discriminating EOAD from bvFTD. This brief tool is sensitive and specific to behavioral disturbances in bvFTD and will be useful for providing accurate and timely diagnosis in this clinical population.

Conflict of Interest

None declared.

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