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Spontaneous Social Behaviors Discriminate "Behavioral Dementias" from Psychiatric Disorders and Other Dementias

Katherine P. Rankin, Ph.D.[1], **Wendy Santos-Modesitt, BA**[1], **Joel H. Kramer, Psy D**[1], **Danijela Pavlic, BA**[1], **Victoria Beckman, BA**[1], and **Bruce L. Miller, MD**[1]

[1]Department of Neurology, University of California San Francisco

Abstract

Objective—Changes in social behavior are often the first symptoms of neurodegenerative disease. Patients with frontotemporal lobar degeneration (FTLD) often go undiagnosed, or are misclassified as psychiatric patients, because in the absence of cognitive deficits, non-experts fail to recognize these social changes as dementia symptoms. The object of this study was to improve screening for behavioral dementia in primary care and mental health settings by quantifying spontaneous social behaviors specific to FTLD.

Method—In a university hospital dementia clinic, examiners blind to subject diagnosis performed one hour of cognitive testing, then completed the Interpersonal Measure of Psychopathy (IMP), an 18-item checklist of observed inappropriate behaviors. Patients then underwent a multidisciplinary evaluation to derive a neurodegenerative or psychiatric diagnosis. Data were collected from 288 subjects: 45 Alzheimer's disease (AD), 40 frontotemporal dementia (FTD), 21 semantic dementia (SD), 13 progressive nonfluent aphasia (PNFA), 14 corticobasal degeneration (CBD), 21 progressive supranuclear palsy (PSP), 37 dementia with Lewy bodies (DLB), 16 vascular dementia, 29 mixed vascular and AD, 35 primary psychiatric disorders, and 17 normal older controls.

Results—Statistical item analyses demonstrated specific patterns of social behavior that differentiated both FTD and SD patients from 1) non-dementing older adults, 2) non-dementing individuals with psychiatric conditions, 3) individuals with cerebrovascular disease, and 4) individuals with other neurodegenerative disorders. SDs verbally and physically interrupted evaluations, spoke perseveratively and tangentially and resisted clinician redirection. FTDs were apathetic or disinhibited and were unconcerned about meeting clinician expectations.

Conclusions—Specific, abnormal interpersonal behaviors can alert non-experts to the need for specialized dementia referral.

INTRODUCTION

An alarming 4.5 million people were diagnosed with Alzheimer's disease (AD) in the U.S. as of the year 2000[1], and the number of individuals diagnosed with the disease is predicted to triple by 2050. AD is the most common and well-known subtype of dementia; however, it typically accounts for only 50-70% of dementia cases, while the rest can be attributed to other neurodegenerative diseases such as vascular dementia (VascD), frontotemporal lobar degeneration (FTLD), corticobasal degeneration (CBD), progressive supranuclear palsy (PSP),

Address for Correspondence and Reprint Requests: Katherine P. Rankin, Ph.D. UCSF Memory and Aging Center 350 Parnassus Avenue, Suite 706 San Francisco, CA 94143-1207 krankin@memory.ucsf.edu.

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and dementia with Lewy bodies (DLB). As distinct treatment regimens develop for each of these dementias, it becomes is increasingly imperative that they are recognized early and are referred to dementia specialists for specialized treatment and inclusion in clinical trials.

Diseases such as PSP, CBD, and DLB characteristically have early motor signs that accompany any cognitive or behavioral symptoms, and which can serve as a red flag to primary care clinicians to initiate a neurologic referral [2-4]. Similarly, variants of FTLD such as the left-temporal predominant type of semantic dementia (SD) and progressive nonfluent aphasia (PNFA) cause easily-observed speech and language deficits that can signal the need for specialty referral [5]. However, patients with two subtypes of FTLD, specifically the frontotemporal dementia (FTD) subtype and patients with the right temporal predominant variety of SD, can present with no appreciable motor, language, memory, or other cognitive symptoms [6, 7], yet may already be experiencing severe frontal or temporal neurodegeneration. Because the only symptoms many of these patients display early in the disease process are altered personality and social behavior, they are frequently misdiagnosed as having a psychiatric condition [8, 9], or the disease is missed entirely by non-experts who believe the patient is merely difficult or odd, but neurologically normal [10]. Misdiagnoses are even more likely because SD and FTD appear at a significantly younger age than classic dementias such as AD and VascD, with an average age of onset in the mid-60's, and cases commonly beginning as early as the 30's and 40's[11]. Even when a neurodegenerative condition is suspected in an FTLD patient, it is often mistaken for AD or VascD [9, 12]. As a result, physicians often fail to refer the patient to a specialty clinic, and may administer incorrect treatments. For example, the current standard pharmaceutical treatment of AD and VascD is an acetylcholinesterase inhibitor, but this treatment can often exacerbate FTLD symptoms rather than relieving them[13]. Particularly in managed care settings, primary care clinicians lack the time and resources needed to provide specialized dementia examinations for their patients, and they will not perform a separate dementia screen unless they already suspect there is a problem.[14, 15] Alternatively, FTLD patients may first present in a mental health setting, where neurological disease may be low on the diagnostic differential.

The magnitude and nature of FTLD behavior deficits, along with the fact that many of these patients are young and still have school-age children, combine to have a more devastating impact on family and caregivers than the burden caused by other dementias [16]. Early, accurate education about disease course and typical expected symptoms, as well as FTLD-specific support mechanisms for the caregiver, can significantly alleviate this burden, but only if the patient is properly diagnosed. Quick, simple, but sensitive mechanisms must be developed to allow mental health and primary care clinicians to screen for these behavioral dementias. We hypothesized that patients with different neurodegenerative diseases would spontaneously display objective social behavior deficits during routine clinical interactions. In particular, we hypothesized that the presence and pattern of unsolicited social behaviors would distinguish 1) FTD and SD patients from healthy older adults, 2) FTD and SD patients from patients with psychiatric features, 3) FTD and SD patients from patients with VascD, who sometimes also exhibit inappropriate social behaviors and personality changes[17, 18], and 4) FTD and SD patients from patients with all other major dementias, including AD, PNFA, CBD, PSP, and DLB.

METHODS

Participants

All subjects were recruited over a 3-year period after being referred to a university hospital neurology clinic specializing in neurodegenerative disorders. Two-hundred and seventy-one patients (157 male, 131 female) were included in this study because they met established research criteria for one of 11 diagnoses. These groups included 45 AD patients (meeting

National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association [19] research criteria); 40 FTD, 21 SD and 13 PNFA patients meeting the Neary[5] research criteria for frontotemporal lobar degeneration; 21 progressive supranuclear palsy (meeting Litvan[3] research criteria); 37 dementia with Lewy bodies (DLB)(meeting McKeith[4] research criteria; 16 vascular dementia (VascD)(meeting Ischemic Vascular Disease research criteria[20]; 29 mixed Alzheimer's disease and vascular disease (Alzheimer's Disease Diagnostic and Treatment Centers criteria)[20]; and 14 corticobasal degeneration (Litvan Criteria[21]). Patients were included in the psychiatric group (PSY: N=35) if 1) the expert diagnostic team determined that no neurodegenerative disease was present to account for the patient's cognitive or behavior symptoms, and 2) evaluation by a geriatric psychiatrist, a psychologist, or a neurologist determined that the patient had a current or past history of bipolar disorder, clinically significant current levels of anxiety or depression, psychotic features not associated with a dementia, or personality pathology consistent with a DSM-IV Axis II disorder. However, patients with clinical paranoia may have been more likely to decline participation in the study, thus it is possible that they were underrepresented in the PSY group compared to the initial clinic subject pool. AD patients were included in the pure AD group only if they met criteria for Probable AD, and no other comorbid conditions were suspected to be present (e.g., psychiatric features, vascular disease, metabolic conditions, etc.). Though many AD patients meeting these criteria were seen during the 3-year course of the study, only the first 45 eligible patients were included in order to limit the disparity between cell sizes across dementia groups. All other diagnostic groups included all eligible, consenting subjects available during the study period.

Normal control (NC) subjects (N=17) were recruited from the San Francisco Bay Area through advertisements in local newspapers and recruitment talks at local senior community centers. Interested individuals underwent telephone screening for a history of problems with their physical or psychiatric health, or a substance abuse history. Information about their current medication status was obtained, and their fluency in English was verified at this time. Individuals were accepted only if they had an informant available who had close contact with the subject for more than 5 years and was willing to answer questions about the subject to corroborate their clinical history. Participants who passed the telephone screen then underwent a 1 hour neuropsychological evaluation, routine labs, and a brain MRI. Following this initial evaluation, a multidisciplinary team consisting of a neurologist, a neuropsychologist, and a nurse reviewed the data to determine if the patient met criteria to be a healthy control. For inclusion as a healthy control subject for this study, subjects must have had a normal neurologic exam, a Clinical Dementia Rating Scale (CDR) score=0, MMSE score equal to or greater than 28/30, and delayed memory performance equal to or greater than the 25th percentile in both verbal and visuospatial domains.

This research was subject to approval by the University of California San Francisco Committee for Human Resources Independent Review Board. Because data were initially collected as part of a clinical evaluation, subjects' data were included only if they later signed a consent form stating that the collected data could be used for research purposes. In all cases, informed consent and assent were gained from both the patient and the primary caregiver.

Participants' ages ranged from 33 to 94 years with a mean of 68.2 (SD=11.9). The majority of the participants were white (87.1%), followed by Chinese (11%), Latino/Hispanic (7%), African American (6%), Japanese (4%), Filipino (3%), Asian Indian (3%) and (2%) unknown. The mean level of education was 15.8 years (SD=2.8). The average Mini Mental State Examination (MMSE) score across the patient groups was 23.2 (SD=6.0), and MMSEs ranged from 0 to 30.

Procedures

All patients presented to a neurology clinic at a university hospital to undergo clinical screening for dementia. Before they underwent neurologic examination or any diagnostic evaluation was performed, cognitive testers blind to patient history performed one hour of testing with patients. These testers included clinical research assistants with a bachelor's degree but no graduate study (36%), psychology postdoctoral students (24%), a neuroscientist (19%) or a neuropsychologist (21%). Immediately after the conclusion of this cognitive testing session, examiners filled out the Interpersonal Measure of Psychopathy (IMP) behavior checklist (see below) describing the patient. After the cognitive testing session, the patient immediately underwent a medical examination conducted by a neurology or psychiatry resident or fellow. This evaluation included a full clinical history as well as a neurologic examination, and family members and caregivers were asked to be present to provide corroboration and increase the reliability of information obtained about the patient. A nurse also interviewed family members and caregivers separately from the patient to obtain additional corroborative information and an assessment of the patient's functional status. After each of these examinations were performed, a clinical conference was held in order to make a diagnostic determination based on the neurologic examination, history and physical, cognitive testing, and functional evaluation, as well as any existing medical records, CT or MRI data, or laboratory values that may have been available. Clinicians at these diagnostic conferences included senior neurologists who specialize in neurodegenerative disease, geriatric psychiatrists, neuropsychologists, pharmacists, nurses, and neurology and neuropsychology fellows. The results of the IMP were not used as part of the diagnostic determination, though the cognitive data from the hour-long evaluation was used. If consensus was not reached about patient diagnosis at this time, additional laboratory work or a structural MRI scan was obtained within one month, after which another diagnostic conference was held. Patients were also typically seen at least once a year for clinical follow-up visits to monitor disease progression and reevaluate diagnosis. The potential for involvement in research was discussed with patients and their caregivers either at the end of their first evaluation day, or during a follow-up visit at the clinic, at which time informed consent to use their data for research purposes was obtained and both the patient and their caregiver signed the consent form. All subjects from whom IMP data were initially collected, but who did not consent to involvement in research, were excluded from analysis.

Measures

Because dementia-related behavior change has been described as “acquired sociopathy,”[22] we wished to use an established behavior instrument designed to assess observed sociopathic behaviors. One factor analysis of sociopathy suggests that it can be divided into two factors, one corresponding to criminal behavior, and the other describing a tendency towards interpersonal coldness and lack of empathy that can lead to subtly inappropriate interpersonal behaviors[23]. The Interpersonal Measure of Psychopathy (IMP)[24] was initially developed with a forensic population, and was designed to assess this second, “coldness”, factor by operationalizing this construct to be represented by a list of objectively observed behaviors. We chose to use a behavioral checklist instead of a subjective assessment of sociopathy, which could vary significantly depending on the rapport between the patient and the evaluator. We were particularly interested in determining if a brief clinical interaction would be adequate time to observe objective behaviors that would significantly correspond with real-life sociopathy, particularly in cases where the clinician had never met the patient and had no previous knowledge of their typical social behavior.

The IMP (Version 1) contains 18 items on which raters are asked to identify the degree to which a behavior typified the patient (1: Not at all; 2: Somewhat; 3: Very well; 4: Perfectly), e.g., “Ignores professional boundaries.” In addition to the primary items, the IMP also has 32

checklist behaviors that could be endorsed if the patient engaged in them at any time during the assessment period (e.g., “touched interviewer.”), which are scored in a binary manner (0: no; 1: yes). All items can be seen in Tables 2 and 3.

RESULTS

IMP Summary Scores

IMP Total scores ranged from 18 to 40 with a mean of 19.9 (SD=3.7) for all groups combined, and IMP Total Items Checked scores ranged from 0 to 8 with a mean of 0.8 (SD=1.6) (Table 1). These low numbers suggest that across the whole sample, the behaviors assessed by the IMP were not frequently endorsed. Data analysis was performed using a GLM procedure in SAS to derive ANCOVA statistics, controlling for sex, age, and MMSE total. Patients diagnosed with FTD (22.1±4.8) and SD (24.7±6.2) had significantly more item endorsements than NC subjects (18.8±2.4) at $p<0.01$ using a Dunnett-Hsu test, controlling for age, sex, and MMSE, for post-hoc comparisons. Only SD patients showed significantly higher numbers of IMP items checked (2.7±2.4) compared to the NC group (0.6±1.9) at $p<0.01$.

IMP Item Analysis

Patient groups were collapsed for the item analysis to answer the questions posed by the four group-comparison hypotheses. The third- and fourth- highest levels of total item endorsement were in the Vascular and Mixed Vascular/Alzheimer's groups, so these were collapsed together into an “Any Vascular” group (AnyV). Patients in the psychiatric disorder group (PSY) were kept as a separate group for analysis. The other dementia groups (AD, PNFA, CBD, PSP, DLB) were collapsed into an “Other Dementia” group (OthD). The SD, FTD, PSY, AnyV, OthD, and NC groups were then compared to determine if there were significant differences in item endorsement by clinicians. For the 18 descriptor items, SAS GLM procedures controlling for age, sex, and MMSE were followed by post-hoc Tukey-Kramer tests to compare the 6 groups, and a $p<0.05$ level of significance was accepted. The descriptor item results can be found in Table 2 and in Figure 1. Checklist items were scored as yes-no items, and the frequency with which they were endorsed by clinicians across the 6 groups was analyzed using a Fisher's Exact Test. The checklist item results are in Table 3 and in Figures 1 and 2.

Hypothesis 1: FTD and SD vs. NC Subjects—Both FTD and SD groups had significantly higher clinician ratings than NCs on the descriptor “Perseverates,” but no checklist items significantly differentiated both groups from controls.

SD patients also differed from the NC group by demonstrating significantly higher level of clinician endorsement of the descriptors “Interrupts,” “Refuses to tolerate interruption,” “Tends to be tangential,” and “Fills in dead space.” Compared to controls, the SD group was also significantly more likely to spontaneously engage in the checklist behaviors, “interrupted exam” (48% of SD patients, compared to 6% of NCs), “changed answer in middle of explanation” (SD= 24%; NC=0%), and “returned often to one event” (SD=29%; NC=0%).

FTD subjects rated higher than NC subjects on the descriptor “Exhibits unusual calmness or ease,” however, FTD subjects did not significantly differ from NCs on frequency of endorsement of any checklist items.

Hypothesis 2: FTD and SD vs. PSY Subjects—Clinicians rated both FTD and SD subjects as significantly higher than PSY subjects on the descriptor, “Exhibits unusual calmness or ease.” Both FTD and SD subjects were also significantly more likely to engage in the checklist behavior, “Interrupted examiner,” (SD=29%; FTD=18%; PSY= 0%).

SD subjects also were rated significantly higher than PSY subjects on the descriptors "Interrupts," "Refuses to tolerate interruption," "Tends to be tangential", and "Fills in dead space." SDs were more likely than PSY subjects to engage in the checklist behaviors, "Interrupted exam," (SD=47%; PSY=3%), "Provided very lengthy answers," (SD=29%; PSY=6%), "Changed answer in middle of explanation," (SD=24%; PSY=3%), "Returned often to one event," (SD=29%; PSY=3%), and "Returned often to one theme," (SD=19%; PSY=3%).

FTD subjects were significantly more likely than PSY subjects to cause clinicians to endorse the descriptors, "Ignores professional boundaries," and "Ignores personal boundaries." No additional checklist items differentiated FTD and PSY subjects.

Hypothesis 3: FTD and SD vs. Any Vascular (AnyV) Subjects—No single IMP item successfully differentiated both the SD and FTD groups from the AnyV group.

However, SD subjects scored higher than the AnyV group on the descriptor items "Interrupts," "Refuses to tolerate interruption," "Tends to be tangential," "Fills in dead space," and "Expresses narcissism." Also, the SD group was significantly more likely to spontaneously engage in the checklist behaviors, "interrupted exam" (SD=48%; AnyV=16%), "interrupted examiner" (SD=29%; AnyV=7%), "changed answer in middle of explanation" (SD=24%; AnyV=7%), "moved about the room," (SD=10%; AnyV=0%), "returned often to one event" (SD=29%; AnyV=4%), and "discussed personal uniqueness" (SD=19%; AnyV=0%).

FTD subjects had significantly higher endorsements rates of the descriptors, "Ignores personal boundaries" and "Exhibits unusual calmness or ease" than AnyV subjects. However, the FTD group did not differ significantly from the AnyV group on any checklist items.

Hypothesis 4: FTD and SD vs. Other Dementia (OthD) Subjects—The IMP showed the greatest discriminative power when differentiating the behavior of FTD and SD subjects from subjects with non-vascular dementias (AD, PNFA, CBD, PSP, and DLB). Both SD and FTD subjects showed significantly higher rates of clinician endorsement of many descriptors, including "Interrupts," "Refuses to tolerate interruption," "Ignores personal boundaries," "Exhibits unusual calmness or ease," "Perseverates," and "Expresses narcissism." Both FTD and SD subjects were more likely than OthD subjects to have a clinician endorse the checklist items "interrupted examiner" (FTD=18%; SD=29%; OthD=1%), "Touched examiner," (SD=14%; FTD=8%; OthD=0%), "Moved about the room," (SD=10%; FTD 8%; OthD=0%), "Discussed personal uniqueness," (SD=19%; FTD=8%; Oth=0%).

In addition, SD subjects showed significantly higher ratings than OthD subjects on the descriptors, "Tends to be tangential," "Fills in dead space," and "Becomes frustrated with argument avoidance." Compared to OthD patients, the SD group was significantly more likely to spontaneously engage in the checklist behaviors "interrupted exam" (SD=48%; OthD=12%), "Provided very lengthy answers," (SD=29%; OthD=6%), "changed answer in middle of explanation" (SD=24%; OthD=2%), "Returned often to one event" (SD=29%; OthD=2%), "Returned often to one theme," (SD=19%; OthD=2%), as well as low-frequency checklist behaviors such as "Expressed personal superiority," (SD=5%; OthD=0%), "Displayed grandiosity," (SD=5%; OthD=0%), "Displayed large gestures," (SD=5%; OthD=0%), "Used voice inflection to emphasize points," (SD=5%, OthD=0%), and "Used dramatic language," (SD=5%; OthD=0%).

FTD subjects significantly differed from OthD subjects by showing higher scores on the descriptors, "Ignores professional boundaries", "Makes personal comments," and "Seeks alliance with examiner." The FTD patients also were more likely than OthD patients to engage in the low-frequency checklist behavior, "Leaned very far forward," (FTD=8%; OthD=1%).

Additional Comparisons—SD patients could also be significantly discriminated from FTD patients based on higher clinician endorsement of the descriptors, “Refuses to tolerate interruption,” “Tends to be tangential,” and “Fills in dead space.”

PSY patients were significantly less likely than NCs to show the checklist behavior, “Displayed grandiosity,” (PSY=0%; NC=12%), but were more likely than OthD patients to engage in the behavior, “Discussed personal uniqueness,” (PSY=6%; NC=12%).

The AnyV group was significantly less likely than NCs to engage in the checklist behavior, “Discussed personal uniqueness,” (AnyV=0%; NC=12%). They were also more likely than the OthD group to engage in the behavior, “Interrupted examiner” (AnyV=7%; OthD=1%), “Touched examiner,” (AnyV=4%; OthD=0%), “Commented on examiner's dress or manner,” (AnyV=11%; OthD=2%), “Repeatedly tried to begin an argument with examiner,” (AnyV=4%; OthD=0%), and “Returned often to one theme,” (AnyV=16%; OthD=2%).

OthD patients were less likely than NCs to engage in the checklist behaviors, “Moved about the room,” (OthD=0%; NC=6%), “Expressed personal superiority,” (OthD=0%; NC=6%), “Displayed grandiosity,” (OthD=0%; NC=12%), “Discussed personal uniqueness,” (OthD=0%; NC=12%).

DISCUSSION

The primary finding of our study was that patients with frontotemporal dementia and semantic dementia spontaneously demonstrate specific social behaviors during clinical interactions that can be used to differentiate them from 1) non-dementing older adults, 2) nondementing individuals with psychiatric conditions, 3) individuals with a dementing condition caused by vascular disease or a combination of vascular disease and Alzheimer's disease, and 4) individuals with other major dementias, including Alzheimer's disease, progressive nonfluent aphasia, progressive supranuclear palsy, corticobasal degeneration, and dementia with Lewy bodies. These behavioral features may be used by clinicians who do not specialize in atypical dementias to screen their patients for dementia specialty referral, increasing the chance of early and accurate differential diagnosis of dementias causing primarily behavioral symptoms. This study also found additional results that are more relevant to differential diagnosis in a specialized setting: 1) that certain social behaviors help discriminate FTD from the behavioral variant of SD, and 2) specific behaviors may help identify the presence of vascular disease in patients with other, non-behavioral dementias.

“Behavioral Dementia” as a New Paradigm

Dementia is classically considered to be a disorder of cognition. Recent challenges to this characterization have been posed by the atypical dementias, but have been slow to reach the primary care and mental health clinicians who are the first to see these patients. While patients presenting with memory, language, or motor symptoms have a greater chance of being appropriately referred to a clinic specializing in dementia diagnosis and treatment, dementia is rarely part of the differential diagnosis for patients with a behavioral presentation in either primary care or mental health settings.

Behavior symptoms are central to the diagnosis of the frontotemporal dementia subtype of FTLD. Standard research criteria for FTD allow a diagnosis based on 1) insidious onset and gradual progression, 2) early decline in social interpersonal conduct, 3) early impairment in regulation of personal conduct, 4) early emotional blunting, and 5) early loss of insight[5]. This disease initially causes neuropathologic changes in the orbitofrontal cortex, the anterior cingulate, and the insula[25], areas directly involved in social and emotional processing, but the

dorsolateral frontal cortex remains unaffected until later. Thus, the frontal-executive cognitive symptoms which result from dorsolateral damage may not appear until years after disease onset, while florid social behavior symptoms will have already disrupted the patient's capacity to function in work, social, and family relationships.

The semantic dementia subtype of FTLD is primarily considered to be a language disorder, the hallmark of which is early neurodegeneration in the left anterior temporal lobe causing a loss of semantic meaning for words and everyday objects. However, as this disease has been more carefully characterized in recent years, it has become apparent that a large proportion of patients with this disease also have prominent behavior symptoms {Perry, 2001 #2842;Rankin, 2005 #3925;Rankin, 2003 #3322}. In addition to left temporal atrophy, the orbitofrontal cortex, anterior cingulate, and insula areas involved in emotional behavior are damaged early in SD, just as they are in FTD[29]. The majority of patients with left anterior temporal atrophy also eventually evidence neurodegeneration of the right temporal lobe and amygdala, areas which are directly responsible for social and emotional processing[30-32]. Making diagnosis even more difficult, this right temporal lobe damage occurs first in a subset of SD patients, so the left-sided damage that would normally cause telltale language symptoms is subtle or absent. Of all FTLD patients, it is this group of patients that is most likely to be misdiagnosed in primary care settings and referred for mental health treatment of their late-onset, bizarre personality and behavior changes. Dementia specialty clinics currently see more than three left-temporal predominant SD patients for every one that is right-temporal predominant[33], and many experts suspect that this is partly due to a referral bias in which these patients are never recognized as having a dementia, and instead undergo long-term psychiatric hospitalizations or live as deteriorating, treatment-resistant social recluses.

Our study found that when taken as a whole, the SD group demonstrated more dramatic and broad behavior changes even than the FTD group, which is consistent with other studies showing poorer emotion recognition[34] and more pervasive loss of empathy {Rankin, 2005 #3925} in SD than in FTD. However, it is likely that the SD group's high IMP scores were generated by the subset of SD patients with right temporal damage, and the wide standard deviations seen in this group suggest that it included some patients, probably with left-temporal predominant disease, who did not show behavioral symptoms during this clinical visit.

Recognizing FTLD Behaviors as Abnormal

The first challenge of primary care and mental health clinicians is to recognize that a patient with a behavioral form of dementia is not simply an “odd” or “difficult” individual who is otherwise neurologically normal. Thus, our first goal was to differentiate FTD and SD patients' spontaneous behavior from what could be expected from healthy, non-dementing older adults. Clinicians in our study were more likely to use the term “perseverates” to describe both FTLD subtypes, meaning that the patients tended to become fixated on one idea or stimulus and failed to allow the clinical interaction to proceed fluidly to the next idea. This trait was further elucidated by the comparison between controls and SD subjects, whose uniquely characteristic pattern of behaviors involved derailing the clinical examination process. Fully one-half of SDs in this study interrupted the clinician or the process of the examination itself, even to the point of standing up and attempting to leave the room prematurely. Approximately one-quarter of them spoke in a tangential, rambling manner that shifted to irrelevant topics, and they were more likely to resist the clinician's attempts to redirect them back to the exam. SD subjects rated higher on both perseverative and tangential speech because they tended to repeatedly shift the discussion to one or two pet topics that were neither initiated by the clinician nor relevant to the exam, then insisted on completing their train of discourse, despite the clinician's protests that they have already heard about it. These same behaviors were seen in only 0-6% of control subjects, and taken together, should be considered abnormal social behavior.

This pattern of behavior may be directly linked to the right temporal damage common to this dementia subtype. The implicit social expectation conveyed in the context of a medical or psychological evaluation assumes the clinician is “in charge” and will determine the course and pace of the interaction. The failure of such a large proportion of SD subjects to recognize this power differential and appropriately defer to this expectation, even when the clinician explicitly reminds them of it by openly interrupting the patient's perseverative or tangential thought process, demonstrates a loss of sensitivity to social signals. The right temporal lobe is involved in many aspects of basic social perception, ranging from identifying emotions in faces, voices, and gestures [32, 35, 36], to higher social processes such as empathy [37]. The controlling, insensitive behavior of these SD subjects may be the practical manifestation of this breakdown of social cognition.

When compared to healthy aging controls, subjects with FTD did not demonstrate this particular set of abnormal social behaviors as a whole, though some patients did engage in one or two of these same behaviors. Though FTD subjects were described as perseverative, they were less likely than SD subjects to interrupt or be tangential. However, they were described as “exhibiting unusual calmness or ease.” This behavior was initially included in the development of the IMP to measure the almost unnatural lack of anxiety seen in many developmental sociopaths. However, in this context, clinicians endorsing this symptom described a subset of FTD patients as qualitatively flat, unresponsive, and lacking normal initiative. Apathy is one of the primary clinical symptoms of FTD[38], and has been directly associated with the medial frontal damage characteristic of this disease [39]. Our study suggests that in a subset of cases, this apathy is observable in the course of a typical clinical interaction, and may provide a red flag for referral. However, it is important for clinicians to note that apathy characterizes only one subset of FTD patients, while others with this diagnosis present with positive symptoms such as disinhibition, hyperkinesis, and logorrhea.

Distinguishing FTLD from a Psychiatric Condition

In everyday clinical practice, behavioral-predominant dementias are routinely mistaken for psychiatric disorders; however, our study suggests that FTLD patients' spontaneous behavior is very different from that of patients with psychiatric conditions. Our group of psychiatric patients was diverse and somewhat atypical, in that it was comprised of patients that presented to a memory clinic complaining of cognitive symptoms, which were subsequently determined to originate in a psychiatric disorder rather than a primary neurodegenerative condition. Diagnoses within this group included anxiety, bipolar and unipolar depression, psychotic disorders, and Axis II personality pathology. However, this group was rated by clinicians as seldom engaging in any of the behaviors measured by the IMP. They did not differ from controls on any descriptor items, and were actually significantly less likely than controls were to behave in a grandiose manner.

SD and FTD patients differed from the PSY group for many of the same reasons they differed from controls. The SD group's pattern of derailing the course of the clinical interaction, described above, also differentiated them from the PSY group, who did not engage in this cluster of behaviors. Both SD and FTD subjects were also considered by clinicians to be significantly more likely than PSY patients to “Exhibit unusual calmness or ease.” Paradoxically, FTD patients were also more likely than PSY patients to ignore professional and personal boundaries, though these behaviors were probably seen in patients exhibiting the disinhibited rather than apathetic phenotype of FTD. These data highlight one of the primary clinical factors that distinguish FTLD from psychiatric disease. The core neuroanatomy of FTD and SD, in which orbitofrontal, anterior cingulate, and insular cortex are damaged, causes an early decrease in emotional reactivity and sensitivity, along with a loss of self-awareness and impression management. Whether they were apathetic or disinhibited, these patients were

observed to be unfazed by the evaluative context of the cognitive exam, often not caring whether or not they made mistakes, they showed little emotional reactivity, and they did not show a tendency to "check in" with the examiner either verbally or via eye-contact to obtain social feedback. In contrast, patients with psychiatric disorders were more likely to be anxious or self-critical, and often required reassurance and feedback from the examiner. PSY patients as a group made an appreciable effort to defer to the examiner, meet expectations, and remain task-focused, in a pattern of behavior opposite to that of the SD patients.

Is Cerebrovascular Disease a "Behavioral Dementia?"

Particularly in cases where patients exhibit some cognitive symptoms such as memory loss or executive deficits, FTLD is misdiagnosed as vascular disease[7]. Both conditions eventually cause a frontally-predominant pattern of cognitive deficits, and both can cause behavioral impulsivity and poor social judgment. One of the most common forms of vascular disease in aging adults does not involve obvious focal strokes, but creates a pattern of leukoencephalopathy, or white matter disease, that interferes with frontal-subcortical circuits and effectively "disconnects" the frontal lobes[40]. Our study found that patients with clinically significant vascular disease, diagnosed alone or mixed with Alzheimer's disease pathology, were more likely than any other non-FTLD patient group to spontaneously exhibit problematic social behaviors during our clinical evaluations. These cerebrovascular patients' scores on IMP items were not significantly different from those of healthy aging control subjects. However, a subset of VascD subjects was more likely than patients with other dementias (AD, PNFA, CBD, PSP, and DLB) to engage in behaviors such as interrupting the examiner while they were speaking, touching the examiner, commenting on the examiner's dress or manner, attempting to argue with the examiner, or returning to the same theme in conversation (4 to 16% of the group for each behavior).

Despite this increased base rate of behavioral irregularities in vascular patients, they could be discriminated from both SD and FTD patients on the basis of numerous behavior differences. Importantly, the cluster of interrupting/controlling behaviors demonstrated by a large proportion of the SD group did not appear in the vascular patients, with the exception that 16% of vascular patients verbally interrupted the examination (compared to almost half of the SD patients, many of whom actually stood up to leave the room). An additional discriminating factor was that SD patients were more likely to behave in a narcissistic manner, with one-fifth of them explicitly raising the topic of their personal uniqueness, while none of the vascular patients did this. The pathological lack of social responsiveness that discriminated FTD subjects from healthy controls and psychiatric patients also significantly differentiated them from vascular patients. In addition, clinicians rated FTD patients as significantly more likely than vascular disease patients to ignore personal boundaries. Overall, discrimination between FTLD and vascular patients may be based on the fact that despite occasionally irritable, impulsive behaviors on the part of some vascular patients, they remain capable of self-reflection, and retain a greater sensitivity to the social and emotional context of the clinical interaction than FTLD patients do.

FTLD Behavior is Highly Divergent from Other Dementias

Our results also showed that the spontaneous behaviors more common in FTLD patients than in controls, psychiatric patients, and vascular patients are not merely a result of "dementia" in general. FTLD patients act quite different from patients with other dementias such as Alzheimer's disease, progressive nonfluent aphasia, corticobasal degeneration, progressive supranuclear palsy, and dementia with Lewy bodies. None of these dementia groups showed a distinctive pattern of social behavior during the evaluation. In fact, the overall trend was that non-FTLD dementia patients were less spontaneously active, thus were less likely to evidence the positive behaviors of the IMP than either FTLD patients or healthy aging controls. For

example, despite the fact that the combined Other Dementia group numbered 130 patients, not a single person was observed to move around the room or speak in a narcissistic, “personally superior” manner, while 6-10% of the normal subjects and even more FTLD patients did these things. Fewer than 3% of Other Dementia patients interrupted the examiner or spoke in the perseverative, tangential manner we observed in approximately one-quarter of FTLD patients. In practical terms, however, using behavior to differentiate FTLD patients from those with other types of dementia may be less useful in a typical primary care or mental health setting, because these other dementias should have telltale memory, language, or motor symptoms that indicate the need for neurologic referral.

Study Limitations

There are some methodological considerations specific to our study that may limit the generalizability of our findings. One issue is the possible circularity of performing behavior ratings on patients who are diagnosed, in part, based on behavioral criteria. This study was performed at a neurology specialty clinic by clinicians who are exposed to dementia patients more frequently than typical primary care or mental health professionals. However, almost 40% of the ratings were performed by bachelor's degree-level research assistants with no formal medical or psychological education, which was done purposely to reduce the chance raters would correctly recognize the patient's disease before they had filled out the IMP. We also specifically selected a measure with an objective behavior-checklist component to reduce the likelihood that the rater's “guess” about patient diagnosis would influence their ratings.

This study was designed to identify FTLD-specific behaviors likely to occur spontaneously in primary care or mental health settings; however, these ratings were performed by clinicians who had been one-on-one with the patient for one hour performing cognitive testing. Important behaviors that might be seen in a more naturalistic clinical interview setting may have either been elicited or suppressed by the cognitive testing context. Also, the typical primary care visit is only 15 minutes in duration, reducing the time in which important patient behaviors might be observed. In mental health settings such as therapy, the clinician does spend 45 minutes to an hour one-on-one with the patient; however, the social dynamic of talk therapy is different from what is seen in other, more goal-directed contexts like a physician's visit or a structured cognitive exam. Some of the behaviors this study suggests are specifically associated with behavioral dementias, such as perseverative, tangential, or narcissistic discourse, may fall within the limits of normal behavior in a therapy session. Clinicians should be careful to recognize context in their interpretation of patient behavior.

The behavior checklist used in this study was not developed for use with dementia patients, thus it was not comprised of a comprehensive list of all behaviors that might be expected from FTLD patients. Despite our use of an imprecise instrument, however, we still found that many spontaneous social behaviors do differentiate FTLD patients from other patients during brief clinical interactions, which suggests that future research with a behavioral checklist tailored to FTLD might show even better results. The behaviors we found that were useful discriminators occurred in no more than half of our patients, which suggests that though these behaviors are fairly specific, they are not highly sensitive. Research to discover additional behaviors that occur in a larger proportion of FTLD patients will allow more of them to be recognized by medical gatekeepers and appropriately referred.

Conclusions

Primary care and mental health professionals are likely to be the first clinicians to recognize that FTLD patients require a referral for a dementia evaluation, thus these clinicians must be able to recognize salient behaviors without needing to perform specialized evaluations. This study demonstrated that FTLD patients are likely to spontaneously exhibit specific patterns of

aberrant social behavior that can be objectively observed by non-experts in a time-limited, problem-focused clinical context. These behaviors are not typical of normal aging, and are not common in psychiatric or cerebrovascular disease, thus should be seen by clinicians as red flags for behavioral dementia.

The most powerful discriminator of the SD subtype of FTLD was a pattern of behavior in which the patient derails the course of the clinical interaction by verbally and physically interrupting the evaluation, speaking at length and repeatedly about one or two irrelevant topics, and resisting the clinician's attempts to interrupt and redirect them. The FTD subtype of FTLD showed no self-consciousness or concern about meeting the clinician's expectations, though they displayed this behavior in the context of two different phenotypes: they either displayed an abnormally flat, apathetic demeanor or were socially disinhibited, readily crossing personal and professional boundaries. When observed in a primary care or mental health context, these symptoms may indicate the need for referral to a dementia specialist for further evaluation.

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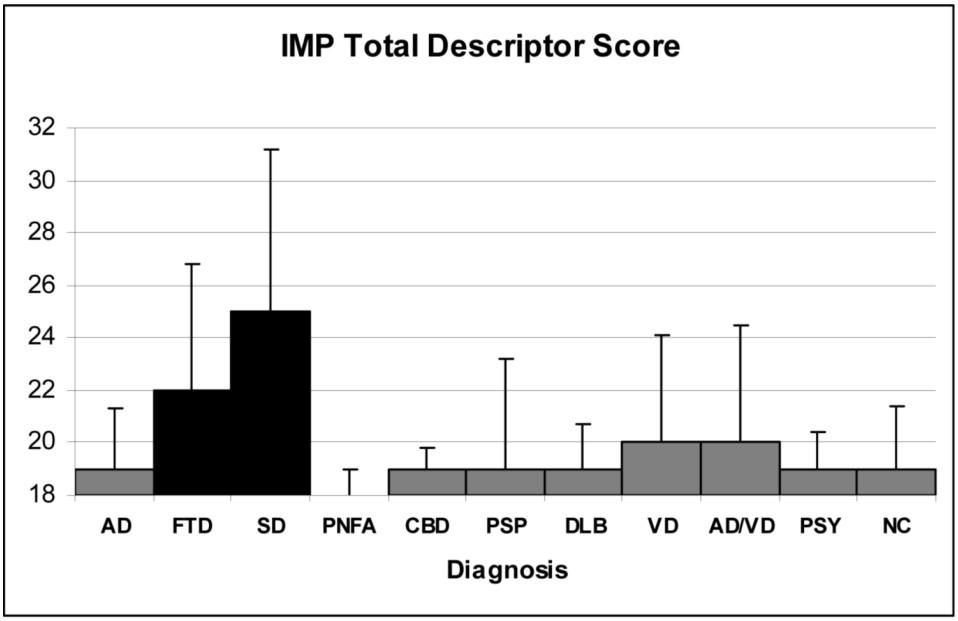

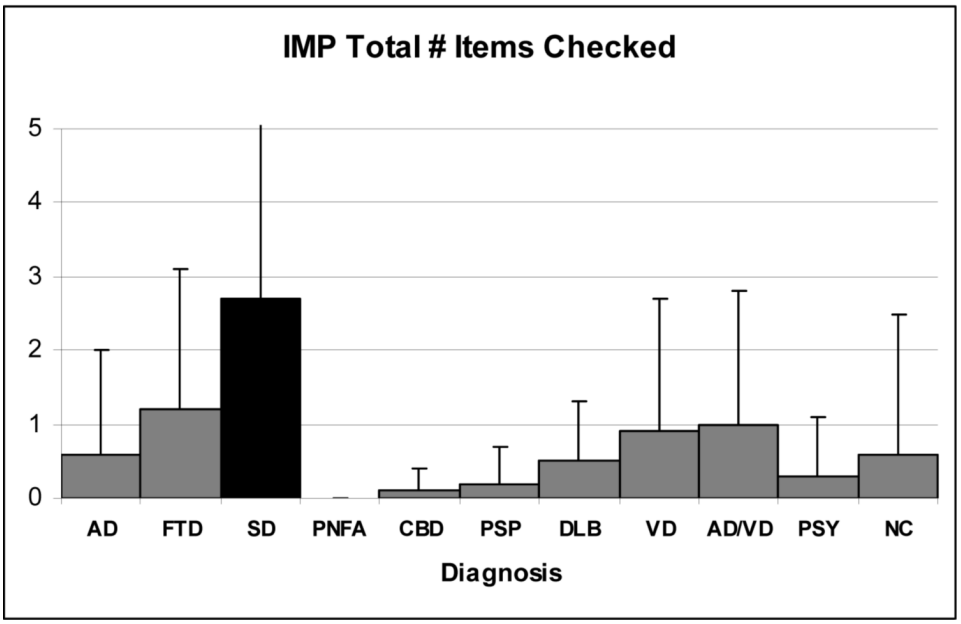

Figure 1.

Clinician ratings of collapsed patient groups on IMP descriptor item total score and # of IMP checklist items endorsed. Patient groups showing significantly higher rates of a behavior compared to normal controls (NC) are marked with black bars; groups with no significant difference from NCs are marked with grey bars. AD=Alzheimer's disease; FTD=frontotemporal dementia, SD=semantic dementia; PNFA=progressive nonfluent aphasia; CBD=corticobasal degeneration; PSP=progressive supranuclear palsy; DLB=dementia with Lewy bodies; VD=vascular dementia; AD/VD=mixed Alzheimer's disease and vascular disease; PSY=psychiatric disorder; NC=normal controls.

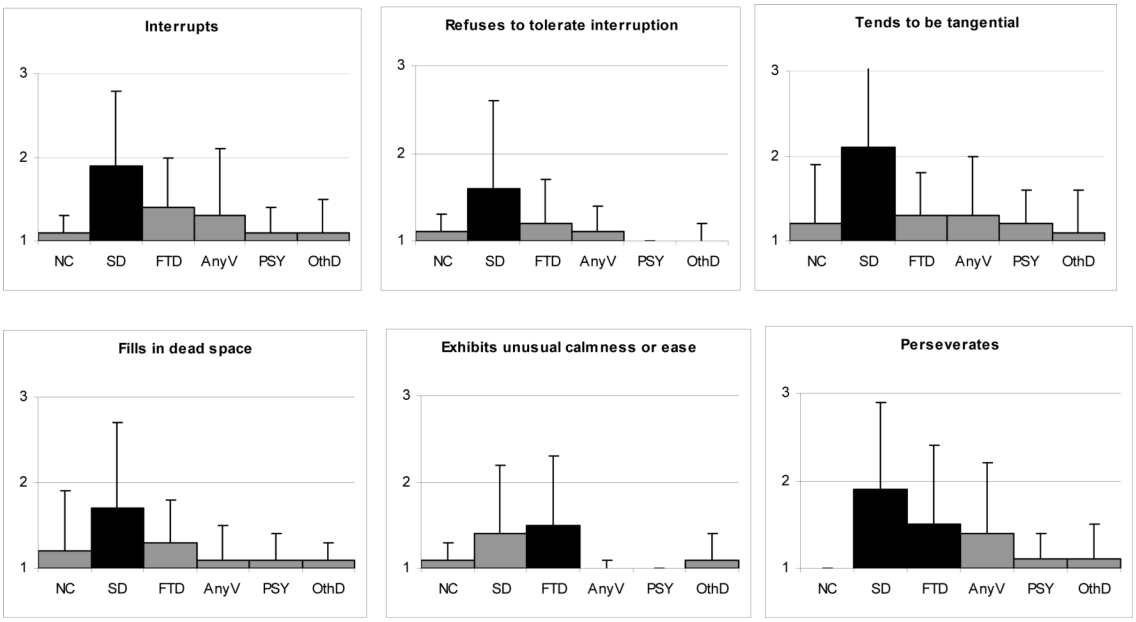

Figure 2.

Clinician ratings of collapsed patient groups on six IMP descriptor items. Patient groups showing significantly higher rates of a behavior compared to normal controls (NC) are marked with black bars; groups with no significant difference from NCs are marked with grey bars. FTD=frontotemporal dementia, SD=semantic dementia; AnyV=vascular dementia and mixed Alzheimer's disease and vascular disease; PSY=psychiatric disorder; OthD=Alzheimer's disease, progressive nonfluent aphasia, corticobasal degeneration, progressive supranuclear palsy, dementia with Lewy bodies.

Table 1

Demographics and summary scores across all patient groups. AD=Alzheimer's disease; FTD=frontotemporal dementia, SD=semantic dementia; PNFA=progressive nonfluent aphasia; CBD=corticobasal degeneration; PSP=progressive supranuclear palsy; DLB=dementia with Lewy bodies; VD=vascular dementia; AD/VD=mixed Alzheimer's disease and vascular disease; PSY=psychiatric disorder; NC=normal controls

Mean (±SD)	Overall F-Statistic	Overall p-value	AD (N=45)	FTD (N=40)	SD (N=21)	PNFA (N=13)	CBD (N=14)	PSP (N=21)	DLB (N=37)	VD (N=16)	AD/VD (N=29)	PSY (N=35)	PATIENT TOTAL (N=271)	NC (N=17)
Sex M/F	χ^2=30.84	p=0.0006	22/23	29/11	14/7	1/12	6/8	14/7	27/10	7/9	16/13	15/20	151/120	6/11
Age	F=30.53†	p<0.0001	75 (9.5)*	59.7 (7.1)	65.9 (7.3)	64.8 (11.4)	62.4 (5.9)	68.6 (7.6)*	74.9 (7.7)*	74.6 (11.1)*	81.5 (5.6)*	56.5 (11.5)	68.7 (11.8)	60.7 (12.0)
Education	F=1.26	n.s.	15.5 (3.0)	16.4 (2.4)	16.3 (2.1)	16.1 (2.9)	14.1 (2.1)	16 (3.2)	16 (3.7)	14.5 (2.9)	15.4 (2.1)	16.3 (2.7)	15.8 (2.8)	16.4 (2.1)
MMSE	F=24.06†	p<0.0001	22.7 (3.6)*	24.3 (6.1)*	18.2 (8.1)*	24.9 (4.5)	19.6 (7.4)*	25.3 (4.2)	22.2 (6.3)*	23.5 (5.5)*	20.0 (6.0)*	28.6 (1.7)	23.2 (6.0)	29.3 (1.3)
IMP Total Score	F=6.81	p<0.0001	19.2 (2.3)	22.1 (4.8)*	24.7 (6.2)**	18.4 (1.0)	18.5 (0.8)	18.9 (4.2)	18.9 (1.7)	20.1 (4.1)	20.0 (4.5)	18.9 (1.4)	20.0 (3.7)	18.8 (2.4)
IMP # Items Checked	F=4.49	p<0.0001	0.6 (1.4)	1.2 (1.9)	2.7 (2.4)**	0.0 (0.0)	0.1 (0.3)	0.2 (0.5)	0.5 (0.8)	0.9 (1.8)	1.0 (1.8)	0.3 (0.8)	0.8 (1.5)	0.6 (1.9)

* p<0.05 compared to NC's (Dunnett's post-hoc test)

** p<0.01 compared to NC's (Dunnett-Hsu post-hoc test controlling for sex, age, and MMSE score)

† F and p values derived from Welch's ANOVA statistic due to a positive Levine's test for inhomogenous variances.

Table 2

Average IMP behavioral descriptor ratings across collapsed diagnostic groups. FTD=frontotemporal dementia, SD=semantic dementia; AnyVasc=vascular dementia and mixed Alzheimer's disease and vascular disease; PSY=psychiatric disorder; Other Dementia=Alzheimer's disease, progressive nonfluent aphasia, corticobasal degeneration, progressive supranuclear palsy, dementia with Lewy bodies; NC=normal controls

	IMP Descriptor	SD (N=21)		FTD (N=40)		Any Vasc (N=45)	PSY (N=35)	Other Dementia (N=130)	NC (N=17)	**Overall F-value	p-value
1	Interrupts	1.9(0.9)	abcd	1.4(0.6)	d	1.3(0.8)	1.1(0.3)	1.1(0.4)	1.1(0.2)	6.60	<0.0001
2	Refuses to tolerate interruption	1.6(1.0)	abcde	1.2(0.5)	d	1.1(0.3)	1.0(0.0)	1.0(0.2)	1.1(0.2)	9.61	<0.0001
3	Ignores professional boundaries	1.2(0.6)		1.3(0.8)	bd	1.1(0.3)	1.0(0.0)	1.0(0.2)	1.0(0.0)	3.81	0.0024
4	Ignores personal boundaries	1.4(1.0)	d	1.4(0.8)	bcd	1.1(0.4)	1.1(0.2)	1.0(0.2)	1.1(0.2)	5.76	<0.0001
5	Tests examiner	1.0(0.0)		1.1(0.3)		1.0(0.3)	1.0(0.0)	1.0(0.2)	1.0(0.0)	0.66	n.s.
6	Makes personal comments	1.2(0.5)		1.3(0.7)	d	1.2(0.5)	1.1(0.3)	1.1(0.3)	1.0(0.0)	2.77	0.0186
7	Makes requests of examiner	1.2(0.7)		1.2(0.5)		1.1(0.5)	1.1(0.2)	1.1(0.2)	1.0(0.0)	1.55	n.s.
8	Tends to be tangential	2.1(1.1)	abcde	1.3(0.5)		1.3(0.7)	1.2(0.4)	1.1(0.5)	1.2(0.7)	8.02	<0.0001
9	Fills in dead space	1.7(1.0)	abcde	1.3(0.5)		1.1(0.4)	1.1(0.3)	1.1(0.2)	1.2(0.7)	7.11	<0.0001
10	Exhibits unusual calmness or ease	1.4(0.8)	bd	1.5(0.8)	abcd	1.0(0.1)	1.0(0.0)	1.1(0.3)	1.1(0.2)	7.81	<0.0001
11	Becomes frustrated with argument avoidance	1.2(0.7)	d	1.1(0.2)		1.0(0.2)	1.0(0.0)	1.0(0.0)	1.0(0.0)	2.40	0.0374
12	Perseverates	1.9(1.0)	ad	1.5(0.9)	ad	1.4(0.8)	1.1(0.3)	1.1(0.4)	1.0(0.0)	7.35	<0.0001
13	Expresses ethical superiority	1.0(0.0)		1.0(0.2)		1.0(0.0)	1.0(0.0)	1.0(0.1)	1.0(0.0)	0.49	n.s.
14	Expresses narcissism	1.3(0.8)	cd	1.3(0.6)	d	1.1(0.3)	1.0(0.2)	1.0(0.1)	1.2(0.6)	5.29	0.0001
15	Incorporates examiner into personal stories	1.1(0.3)		1.1(0.2)		1.1(0.4)	1.0(0.2)	1.0(0.0)	1.0(0.0)	1.25	n.s.
16	Seeks alliance with examiner	1.1(0.3)		1.2(0.5)	d	1.1(0.3)	1.1(0.3)	1.0(0.2)	1.0(0.0)	2.78	0.0182
17	Displays showmanship	1.1(0.5)		1.0(0.4)		1.0(0.0)	1.0(0.2)	1.0(0.1)	1.0(0.0)	1.72	n.s.
18	Is angry	1.2(0.7)		1.1(0.3)		1.1(0.3)	1.1(0.3)	1.1(0.4)	1.0(0.0)	0.49	n.s.
	IMP Descriptor TOTAL	24.7 (6.2)	abcd	22.1 (4.8)	abcd	20.0 (4.0)	18.9 (1.4)	18.9 (1.9)	18.8 (2.4)	13.87	<0.0001

a = significantly different from NC group ($p<0.05$ Tukey-Kramer-Kramer post-hoc test)

b = significantly different from PSY group ($p<0.05$ Tukey-Kramer post-hoc test)

c = significantly different from Any Vascular (AnyV) group ($p<0.05$ Tukey-Kramer post-hoc test)

d = significantly different from Other Dementia (OthD) group ($p<0.05$ Tukey-Kramer post-hoc test)

e = significantly different from FTD group ($p<0.05$ Tukey-Kramer post-hoc test)

** Omnibus F-statistic for effect of diagnosis across all 6 groups, controlling for age, sex, and MMSE

Table 3

Percentage of each diagnostic category exhibiting IMP behavior checklist items. FTD=frontotemporal dementia, SD=semantic dementia; AnyVasc=vascular dementia and mixed Alzheimer's disease and vascular disease; PSY=psychiatric disorder; Other Dementia=Alzheimer's disease, progressive nonfluent aphasia, corticobasal degeneration, progressive supranuclear palsy, dementia with Lewy bodies; NC=normal controls

		SD (N=21)		FTD (N=40)		PSY (N=35)	Any Vasc (N=45)		Other Dementia (N=130)		NC (N=17)	Overall Fisher's Exact p-value
1A	Interrupted exam	47.6%	abcd	10.0%		2.9%	15.6%		11.5%		5.9%	<0.0001
1B	Interrupted examiner	28.6%	bcd	17.5%	bd	0.0%	6.7%	d	0.8%		5.9%	<0.0001
3A	Called examiner by first name	0.0%		5.0%		0.0%	0.0%		1.5%		0.0%	0.0233
3B	Asked for something examiner had in their possession	0.0%		2.5%		0.0%	0.0%		0.0%		0.0%	n.s.
4A	Touched examiner	14.3%	d	7.5%	d	2.9%	4.4%	d	0.0%		0.0%	<0.0001
4B	Leaned very far forward	4.8%		7.5%	d	0.0%	4.4%		0.8%		5.9%	<0.0001
5A	Asked about examiner's credentials	0.0%		2.5%		0.0%	2.2%		2.3%		0.0%	0.0404
5B	Asked examiner general psychology or other questions	0.0%		0.0%		2.9%	0.0%		0.8%		0.0%	n.s.
5C	Asked to see identification	0.0%		2.5%		0.0%	0.0%		0.0%		0.0%	n.s.
6A	Insulted examiner's dress or manner	0.0%		5.0%		0.0%	0.0%		0.8%		0.0%	0.0257
6B	Commented on examiner's dress or manner	4.8%		7.5%		5.7%	11.1%	d	2.3%		0.0%	<0.0001
8A	Provided very lengthy answers	28.6%	bd	7.5%		5.7%	11.1%		6.2%		5.9%	<0.0001
8B	Changed answer in middle of explanation	23.8%	abcd	2.5%		2.9%	6.7%		2.3%		0.0%	<0.0001
10A	Put feet up	4.8%		0.0%		0.0%	0.0%		0.0%		0.0%	n.s.
10B	Stretched often	0.0%		0.0%		0.0%	0.0%		0.8%		5.9%	n.s.
10C	Moved about the room	9.5%	cd	7.5%	d	0.0%	0.0%		0.0%	a	5.9%	<0.0001
11A	Repeatedly tried to begin an argument with examiner Became angry or frustrated when examiner agreed with	0.0%		2.5%		0.0%	4.4%	d	0.0%		0.0%	0.0101
11B	subject	0.0%		0.0%		0.0%	0.0%		0.0%		0.0%	--
12A	Returned often to one event	28.6%	abcd	2.5%		2.9%	4.4%		2.3%		0.0%	<0.0001
12B	Returned often to one theme (e.g., winning, intelligence)	19.1%	bd	5.0%		2.9%	15.6%	d	2.3%		0.0%	<0.0001
13A	Expressed overt desire to help others	0.0%		2.5%		0.0%	2.2%		0.0%		0.0%	0.0436
13B	Made references to own truthfulness	0.0%		0.0%		0.0%	0.0%		0.0%		0.0%	--

		SD (N=21)		FTD (N=40)		PSY (N=35)		Any Vasc (N=45)		Other Dementia (N=130)		NC (N=17)	Overall Fisher's Exact p-value
13C	Indicated that others are “not as good” as subject is	0.0%		0.0%		0.0%		0.0%		0.8%		0.0%	n.s.
14A	Expressed personal superiority	4.8%	d	2.5%		0.0%		2.2%		0.0%	a	5.9%	0.0023
14B	Displayed grandiosity	4.8%	d	2.5%		0.0%	a	2.2%		0.0%	a	11.8%	<0.0001
14C	Discussed personal uniqueness	19.1%	cd	7.5%	d	5.7%	d	0.0%	a	0.0%	a	11.8%	<0.0001
16A	Excessive smiling	4.8%		2.5%		0.0%		0.0%		0.8%		0.0%	0.0278
16B	Verbal expression of communality	4.8%		0.0%		0.0%		2.2%		0.8%		0.0%	0.0313
16C	Sought interviewer's agreement of subject's views	0.0%		2.5%		0.0%		2.2%		0.0%		0.0%	0.0439
17A	Displayed large gestures	4.8%	d	2.5%		0.0%		0.0%		0.0%		0.0%	0.0205
17B	Used voice inflection to emphasized points	4.8%	d	2.5%		0.0%		0.0%		0.0%		0.0%	0.0205
17C	Used dramatic language	4.8%	d	2.5%		0.0%		0.0%		0.0%		0.0%	0.0205
		2.7		1.2		0.3		1.0					
	IMP TOTAL # CHECKED	(2.4)	abcde	(1.9)	d	(0.8)		(1.8)		0.4 (1.0)		0.6 (1.8)	<0.0001

a = significantly different from NC group ($p<0.05$)

b = significantly different from PSY group ($p<0.05$)

c = significantly different from Any Vascular (AnyV) group ($p<0.05$)

d = significantly different from Other Dementia (OthD) group ($p<0.05$)

e = significantly different from FTD group ($p<0.05$)