Published in final edited form as:
J Neuropsychiatry Clin Neurosci. 2009 ; 21(3): 299–306. doi:10.1176/appi.neuropsych.21.3.299.

Generalized and Symptom-Specific Insight in Behavioral Variant Frontotemporal Dementia and Primary Progressive Aphasia

Sarah Jane Banks, PhD and **Sandra Weintraub, PhD**
Cognitive Neurology and Alzheimer's Disease Center, Northwestern University Feinberg School of Medicine, 320 E Superior 11-569, Chicago, IL, 60613, USA

Abstract

Behavioral variant frontotemporal dementia (bvFTD) and primary progressive aphasia (PPA) are related dementias with different presenting symptoms, but with increasing symptom-overlap as they progress. Loss of insight is associated with early bvFTD, but not PPA. This study used the Frontal Behavioral Inventory (FBI) to compare patient and caregiver concepts of symptom presence and severity. BvFTD patients were found to have worse insight overall than PPA patients. However, the PPA group showed reduced insight into behavioral symptoms, and the bvFTD groups had intact insight into some language symptoms. Theoretical and clinical implications are discussed.

Keywords

Anosognosia; awareness; dementia; primary progressive aphasia; frontotemporal dementia

Anosognosia, or loss of insight for symptoms, has been reported in various neurological disorders (Prigatano, 1991) including dementia (Bozzola, Gorelick, & Freels, 1992; Migliorelli, Teson, Sabe, Petracca et al., 1995). An intriguing dichotomy in insight exists between two variants of dementia caused by frontotemporal lobar degeneration (FTLD), namely, the behavioral variant (bvFTD) and the language variant (primary progressive aphasia or PPA). A core diagnostic criterion for bvFTD is the early loss of insight (which is defined as "a lack of awareness of mental symptoms evidenced by frank denial of symptoms or unconcern about the social, occupational, and financial consequences of mental failure" (Neary et al., 1998), thus combining both a frank loss of insight (anosognosia) with a lack of concern about acknowledged symptoms (anosodiaphoria)) although studies indicate that some bvFTD patients show partially intact insight early in their disease course (Evers, Kilander, & Lindau, 2007). In PPA, studies indicate that insight is spared early in the disease, but diminishes over time (Eslinger et al., 2005; Marczinski, Davidson, & Kertesz, 2004).

With increasing disease duration, the symptom profiles of these two related dementias become less distinct: symptoms of aphasia can emerge later in the course of bvFTD (Blair, Marczinski, Davis-Faroque, & Kertesz, 2007), and PPA patients often become behaviorally more similar to bvFTD patients (Marczinski et al., 2004). Few studies have assessed insight in PPA, but evidence does point to loss of insight into select symptoms in this disorder. This is consistent with evidence from other neurological diseases, which demonstrate that loss of insight is sometimes quite radical, with a total denial of a particular symptom, but in other cases insight can be only partially diminished (McGlynn & Schacter, 1989; Prigatano, 1991). The symptoms seen in dementias caused by FTLD can grossly be divided into two categories: behavioral

Reprints: Sarah Banks, Montreal Neurological Institute, Department of Neurology and Neurosurgery, 3801 University Street, Montreal Quebec H3A 2B4, Canada, sarah.banks@mail.mcgill.ca, phone: +01 (514) 398 6644 ext. 00262.

symptoms such as disinhibition, apathy or aspontaneity, and cognitive symptoms such as aphasia or difficulties with attention or executive functions. In the frontotemporal dementias and other disorders, including Alzheimer's disease, studies suggest that behavioral symptoms are more vulnerable to loss of insight than certain cognitive symptoms (S. Banks & S. Weintraub, 2008; Starkstein, Jorge, Mizrahi, & Robinson, 2006). In PPA, language is the most affected domain. Few studies have assessed insight into language symptoms, although the evidence to date points to reduced insight in some patients with PPA (S.J. Banks & Weintraub, in press), with behavioral symptoms such as apathy most often being associated with reduced insight (S. Banks & S. Weintraub, 2008).

Levels of insight can be assessed by administering identical questionnaires to patients and their caregivers, and calculating the discrepancy between their responses. This method has been applied to the study of insight into particular symptoms such as empathy (Rankin, Baldwin, Pace-Savitsky, Kramer, & Miller, 2005) and disinhibition (Starkstein, Garau, & Cao, 2004), in isolation. However, this technique has rarely been used to compare insight across a range of symptoms in a particular disease. The current study compared patient and caregiver ratings on a measure specifically designed to capture the spectrum of symptoms seen in FTLD, the Frontal Behavioural Inventory (FBI (Kertesz, Davidson, & Fox, 1997)). Questions on the FBI survey cognitive symptoms, including aphasia and inattention, and behavioral symptoms, including apathy and disinhibition. Assuming that the caregiver has more objectivity than the patient, this method permits the evaluation of patients' insight into disease-related changes by comparing the total FBI scores in both groups. In addition, insight into specific symptoms can be investigated by comparing caregiver and patient scores on individual items.

The aims of this study were two-fold. The first was to compare patients' and respective caregivers' scores on the FBI, with the hypothesis that preserved insight in the PPA group would be reflected in a smaller discrepancy between their and their caregivers' scores than in the bvFTD group. The second aim was to assess symptom-specific insight by comparing patient-caregiver discrepancy scores on individual items on the FBI. For all groups, it was predicted that behavioral symptoms would be associated with greater symptom discrepancy scores than cognitive symptoms.

Methods

Subjects

Patients with bvFTD, PPA and Probable Alzheimer's Disease (PrAD) with similar disease duration were recruited for this study from the Clinical Core of the Northwestern Alzheimer's Disease Center and informed consent was obtained from each patient and his/her caregiver on a protocol approved by the Institutional Review Board at Northwestern University. The most recent research consensus criteria were used for diagnosis (McKhann et al., 1984; Mesulam, 2001; Neary et al., 1998), and diagnoses were made via consensus among a team of behavioral neurologists and neuropsychologists. The Mesulam criteria used to diagnose PPA do not subtype further, although other groups use the Neary criteria and subtype into semantic dementia and progressive nonfluent aphasia. The current study employed the Mesulam criteria exclusively, and hence all patients with 2 years of relatively isolated aphasia, in addition to the other criteria, were included. This group includes patients with varying degrees of fluency in their output, as well as variation in comprehension deficits and agrammatism. Although the Neary criteria stipulate loss of insight as a core criterion for bvFTD, this criterion is open to interpretation as has been discussed elsewhere (Evers et al., 2007). BvFTD patients in the current study were judged clinically to have reduced insight into some aspect of their disease, and hence met diagnostic criteria. The diagnostic criteria for PPA do not specify a required level of insight. The PrAD group was included as a disease control group, since insight has been well researched (Clare, Wilson, Carter, Roth, & Hodges, 2004; Dalla Barba, Parlato,

Iavarone, & Boller, 1995; Starkstein, Sabe, Chemerinski, Jason, & Leiguarda, 1996; Starkstein et al., 2006) and hence is better understood in this condition. Only those patients who were able to complete a clinical neuropsychological evaluation and clinically judged to have adequate language comprehension to complete the study were included. In addition, only patients with mild or moderate levels of dementia, as determined by a Mini-Mental Status Examination (MMSE (Folstein, Folstein, & McHugh, 1975)) score greater than or equal to 10, and a Clinical Dementia Rating scale (CDR (Hughes, Berg, Danziger, Coben, & Martin, 1982; Morris, 1993)) global score less than or equal to 2, were included. Demographic and disease-severity information is included in Table 1.

Procedures

The FBI was developed as a structured caregiver interview that specifically targets common symptoms in FTLD, and has been shown to have strong psychometric properties (Kertesz et al., 1997; Kertesz, Nadkarni, Davidson, & Thomas, 2000). The version used in the current study was slightly modified by the original author, who standardized it and found it to be equivalent to the earlier versions (pers comm. Kertesz 2004). One question is asked per symptom, with a total of 24 questions. Half of the questions address “negative” symptoms, such as apathy and withdrawal, and half of the questions positive symptoms, such as disinhibition. Each symptom is rated on a Likert scale ranging from 0 (none/never) to 3 (severe/always). In this study, the FBI was given to the caregiver and also to the patient in the course of separate structured interviews. Each of the examiners who completed the questionnaires with the participants was trained by the lead author, to establish that the participants received the same information and instructions.

Data Analysis

FBI discrepancy scores were calculated by subtracting the total caregiver FBI score from the total patient FBI score. Since a higher FBI score implies more, or more severe, symptoms, a negative discrepancy score indicates loss of insight; the more negative the discrepancy, the less insight. The FBI discrepancy scores for each of the subgroups were not normally distributed, and large differences existed between the variance of scores in each subgroup. Given these violations of the assumptions necessary for parametric comparisons, in addition the ordinal nature of the data, nonparametric statistics were employed. Total discrepancy scores were compared among the three groups using the Kruskal-Wallis test and between groups with Mann-Whitney tests, with a Bonferroni correction (a lowered alpha of .017 accepted as significant).

To assess symptom-specific insight, patient-caregiver discrepancy scores for individual items on the FBI were identified for item analysis. In order to focus the analysis on symptoms which occurred with adequate frequency in both PPA and bvFTD groups (and hence not compare symptoms where large numbers of the patients in both or either group did not suffer from the symptom), and to avoid excessive numbers of comparisons, the caregiver responses were examined to exclude items that were rarely endorsed. Caregiver responses were then ranked, and the 7 most commonly endorsed symptoms picked for further analysis, excluding all other items from further analysis. This subgroup of items was selected to avoid excessive comparisons and hence a potential increase in Type I error. Details of item selection are explained in the results section. The individual symptom discrepancy scores for these items (i.e., patient’s symptom score minus caregiver’s symptom score) were then calculated. Wilcoxon signed ranks tests were used to test whether patient and caregiver scores differed significantly for each symptom. All tests were two-tailed.

Results

First, overall differences in insight among groups were compared using the FBI Discrepancy Score. Figure 1 shows the distribution of scores. There was a significant effect of diagnosis (H (2)= 18.26, $p < .0005$). Comparisons between groups indicated that the PPA patients' discrepancy scores were significantly closer to zero, i.e., better patient-caregiver agreement than the bvFTD ($U = 9$, $p < .0005$), and the PrAD ($U = 61$, $p < .0005$) groups. The PrAD and bvFTD groups did not differ significantly. Data were also analyzed by dividing both the patient and caregiver total FBI scores by the number of symptoms that the caregiver endorsed, then comparing the difference between patient and caregiver scores within each of the groups. This step eliminates any bias resulting from the larger number of symptoms that bvFTD patients typically demonstrate on the FBI (Kertesz et al., 1997). The same pattern found in the original analysis was evident (significant effect of diagnosis (H (2)= 19.15, $p < .0005$), no difference between AD and bvFTD groups, PPA groups showed better agreement with their caregivers compared with AD group ($U = 51.5$, $p < .0005$) and the bvFTD group ($U = 10.0$, $p < .0005$)). In addition, given the wide variance in scores seen in each of the groups, correlations were performed with various disease-severity measures (MMSE, CDR, Activities of Daily Living Questionnaire (Johnson, Barion, Rademaker, Rehkemper, & Weintraub, 2004)) for each of the groups. None of these correlations were significant.

Subsequent to these analyses, symptoms were ranked in terms of the frequency with which they were endorsed by caregivers in order to select symptoms that would be used for symptom-specific analysis. Overall, most symptoms were less frequently endorsed by PPA caregivers than by bvFTD caregivers. Therefore, the seven symptoms most frequently endorsed by PPA caregivers were selected. The frequency of endorsement, and ranking of these symptoms for the groups are presented in Table 2.

Wilcoxon signed ranks tests on the FBI Symptom Discrepancy scores (patient score minus caregiver score) for each of the seven symptoms, displayed in Table 3, indicated that the PPA group demonstrated significant differences between caregiver and patient responses only for Apathy and Aspontaneity; the BvFTD group, patients' and caregivers' responses differed significantly for all symptoms except Aphasia; the PrAD group demonstrated significant differences for all symptoms except Aphasia.

Discussion

This study assessed insight in PPA, bvFTD, and PrAD by analyzing discrepancy scores between patients' and caregivers' responses to the Frontal Behavioral Inventory, a measure that quantifies behavioral and cognitive symptoms associated with frontotemporal lobar degeneration. When discrepancy scores were compared, bvFTD patients were found to disagree with their caregivers more than PPA patients on their overall symptom frequency and intensity. However, there was substantial variability among patients in the bvFTD group, with some having similar levels of insight to PPA patients. PPA patients were more likely to be in closer agreement with their caregivers. There was also a relatively wide range of discrepancy scores within the PPA group, suggesting that some patients do, in fact, demonstrate poor insight. The PrAD patients did not differ significantly from the bvFTD patients, and showed the greatest variability in the degree of loss of insight. When symptom-specific insight was analyzed, bvFTD and PrAD patients disagreed with their caregivers for all symptoms analyzed, except Aphasia. PPA patients, however, disagreed with their caregivers only for Apathy and Aspontaneity. PPA patients tended to rate their language and other cognitive symptoms similarly to their caregivers' ratings.

The majority of bvFTD patients in this study showed poor insight. However, there was a wide range of FBI discrepancy scores in this group. The finding that some patients with bvFTD may have relatively intact insight was not expected, given that loss of insight is a core diagnostic criterion for bvFTD by Neary critieria (Neary et al., 1998). This finding echoes that of a recent study investigating the empirical basis of this criterion (Evers et al., 2007). Evers *et al.* found 3 of 8 bvFTD patients to have intact insight when they used a semi-structured interview method directly asking patients about their disease. Another study found that even when bvFTD patients acknowledged their behavioral symptoms, they still did not express concern about how these symptoms might affect them or their families (Mendez & Shapira, 2005). It may be that those bvFTD patients who were in closer agreement to their caregivers in the current study also demonstrated this pattern of anosodiaphoria (i.e., lack of concern regarding symptoms (Critchley, 1953)) as opposed to a frank anosognosia.

Another surprising finding was the lack of significant difference in levels of insight between the bvFTD and PrAD groups. The PrAD group also demonstrated the widest range of FBI discrepancy scores, suggesting that some of these patients had quite intact insight, whereas others had poor insight. Previous studies regarding insight in PrAD also demonstrate variable levels of insight. The involvement of more frontal regions of the brain has been proposed as an explanation for reduced insight in some PrAD patients (Michon, Deweer, Pillon, Agid, & Dubois, 1994). The lack of association between level of insight and disease severity measures further suggests that insight is not simply lost with progression of disease, but a more complex (likely neuroanatomical) explanation is needed.

The results of this study suggested that behavioral symptoms and non-language cognitive symptoms are more commonly associated with loss of insight than language symptoms. Research in various neurological disorders points to the symptom-specificity of insight (Barrett, Eslinger, Ballentine, & Heilman, 2005; Breier et al., 1995; von Hagen & Ives, 1937). With PrAD patients, Starkstein observed that insight for cognitive symptoms is distinct from insight for behavioral symptoms (Starkstein et al., 1996), and others have reported that loss of insight is commonly associated with behavioral symptoms in dementias caused by FTLD (Eslinger et al., 2005). In the present study, the bvFTD and PrAD patients behaved in a very similar manner in terms of symptom-specific insight, whereas PPA patients lost insight only into apathy and aspontaneity, which are (arguably closely related) behavioral symptoms. Eslinger et al. (Eslinger et al., 2005) suggested that apathy and aspects of empathy were particularly sensitive to loss of insight in both bvFTD (they labeled these patients “Social/ Dysexecutive” subtype) and the semantic dementia subtype of PPA; however their bvFTD group differed from their PPA group in terms of insight into cognitive symptoms. They also found bvFTD patients to show poor insight into cognitive symptoms such as memory and attention, whereas PPA patients complained of cognitive symptoms to a similar degree as their caregivers.

Numerous studies in PrAD have suggested that loss of insight into apathy is particularly common (Ott, Noto, & Fogel, 1996; Starkstein et al., 1996). It could be suggested that apathy and insight are not, in fact, dissociable, but that the lack of concern seen in apathy is conceptually related to anosognosia, or at least anosodiaphoria. Attempts to treat apathy in neurological and psychiatric diseases with various medications have had mixed, but sometimes encouraging, results (Deakin, Rahman, Nestor, Hodges, & Sahakian, 2004; Padala, Burke, Bhatia, & Petty, 2007; Pitkala, Laurila, Strandberg, & Tilvis, 2004). If insight and apathy are strongly intertwined; successfully reducing apathy with medication may affect insight. This concept is yet to be explored.

Some of the symptoms investigated (e.g., apathy, indifference) may also reflect mood disturbances, which have proved to be common in PPA (Medina & Weintraub, 2007) and

Alzheimer's disease (Migliorelli, Teson, Sabe, Petracchi et al., 1995) but not to the same degree in bvFTD (S. J. Banks & S. Weintraub, 2008), and which may relate to an increased rate of anosodiaphoria, or may also disturb a potential mechanism of insight, that is somatic "tagging"(Bechara, Damasio, Damasio, & Lee, 1999) of information by the emotion network, making the information (in this case, about disease symptoms) more salient. Further research into this area is warranted.

Insight into aphasia was intact even in the bvFTD and PrAD groups whereas loss of insight for other cognitive symptoms was common. This is interesting in light of the underlying neuroanatomy. Aphasia is associated with damage to the left hemisphere perisylvian language region. Anosognosia, for the most part, is considered to be a right hemisphere phenomenon (Heilman, Barrett, & Adair, 1998; Prigatano, 1991). It could be argued that aphasia is in some way 'protected' from loss of insight due to the hemispheric localization of language. However, some patients with Wernicke's aphasia appear to show loss of insight into their disordered speech despite the left hemisphere locus of damage (Shuren, Hammond, Maher, Rothi, & Heilman, 1995; Weinstein, Cole, Mitchell, & Lyerly, 1964). Perhaps not surprisingly, those PPA patients who show reduced insight produce language with reduced meaningful content, similar to Wernicke's patients (S.J. Banks & Weintraub, in press). However, it is yet to be established whether patients ever lose insight specifically into their language symptoms. The relationship between loss of insight in dementia and language symptoms warrants further investigation.

The lack of insight for even certain cognitive symptoms in bvFTD may be considered consistent with findings in the literature that these patients lose their sense of "selfhood" (Miller et al., 2001). It is possible that they no longer have a good sense of how they used to be, and hence they are unable to realistically compare their ability now to their ability before their disease onset. Rankin has revealed a tendency for bvFTD patients to overestimate positive aspects of their personalities such as assuredness and extroversion, while underestimating negative qualities such as cold-heartedness (Rankin et al., 2005). It could be argued that bvFTD patients similarly hold a delusional belief that they are not impaired. During the disease process in bvFTD, patients may not passively lose awareness into their symptoms, but actively develop a new, and positive, self-view. Results from the current study suggest that PPA patients, in contrast, will sometimes actually be more critical of their abilities than their caregivers, potentially related to increased levels of depressive symptomatology in these patients (Medina & Weintraub, 2007).

A number of important limitations to this study should be discussed. Our patients were matched in terms of disease duration, but differed on other indices of dementia severity. The CDR, with its emphasis on memory, may not be as accurate in assessing severity in non-Alzheimer's dementias as it is in Alzheimer's disease. Future studies may use other strategies in matching the patient groups. In addition, the patients were relatively homogenous in terms of disease duration, preventing analysis of the impact of this variable on insight. Discrepancy techniques, by definition, rely on the subjective responses of both patients and caregivers, which not only adds between-subject variability but may also be affected by factors other than the patients' actual symptoms, such as caregiver distress (which has been previously found to be higher when the patient has reduced awareness (DeBettignies, Mahurin, & Pirozzolo, 1990)) or quality of caregiver observation. This technique also fails to establish what aspect of insight is failing, for example whether there is a break down in general self-awareness, or a more specific self-monitoring deficit (for discussions of these components of insight see (S. Banks & S. Weintraub, 2008; Barrett et al., 2005; O'Keeffe et al., 2007)). Finally, the group sizes, while typical of studies with these less common dementia populations, were not large. This limited the power of the statistical comparisons.

Reduced insight has important clinical implications in terms of caregiver burden, treatment compliance and prognosis. Better understanding of this phenomenon in dementias caused by FTLD will result in improved caregiver education, which has been shown to be beneficial in informing caregivers and enhancing coping strategies (S. J. Banks, Rogalski, Medina, Skoglund, & Morhardt, 2006). Currently, quantification of loss of insight is not a common part of the neurological or neuropsychological examination, but it may be an important addition, especially when loss of insight is considered a diagnostic sine qua non for bvFTD.

Acknowledgments

The work in this report was supported by Northwestern Alzheimer's Disease Core Center grant, P30 AG13854, from the National Institute on Aging to Northwestern University. Jennifer Medina, Jason Osher and Rebecca Gavett kindly assisted with data collection.

References

Banks S, Weintraub S. Self-awareness and self-monitoring of cognitive and behavioral deficits in behavioral variant frontotemporal dementia, primary progressive aphasia and probable Alzheimer's disease. Brain Cogn 2008;67:58–68. [PubMed: 18194832]

Banks SJ, Rogalski E, Medina JE, et al. Organizing a Series of Education and Support Conferences for Caregivers of Individuals with Frontotemporal Dementia and Primary Progressive Aphasia. Alzheimer's Care Quarterly 2006;7:243–250. [PubMed: 20596301]

Banks SJ, Weintraub S. Neuropsychiatric symptoms in behavioral variant frontotemporal dementia and primary progressive aphasia. J Geriatr Psychiatry Neurol 2008;21:133–141. [PubMed: 18474722]

Banks SJ, Weintraub S. Cognitive deficits and reduced insight in primary progressive aphasia. American Journal of Alzheimer's Disease and Other Dementias. in press.

Barrett AM, Eslinger PJ, Ballentine NH, et al. Unawareness of cognitive deficit (cognitive anosognosia) in probable AD and control subjects. Neurology 2005;64:693–699. [PubMed: 15728294]

Bechara A, Damasio H, Damasio AR, et al. Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. J Neurosci 1999;19:5473–5481. [PubMed: 10377356]

Blair M, Marczinski CA, Davis-Faroque N, et al. A longitudinal study of language decline in Alzheimer's disease and frontotemporal dementia. Journal of the International Neuropsychological Society 2007;13:237–245. [PubMed: 17286881]

Bozzola FG, Gorelick PB, Freels S. Personality changes in Alzheimer's disease. Archives of Neurology 1992;49:297–300. [PubMed: 1536633]

Breier JI, Adair JC, Gold M, et al. Dissociation of anosognosia for hemiplegia and aphasia during left-hemisphere anesthesia. Neurology 1995;45:65–67. [PubMed: 7824138]

Clare L, Wilson BA, Carter G, et al. Awareness in early-stage Alzheimer's disease: relationship to outcome of cognitive rehabilitation. Journal of Clinical and Experimental Neuropsychology 2004;26:215–226. [PubMed: 15202541]

Critchley, M. The Parietal Lobes. London: Edward Arnold; 1953.

Dalla Barba G, Parlato V, Iavarone A, et al. Anosognosia, intrusions and 'frontal' functions in Alzheimer's disease and depression. Neuropsychologia 1995;33:247–259. [PubMed: 7746367]

Deakin JB, Rahman S, Nestor PJ, et al. Paroxetine does not improve symptoms and impairs cognition in frontotemporal dementia: a double-blind randomized controlled trial. Psychopharmacology 2004;172:400–408. [PubMed: 14666399]

DeBettignies BH, Mahurin RK, Pirozzolo FJ. Insight for impairment in independent living skills in Alzheimer's disease and multi-infarct dementia. J Clin Exp Neuropsychol 1990;12:355–363. [PubMed: 2341561]

Eslinger PJ, Dennis K, Moore P, et al. Metacognitive deficits in frontotemporal dementia. Journal of Neurology, Neurosurgery & Psychiatry 2005;76:1630–1635.

Evers K, Kilander L, Lindau M. Insight in frontotemporal dementia: conceptual analysis and empirical evaluation of the consensus criterion “loss of insight” in frontotemporal dementia. Brain Cognition 2007;63:13–23.

Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatry Research 1975;12:189–198.

Heilman KM, Barrett AM, Adair JC. Possible mechanisms of anosognosia: a defect in self-awareness. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences 1998;353:1903–1909.

Hughes CP, Berg L, Danziger WL, et al. A new clinical scale for the staging of dementia. British Journal of Psychiatry 1982;140:566–572. [PubMed: 7104545]

Johnson N, Barion A, Rademaker A, et al. The Activities of Daily Living Questionnaire: a validation study in patients with dementia. Alzheimer Dis Assoc Disord 2004;18:223–230. [PubMed: 15592135]

Kertesz A, Davidson W, Fox H. Frontal behavioral inventory: diagnostic criteria for frontal lobe dementia. Can J Neurol Sci 1997;24:29–36. [PubMed: 9043744]

Kertesz A, Nadkarni N, Davidson W, et al. The Frontal Behavioral Inventory in the differential diagnosis of frontotemporal dementia. J Int Neuropsychol Soc 2000;6:460–468. [PubMed: 10902415]

Marczinski CA, Davidson W, Kertesz A. A longitudinal study of behavior in frontotemporal dementia and primary progressive aphasia. Cogn Behav Neurol 2004;17:185–190. [PubMed: 15622012]

McGlynn SM, Schacter DL. Unawareness of deficits in neuropsychological syndromes. Journal of Clinical and Experimental Neuropsychology 1989;11:143–205. [PubMed: 2647781]

McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer’s disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer’s Disease. Neurology 1984;34:939–944. [PubMed: 6610841]

Medina J, Weintraub S. Depression in Primary Progressive Aphasia. J Geriatr Psychiatry Neurol 2007;20:153–160. [PubMed: 17712098]

Mendez MF, Shapira JS. Loss of insight and functional neuroimaging in frontotemporal dementia. Journal of Neuropsychiatry and Clinical Neurosciences 2005;17:413–416. [PubMed: 16179666]

Mesulam MM. Primary progressive aphasia. Annals of Neurology 2001;49:425–432. [PubMed: 11310619]

Michon A, Deweer B, Pillon B, et al. Relation of anosognosia to frontal lobe dysfunction in Alzheimer’s disease. J Neurol Neurosurg Psychiatry 1994;57:805–809. [PubMed: 8021665]

Migliorelli R, Teson A, Sabe L, et al. Anosognosia in Alzheimer’s disease: a study of associated factors. Journal of Neuropsychiatry and Clinical Neurosciences 1995;7:338–344. [PubMed: 7580194]

Migliorelli R, Teson A, Sabe L, et al. Prevalence and correlates of dysthymia and major depression among patients with Alzheimer’s disease. Am J Psychiatry 1995;152:37–44. [PubMed: 7802118]

Miller BL, Seeley WW, Mychack P, et al. Neuroanatomy of the self: evidence from patients with frontotemporal dementia. Neurology 2001;57:817–821. [PubMed: 11552010]

Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology 1993;43:2412–2414. [PubMed: 8232972]

Neary D, Snowden JS, Gustafson L, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology 1998;51:1546–1554. [PubMed: 9855500]

O’Keeffe FM, Murray B, Coen RF, et al. Loss of insight in frontotemporal dementia, corticobasal degeneration and progressive supranuclear palsy. Brain 2007;130:753–764. [PubMed: 17347257]

Ott BR, Noto RB, Fogel BS. Apathy and loss of insight in Alzheimer’s disease: a SPECT imaging study. Journal of Neuropsychiatry and Clinical Neurosciences 1996;8:41–46. [PubMed: 8845700]

Padala PR, Burke WJ, Bhatia SC, et al. Treatment of apathy with methylphenidate. Journal of Neuropsychiatry and Clinical Neurosciences 2007;19:81–83. [PubMed: 17308232]

Pitkala KH, Laurila JV, Strandberg TE, et al. Behavioral symptoms and the administration of psychotropic drugs to aged patients with dementia in nursing homes and in acute geriatric wards. International Psychogeriatrics 2004;16:61–74. [PubMed: 15190997]

Prigatano, GP. Disturbances of self-awareness of deficit after traumatic brain injury. In: Schacter, DL.; Prigatano, GP., editors. Awareness of deficit after brain injury. New York: Oxford University Press; 1991. p. 111-126.

Rankin KP, Baldwin E, Pace-Savitsky C, et al. Self awareness and personality change in dementia. Journal of Neurology, Neurosurgery and Psychiatry 2005;76:632–639.

Shuren JE, Hammond CS, Maher LM, et al. Attention and anosognosia: the case of a jargonaphasic patient with unawareness of language deficit. Neurology 1995;45:376–378. [PubMed: 7854542]

Starkstein SE, Sabe L, Chemerinski E, et al. Two domains of anosognosia in Alzheimer's disease. Journal of Neurology, Neurosurgery and Psychiatry 1996;61:485–490.

Starkstein SE, Garau ML, Cao A. Prevalence and clinical correlates of disinhibition in dementia. Cognitive and Behavioral Neurology 2004;17:139–147. [PubMed: 15536301]

Starkstein SE, Jorge R, Mizrahi R, et al. A diagnostic formulation for anosognosia in Alzheimer's disease. Journal of Neurology, Neurosurgery and Psychiatry 2006;77:719–725.

von Hagen KO, Ives ER. Anosognosia (Babinski) imperception of hemiplegia. Report of six cases, one with autopsy. Bulletin of Los Angeles Neurological Society 1937;2:95–103.

Weinstein EA, Cole M, Mitchell MS, et al. Anosognosia and Aphasia. Archives of Neurology 1964;10:376–386. [PubMed: 14107687]

Table 1

Demographic and disease severity data for participants*

	PPA	bvFTD	PrAD
N	16	10	23
Age	**68.44** (8.16)	**63.70** (6.61)	**79.46** (8.00)
Education (Years)	**15.57** (2.79)	**15.90** (2.33)	**13.50** (3.53)
Duration of disease (Years)	**4.32** (1.74)	**4.90** (2.64)	**5.58** (3.59)
CDR	**0.53** (0.38)	**1.11** (0.55)	**1.27** (0.49)
MMSE (max = 30)	**20.88** (7.56)	**24.00** (4.16)	**20.21** (4.58)
NPI-Q (symptoms, max = 12)	**2.19** (2.23)	**4.22** (2.39)	**3.39** (2.70)
BNT (max = 60)	**38.92** (20.84)	**41.70** (18.67)	**38.52** (13.49)

* Mean scores (with standard deviations) for CDR, MMSE, NPI-Q (Neuropsychiatric Inventory Questionnaire) and BNT (Boston Naming Test). ANOVA with planned comparisons indicated that PrAD patients were significantly older than PPA and bvFTD patients ($p<.005$). PPA patients had significantly lower CDR scores and ADL-Q scores than bvFTD or PrAD patients ($p<.005$).

Table 2

Percentage of caregivers endorsing symptoms selected for symptom-specific analyses for bvFTD and PPA groups (i.e., score >0). 1 indicates the most frequently endorsed item.

		PPA % endorsement	PPA caregivers' rank	BvFTD % endorsement	BvFTD caregivers' rank	PrAD % endorsement	PrAD caregivers' rank
Symptom	Logopenia	90.0	1	62.5	2	62.5	6
	Aphasia	81.2	2	40.0	6	25.0	11
	Inattention	62.5	3	100.0	1	82.5	2
	Apathy	53.8	4	90.0	2	79.2	3
	Disorganization	43.8	5	100.0	1	83.3	2
	Aspontaneity	43.7	6	100.0	1	95.8	1
	Indifference	43.7	6	70.8	2	70.8	4

Table 3

Wilcoxon signed ranks tests for each of the seven symptoms

		PPA Z	BvFTD Z	PrAD Z
Symptom	Logopenia	−0.49	1.98*	2.49 *
	Aphasia	−0.79	1.86	−0.15
	Inattention	−2.77	2.57*	3.21 **
	Apathy	2.53*	2.70*	3.57***
	Disorganization	0.95	2.70*	3.77***
	Aspontaneity	2.12*	2.20*	3.99***
	Indifference	0.33	2.59*	2.93 *

Note: significant differences between caregiver and patient ratings are indicated by asterisks:

* $p < .05$,

** $p < .005$,

*** $p < .0005$