

Review Article

Neuropsychiatric Characteristics of Alzheimer's Disease and the Behavioral Variant of Frontotemporal Dementia

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Abstract

Neurodegenerative dementias that occur in adults can present with significant behavioral symptoms in addition to the cognitive syndrome. These can be disruptive for the families who take care for these patients and cause a significant burden on the medical system. The incidence of Alzheimer's disease (AD) is frequently greater in patients over 65 years of age, whereas the behavioral variant of frontotemporal dementia (bvFTD) is more common in subjects younger than 65. All the same, AD can have an early onset and present with behavioral symptoms that resemble bvFTD. Similarly, bvFTD can begin after age 65, thereby mimicking an AD syndrome. Whereas an amnesic syndrome along with deterioration in other cognitive domains, mood-related symptoms, psychosis and functional disabilities are the main elements characterizing AD, a dysexecutive syndrome accompanied by other neuropsychological detriments, a profound lack of social cognition and functional deterioration are the most prominent signs suggesting the presence of bvFTD. It should be noted, however, that in some cases, especially those in which AD begins before age 65, clinical differentiation of the two disease processes can be difficult. In this manuscript, the most salient aspects of AD and bvFTD and the key signs that might contribute to differential diagnosis of the two disorders are highlighted. Proper diagnosis of AD and bvFTD has important implications for treatment because there are symptomatic therapies for these two types of dementia. Additionally, their appropriate identification may contribute to long-term planning of the care of these patients.

ABBREVIATIONS

AD: Alzheimer's Disease; FTD: Frontotemporal Dementia; bvFTD: Behavioral Variant of Frontotemporal Dementia; MCI: Mild Cognitive Impairment; VD: Vascular Dementia; ADL: Activities Of Daily Living; CSF: Cerebro Spinal Fluid; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography; SPECT: Single-Photon Emission Computed Tomography; DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders 4th Edition; ICD-10: International Statistical Classification of Diseases and Related Health Problems 10th Edition; NIA-AA: National Institute on Aging - Alzheimer's Association guidelines; DSM-5: Diagnostic and Statistical Manual of Mental Disorders 5th Edition

INTRODUCTION

Dementia is a salient issue in global health in the 21st century for several reasons. First, its consequences are disastrous because both important economic costs and intense caregiver burdens are associated with this class of neurodegenerative disorder [1]. Second, because increased age is the most important risk factor for dementia [1], the marked increase in elderly people that currently characterizes societies around the world [2] makes this disease particularly worrisome. For example, according to some estimates, the percentage of the global population over the age of 60 will increase from 10.0% in 2000 to 21.8% in 2050 and to 32.2% in 2100 [3]. Other figures indicate that approximately 24.3

million people age 60 or older suffered from dementia worldwide in 2001, whereas 43.3 million and 81.1 million might suffer from this condition in 2020 and 2040, respectively [4]. Due to the rising trend in the occurrence of dementia across the global population, early-onset dementia (EOD), which is understood as a syndrome that differs from late-onset dementia (LOD) because its clinical manifestation occurs prior to the age of 65, is currently widely recognized [5]. To illustrate this point, the World Alzheimer Report estimated that between 2 and 10% of all cases of dementia begin before the age of 65 [6]. Additionally, it was recently reported that the number of patients suffering from EOD is greater than expected. For example, more than 42,000 people currently suffer from symptoms of EOD in the UK, and this number is more than 2-fold higher than the previous estimate of 17,000 [7]. Accordingly, the prevalence of dementia among persons aged 30-64 has been reported to be 54.0 per 100,000 (95% CI 45.1 to 64.1 per 100,000), whereas this prevalence has been reported to be 98.1 per 100,000 among persons aged 45-64 (95% CI 81.1 to 118.0 per 100,000) [8].

The diagnosis of dementia and the proper identification of its particular type are crucial for tackling its likely devastating consequences and also for offering appropriate treatment [9]. Moreover, the diagnosis of EOD entails particular challenges. On the one hand, the time devoted to diagnosing EOD exceeds that for LOD, particularly for persons who present with a suspected dementia at a young age [10]. On the other hand, over-diagnosis has frequently been reported [11]. Furthermore, regarding the most common types of dementia, different studies variously indicate that Alzheimer's disease (AD), vascular dementia (VD) and frontotemporal dementia (FTD) or AD and FTD alone represent the most frequent cases of EOD [7]. In light of these estimates, it should be noted that differential diagnosis of AD and FTD is particularly challenging and complex. There can be significant overlap between these dementias [12,13], and the diagnosis of FTD is also associated with a requirement for additional time for making a diagnosis [10]. The general aim of this article is to describe certain key points in the process of diagnosing dementia. Specifically, this article will focus on the clinical features of AD and the behavioral variant of FTD (bvFTD). Abnormal behaviors are a common issue that can be identified across different types of dementia. The similarities and differences in the distinctive patterns of behavioral disorders of AD and bvFTD will be analyzed in this article, and key elements that will facilitate differential diagnosis of these disorders will be identified.

Diagnosis of dementia

Based on reviews of the literature related to the diagnosis of dementia in clinical practice [14,15] and on diverse diagnostic protocols for specific types of dementia that have been designed for research purposes [16-21], it is possible to infer a conceptualization of the disease. Dementia can be defined as an acquired neuropsychiatric disease of cerebral etiology characterized by the initiation of a neurodegenerative or neurovascular process associated with marked impairment in one or more cognitive domains including attention, memory, language, visuospatial skills and executive functions. These cognitive deficits must be sufficiently intense to generate

functional disabilities in the performance of the activities of daily living and may also occur in combination with changes in personality and the presence of neuropsychiatric symptoms that include, among others, depression, apathy, agitation, irritability or lability, hallucinations and delusions. The clinical picture has to include a deterioration of previous levels of functioning and performing, and its explanation must exclude the presence of delirium or any major psychiatric disorder. Table (1) summarizes the main elements that should be considered in identifying a demential syndrome.

The diagnostic process of identifying dementias includes two primary steps that are closely related. First, it must be determined whether an observed case is actually a case of dementia [22,23]. Such an analysis should be performed based solely on the DSM-IV-TR [22] or the ICD-10 [24]; however, both guides can be considered for complex cases [24]. Second, it is necessary to identify which type of dementia affects the patient in question [22,23] through the examination of specific criteria that have been identified for each type [23,24]. It should be noted that the DSM-5 has adopted the term 'major neurocognitive disorder' as a new nomenclature for dementia. Furthermore, a distinction between 'major neurocognitive disorder' (linked with the typical conceptualization of dementia) and 'mild neuro cognitive disorder' (seemingly associated with the syndrome currently known as mild cognitive impairment) is made in this manual [25]. Table (1) presents a comparison of the main criteria for diagnosing dementia. Notably, the diagnostic process for dementia requires the collection of a clinical history from the patient and from an additional collateral source such as a spouse or close relative. The compilation of information must be focused on cognitive changes and their plausible consequences in the performance of activities of daily living. Moreover, information related to neuropsychiatric manifestations should be collected. Comorbidities, the patient's education level and family disease history should be explored. Neurological and physical examinations are also important in conjunction with neuropsychological assessment and laboratory tests. Structural brain images, i.e. computed tomography (CT) or, preferably, magnetic resonance imaging (MRI), are necessary to observe the characteristic pattern of brain atrophy in neurodegenerative diseases and to assess vascular involvement in dementias [26]. Findings related to genetic and cerebrospinal fluid (CSF) biomarkers and functional brain images can also contribute to appropriate diagnosis; however, the value of such indicators has not yet been completely clarified [27].

Diagnosis of AD and bvFTD

As previously discussed, to correctly diagnose AD and bvFTD, it is necessary to revise the specific criteria that have been proposed for each type of dementia. Thus, the reliability and validity of clinical diagnoses for dementia vary according to type [28]. Regarding AD, it has been suggested that the NINCDS-ADRDA criteria proposed by McKhann and colleagues [17] remain the best guidelines for making appropriate diagnoses [22,29]. These criteria display a rather high, though variable, sensitivity that ranges from 70.9% to 87.3% and a specificity of approximately 70% [30,31]. They are highly recommended [18,26] and have recently been updated to incorporate the heterogeneity of different forms of presentation of AD, such as

Table 1: *Comparison of the main symptoms suggestive of dementia according to various current diagnostic criteria.

			DSM-IV-TR	ICD-10	NIA-AA	DSM-5
Domain Involved						
Cognition			+	+	+	+
	Attentional capacities				*	*
	Episodic memory				*	*
		Amnesia in general	+			
		Short-term memory (learning skills)	+	+		
		Long-term memory	+	(°)		
	Language				*	*
		Aphasia	+	+		
	Constructional abilities				*	*
		Apraxia	+			
	Visuospatial abilities				*	*
		Agnosia	+			
	Executive functions				*	*
		Abstract thinking	+	+		
		Judgment	+	+		
		Problem solving	+	+		
	Other cognitive abilities					
		Reading			(°)	(°)
		Calculation		(°)	(°)	(°)
Neuropsychiatric Signs				(°)	+	+
	Personality				(°)	(°)
	Behavioral and emotional function				(°)	(°)
	Emotional control			(°)	(°)	(°)
Functionality in ADL				+	+	+
	Activities of daily living			+	+	+
	Work		*		(°)	(°)
	Motivation			(°)	(°)	(°)
	Social behavior, function and activities and relationships with others		*	(°)	(°)	(°)
Other elements						
	Delirium or a major psychiatric disorder do not explain the origin of the disease		+	+	+	+
	Global impairment				+	+
	Progressive deterioration			(°)	+	+
	Decline from previous level of functional capacity before illness		+	+	+	+
	Duration of symptoms greater than 6 months			+		
	Normal consciousness			+		
	Assumed neurobiological cause		+	+	+	+
	Mental retardation as cause			(°)		

Abbreviations: *Mainly based on and modified from [21]. The remaining information was obtained from [16, 15], [18] and [25].
 DSM-IV-TR - Diagnostic and Statistical Manual of Mental Disorders 4th Edition [14]; ICD-10 -International Statistical Classification of Diseases and Related Health Problems 10th Edition [15]
 NIA-AA - National Institute on Aging - Alzheimer's Association guidelines [18]
 DSM-5 -Diagnostic and Statistical Manual of Mental Disorders 5th Edition [25]
 ADL - Activities of daily living
 + impairment in the domain is always required for diagnosis; * one or more of these indicators is required; and (°) optionally, strengthens the diagnosis.

amnesic/non-amnesic expression together with visuospatial, language and dysexecutive presentations [18]. Concerning bvFTD, the Lund and Manchester diagnostic criteria developed by Nearing and collaborators [19] for labeling the spectrum of frontotemporal dementia (FTD) are the best known and best respected criteria [23,29,32], although they have been criticized for their apparent low sensitivity [33,34]. These guidelines are reported to display appropriate diagnostic accuracy with a sensitivity of 85% and a specificity of 99% [35]. Nonetheless, as with AD, the diagnostic criteria for FTD have also been revised [37], and attempts to broaden their use are currently being made [38]. These new guidelines, which are designated the FTDC, have higher sensitivity than the previous criteria [39] and include details necessary for the proper identification of bvFTD [37]. It is relevant to highlight that both sets of diagnostic criteria suggest only probable diagnoses for these diseases. Definitive diagnoses are only possible after post-mortem examination of histopathological indicators of amyloid plaques (extracellular beta-amyloid proteins), inflammatory cells and neurofibrillary tangles (intracellular abnormal aggregates of tau protein) for AD [26] or a set of neuronal inclusions that has collectively been termed Pick's bodies for FTD [40]. These cellular anomalies are proteinopathies such as tauopathies, TDP-43 proteinopathies or fusopathies [41]. In AD, all of the aforementioned pathological indicators may be found in the medial temporal zone [40] and observed as characteristics of bilateral hippocampal atrophy [26], whereas in FTD they can be indicators of frontal and/or temporal degeneration [26]. It should be noted that bvFTD may be primarily associated with orbitofrontal anomalies and that these anomalies may explain the breakdown in social cognition and the distinctive behavioral disorder suggested by the name of this dementia. In contrast, the two other primary types of FTD, i.e., semantic dementia (SD) and the non fluent form of progressive primary aphasia (nfPPA), may be more closely associated with anterolateral temporal and hippocampal impairments or perisylvian atrophy, respectively, and these alterations may reflect the characteristic language disorders associated with these dementias [29,42]. SD presents with fluent and well-articulated speech; however, a marked lack of content words is associated with the language of patients suffering from this pathology [43,44]. Otherwise, nfPPA is associated with impairment of the motor components of speech together with grammatical, syntactic and phonetic errors, but comprehension is rather well preserved [44,45].

Clinical profiles of AD and bvFTD

Due to their primary manifestations, both AD and bvFTD are salient among other similar pathologies because of their interesting clinical profiles. On the one hand, AD is the most common dementia that has been described [1]; on the other hand, bvFTD is perhaps one of the most striking demential syndromes and is also the second most frequent dementia in pre-senile cohorts [42]. To differentiate between these two syndromes, it may be useful to contrast their clinical profiles in terms of evolution, cognitive characteristics, neuropsychiatric and behavioral symptoms and performance in the activities of daily living. A diagnosis of dementia requires the detection of cognitive impairment through a combination of history-taking from the patient and a knowledgeable informant or an

objective cognitive assessment. Neuropsychological assessment should be performed when routine history and bedside mental status examination cannot provide a confident diagnosis [18]. Neurological examination may reveal neurological signs that are very informative for differential diagnosis. Unlike AD, 10% of frontotemporal dementia patients present signs of motor neuron disease, mainly muscle atrophy, weakness and fasciculations in the upper extremities and in the tongue. Patients with FTD may also present extra pyramidal signs. In fact, FTD symptoms overlap with those of corticobasal degeneration and progressive supranuclear palsy [46,47].

AD and bvFTD: Progression

Regarding the diagnostic criteria for AD and bvFTD, a few elements that are related to the progression of these types of dementia should be mentioned. AD is thought to begin between the ages of 45 and 90 [17], whereas bvFTD appears prior to the age of 65 [19]. These dementias share an insidious beginning followed by a gradual progression [24,29,42] that ultimately results in debilitating global cognitive impairment, bedridden status or even death [48]. Furthermore, survival and life expectancy in AD may be greater than in bvFTD [49].

AD and bvFTD: Neuropsychological characterization

Concerning cognitive disorders associated with AD and bvFTD, the diagnostic criteria for these two dementias strongly suggest that episodic memory impairment is the central cognitive detriment found in AD and that aphasia, apraxia and/or agnosia may accompany its clinical picture [24]; in contrast, executive dysfunction is the key sign of bvFTD [29, 42]. In fact, it has been stressed that patients with bvFTD may present a memory capacity that is relatively conserved [29]; however, other evidence contradicts this assertion, showing that memory impairments like those that occur in AD can be found indeed in bvFTD [50]. It has been indicated that 10% of pathologically confirmed cases with bvFTD have marked episodic memory deficits during the initial stages of the disease [51]. Additionally, medial temporal shrinkage observed with brain imaging and significant hippocampal atrophy identified through post-mortem observation has been encountered in patients with FTD, even early in the progression of the disease [51]. The existing evidence suggests that patients with severe memory impairment have pathological changes linked to TDP-43 inclusions [51]. TDP-43 immunoreactivity is frequently reported in hippocampal sclerosis (HS), perhaps reflecting an association between TDP-43 inclusion and HS [52]. All the same, attentional disorders, language impairment, visuospatial disabilities and motor control involvement have been reported in both types of dementia [23,29,40]. In short, heterogeneous or multi-domain cognitive impairment can be observed in both pathologies, but episodic memory disorder predominates in AD and severe executive dysfunction predominates in bvFTD.

AD and bvFTD: Neuropsychiatric symptomatology

Considering the neuropsychiatric and behavioral symptoms of AD and bvFTD, it is notable that diagnosis of either dementia is possible only if a patient's symptoms cannot be explained by the presence of delirium [14,15] or a major psychiatric disorder.

Both diseases can present with depression, apathy, mood disorders or other signs according to the diagnostic criteria; however, a set of key symptoms associated with a lack of social cognition that is observed in bvFTD has not been linked to AD. A disruptive change in personality characterized by aggressiveness, impulsiveness, disinhibited behavior, inappropriateness and a combination of obsessions/compulsions and ritualistic acts or hoarding are observed in bvFTD [32,42,53]. This change in personality is occasionally accompanied by hyperorality and utilization behaviors [53]. In contrast, AD is strongly connected with a high presence of depressed mood [24,54], a situation that has apparently not been linked to bvFTD [54]. Although cognitive disorders have been emphasized as the critical dysfunctions associated with every type of dementia, it has been stated that neuropsychiatric symptoms are always present in combination with these cognitive disorders. Pursuing this line of reasoning, it has been reported that nearly all patients with dementia suffer from some type of neuropsychiatric symptoms during the progression of the disease [55]. These symptoms are known to frequently manifest very early in the disease, that is to say, in prodromal phases such as MCI [54,56]. It has been reported that 75% of dementia patients have experienced a neuropsychiatric symptom within the last month (apathy 36%, depression 32%, Agitation 30%) and that 80% have experienced at least one symptom since the beginning of the neuropsychological impairment. A 97% prevalence of any neuropsychiatric symptom among dementias was reported in a follow-up of 5 years, during which depression (77%), apathy (71%) and anxiety (62%) were the most frequent symptoms [55]. Apathy and agitation/aggression have been reported in both AD and bvFTD [54]. In addition, it has been indicated that patients with AD may experience a higher frequency of delusions and depression [57,58], whereas patients suffering from various types of FTD may primarily show behavioral disorders including impulsivity, aggression, disinhibition, compulsive behavior, hyper sexuality and personality changes, the latter being particularly salient in bvFTD [59].

AD and bvFTD: Functional impairment in the activities of daily living

The diagnostic guidelines for both diseases emphasize the requirement for the presence of functional impairment in the activities of daily living. The literature related to AD and bvFTD reports findings that seem to be common to all dementias. In both pathologies, complex or instrumental activities are affected earlier than basic activities [60]. Furthermore, moderate levels of functional decline in domains such as self-care, household tasks, employment and recreation, shopping, finances, travel and communication have been described for both AD and bvFTD [60], although it seems that the functional impairments exhibited in bvFTD are greater than those observed in AD [61].

AD and bvFTD: Neuropsychological assessment

It has been noted above that, broadly speaking, dementia is a complex neurobiological pathology that can involve the following three spheres: cognitive impairment, neuropsychiatric disorders and functional disability. Moreover, AD and bvFTD present with different clinical profiles in which these three domains vary,

exhibiting different specifics. Given that neuropsychological assessment is a clinical tool that contributes to the collection of clinical information for the purpose of assisting patients with cognitive complaints [62,63], it is important to stress its relevance as a crucial procedure for the differential diagnoses of various types of dementia such as AD and bvFTD. Neuropsychological assessments use diverse instruments and tests to evaluate the manifestations observed in dementias [40,62,64-66]. For example, to identify elements pertinent to the differentiation of AD and bvFTD, cognitive screening tools may be convenient if they can be used to quickly and simultaneously explore conditions related to several cognitive domains [66]. Internationally, the most frequently utilized test for the assessment of cognitive impairment is the Mini Mental State Examination (MMSE), although this test has many limitations [66]. The Addenbrooke's Cognitive Examination - Revised (ACE-R) is also a practical screening tool that aims to evaluate cognitive functions. Unlike the MMSE, the ACE-R has the key advantage of providing a statistical value for the differentiation of different dementias and includes a rating for the MMSE within its scoring [61]. In this sense, the ACE-R might be an interesting test for use in the identification of the type of syndrome in question. The Montreal Cognitive Assessment (MoCA), which was originally designed for the identification of mild cognitive impairment, might be another appropriate instrument for quickly examining many neuropsychological functions and assessing global cognitive efficiency where the occurrence of any neurodegenerative disease is suspected. Furthermore, the Frontal Assessment Battery (FAB) [67] and the Instituto de Neurología Cognitiva (INECO) Frontal Screening (IFS) [68] may be valuable for distinguishing AD and bvFTD because these tools were designed for rapid assessment of executive dysfunction in dementia and have been reported to be effective in differentiating between these dementias [69,70]. Regarding the documentation of neuropsychiatric and behavioral symptoms, certain scales can be mentioned because of their usefulness. The Neuropsychiatric Inventory Questionnaire (NPI-Q) [71] might aid in the identification of hallucinations, delusions, depression, apathy and other signs that occur in both pathologies. The Cambridge Behavioral Inventory (CBI) can also be used to assess behavioral alterations in neurodegenerative diseases; however, the CBI is more extensive than the NPI-Q and includes questions that address cognitive changes as well. Additionally, the Frontal Systems Behavioral Scale (FrSBe) may be worthwhile for evaluating dysexecutive conduct, especially if its strengths in discriminating between AD and FTD are considered [72]. Concerning functional capacity, it should be noted that a comprehensive neuropsychological evaluation needs to consider functional assessment in activities of daily living (ADL) [63]. It has been stated that unlike AD, functional impairment in bvFTD is not always captured by cognitive tests and might be associated with behavioral disturbances [61]. Functional capacity might be assessed by specific instruments such as the Functional Activities Questionnaire (FAQ) [73] and the Activities of Daily Living Questionnaire (ADLQ) [74]. The ADLQ has proved to be an excellent scale for measuring functional impairment and describing the overall performance profiles associated with various ADL [74], including the use of technology in its revised version, the T-ADLQ (Technology-Activities of Daily Living Questionnaire) [75]. In addition to these

tools, the Clinical Dementia Rating Scale (CDR) might be useful both as an instrument for functional assessment and a rating of the severity of the dementia in question [76]. Knopman and colleagues (2008) [77] incorporated two domains to the original CDR, namely Language and Behavior and Comportment and Personality, to identify aspects that might characterize patients with frontotemporal degeneration. These domains were included in a sum of scores of other domains (the 'sum of boxes'), but they are not used to obtain a 'global' indicator of the severity of the dementia in question [77]. A more detailed review of other relevant instruments for assessing dementias is beyond the scope of this article.

AD and bvFTD: Information obtained through brain imaging

Although in a typical syndrome of dementia examination by brain imaging is not mandatory for making a diagnosis [22], neuroimaging obtained through CT or MRI can be very useful. On the one hand, CT is capable of detecting tumors, hemorrhages and, in general terms, gross brain anomalies [78]. On the other hand, MRI permits a more accurate and detailed assessment of structural patterns of brain atrophy that may lead to a better understanding of the structures involved in the neurodegenerative process and thereby contribute to differential diagnosis [22]. MRI studies have shown that AD is usually characterized by global shrinkage with prominent atrophy of the medial temporal lobe. However, atypical forms of AD featuring both frontal involvement and prominent posterior atrophy have been described, and these are especially prevalent among younger patients with AD [79]. In contrast, bvFTD is characterized by atrophy of the mesial frontal, orbitofrontal, and anterior insular cortices in the coronal plane. The presence of an apparently normal MRI on visual inspection does not completely exclude a diagnosis of bvFTD, mainly because the changes can be subtle at the early stage of the disease [77]. Functional neuroimaging techniques such as positron emission tomography (PET) with fluorodeoxy glucose ([¹⁸F]-FDG) can reveal alterations in brain metabolism that may precede structural changes in the brain. FDG-PET in AD

has shown hypometabolism in the temporal, parietal and, most notably, the posterior singular areas, discriminating AD patients from controls with sensitivity and specificity of 85% to 90% [79]. Although its clinical use is accepted, brain amyloid imaging with PET in AD requires careful interpretation because both patients with AD or other neurodegenerative disorders and cognitively healthy elderly subjects might show increased levels of beta-amyloid plaques in this examination [80]. At present, PET is not routinely advised because it has not yet been fully clarified whether this examination makes an additional diagnostic contribution over clinical diagnosis and structural imaging. In bvFTD, hypometabolism is detected consistently and reliably in frontal brain regions before changes are visible through structural MRI. Thus, FDG-PET is perhaps the most sensitive diagnostic tool currently available for diagnosing bvFTD [46,47]. Single-photon emission computed tomography (SPECT) with hexamethylpropyleneamine oxime ([^{99m}Tc]) has indicated that AD is characterized by bilateral temporoparietal hypoperfusion. Nevertheless, the application of SPECT in clinical routine has been hampered by false-positive findings and insufficient added value over MRI. Frontal hypoperfusion can be observed through SPECT in bvFTD; however, the specificity of these changes has not yet been fully clarified [47]. Currently, functional neuro imaging is generally suggested in cases with a suspicion of either AD or bvFTD and a normal structural MRI [47].

DISCUSSION & CONCLUSION

AD and bvFTD are markedly different types of dementia that should be specifically accounted for when considering the relevance of EOD. Health professionals should be aware of the distinctive clinical features of AD and bvFTD to enable early detection. A summary of the main differences and similarities between AD and bvFTD is presented in Table (2). Although AD is predominantly marked by an amnesic syndrome in terms of cognitive performance [1] whereas bvFTD is characterized by profound executive dysfunction [29,42], both types of dementia can present with multi-domain cognitive impairment [23,29,40]. Moreover, although neuropsychiatric symptoms such as apathy,

Table 2: Comparison of the clinical profiles of Alzheimer's disease and behavioral variant of frontotemporal dementia across three spheres of clinical signs: cognitive characterization, neuropsychiatric symptoms and functional capacity.

	AD	bvFTD
General	The demential syndrome cannot be explained by delirium or by the presence of any major psychiatric disorder.	
Cognitive Characterization*	Multi-domain cognitive impairment.	
	Episodic memory mainly impaired.	Predominant executive dysfunction.
Neuropsychiatric Symptoms**	Depression, apathy and anxiety are highly common in both.	
	High frequency of delusions and depression.	Impulsivity, aggression, disinhibition, compulsive behavior, hyper sexuality and personality changes.
Functional Capacity in ADL***	Instrumental ADL are affected earlier than basic in both types of dementia.	
	Functional impairment associated with bv FTD may be greater than that associated with AD.	
	Impairments in the performance of ADL such as self-care, household tasks, employment and recreation, shopping, finances, travel and communication increase progressively in both.	

Abbreviations: AD - Alzheimer's disease

bvFTD - Behavioral variant of frontotemporal dementia.

ADL = Activities of daily living.

* For further details, see [1,12,13,15,16,19,23,24,26,28,30]

** For further details, see [12,13,15,16,24,26,34-36,53]

*** For further details, see [12,13,15,16,24,36,38,39]

depression and anxiety may be common elements in these dementias [55], depression and delusions may be more frequent in AD [57,58], and a marked change in personality that is based on an impairment in social cognition is the pathognomonic symptom of bvFTD [44]. Regarding functional capacity, both AD and bvFTD present with progressive impairment in the performance of basic and instrumental ADL, including impairment in areas such as self-care, household tasks, employment and recreation, shopping, finances, travel and communication. Nonetheless, bvFTD has been associated with greater functional impairment than AD [60,61]. CSF, MRI, PET, SPECT and cognitive assessments are sophisticated and expensive tools that are frequently not available to the general practitioner in the context of primary care. All the same, given that neuropsychological assessments permit the exploration of the salient differences in the symptoms that emerge from different neurodegenerative disorders, they are helpful tools for the differential diagnoses of AD and bvFTD in particular and of other dementias in general. Indeed, considering that it has been convincingly demonstrated that diagnosis of dementia is eminently clinical [22,29], neuropsychological assessments are crucial because they permit gathering of information pertinent to each case, ranging from patients' clinical histories to their current cognitive status, neuropsychiatric and behavioral symptoms and current functional capacity. Thus, neuropsychological assessments are extremely useful for clinicians, neuropsychologists, neurologists and psychiatrists due to their contributions to the documentation of the key indicators required for diagnosis [65].

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