Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria

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Article abstract—*Objective:* To improve clinical recognition and provide research diagnostic criteria for three clinical syndromes associated with frontotemporal lobar degeneration. *Methods:* Consensus criteria for the three prototypic syndromes—frontotemporal dementia, progressive nonfluent aphasia, and semantic dementia—were developed by members of an international workshop on frontotemporal lobar degeneration. These criteria build on earlier published clinical diagnostic guidelines for frontotemporal dementia produced by some of the workshop members. *Results:* The consensus criteria specify core and supportive features for each of the three prototypic clinical syndromes and provide broad inclusion and exclusion criteria for the generic entity of frontotemporal lobar degeneration. The criteria are presented in lists, and operational definitions for features are provided in the text. *Conclusions:* The criteria ought to provide the foundation for research work into the neuropsychology, neuropathology, genetics, molecular biology, and epidemiology of these important clinical disorders that account for a substantial proportion of cases of primary degenerative dementia occurring before the age of 65 years.

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Frontotemporal lobar degeneration (FTLD) is the third most common cause of cortical dementia, following AD and Lewy body disease. In the past few years FTLD has been studied extensively, and substantial progress has been made in understanding its associated clinical syndromes and underlying pathologic changes. This report provides a consensus statement based on a conference of international investigators familiar with the disorder, and provides an update and extension of previously proposed clinical and pathologic diagnostic criteria for frontotemporal dementia (FTD).[1]

FTLD encompasses two major pathologic substrates which affect primarily the frontal or temporal cortex, in some patients asymmetrically. Three prototypic neurobehavioral syndromes can be produced by FTLD. Results of the consensus conference presented here describe these three behavioral conditions. The most common clinical manifestation of FTLD is a profound alteration in personality and social conduct, characterized by inertia and loss of volition or social disinhibition and distractibility, with relative preservation of memory function (FTD).[2-5] There is emotional blunting and loss of insight. Behavior may be stereotyped and perseverative. Speech output is typically economical, leading ultimately to mutism, commensurate with the patient's amotivational state, although a press of speech may be present in some overactive, disinhibited patients. Cognitive deficits occur in the domains of attention, abstraction, planning, and problem solving, in keeping with a frontal "dysexecutive" syndrome, whereas primary tools of language, perception, and spatial functions are well preserved. Patients are not clinically amnesic. They are typically oriented and negotiate their local environment without becoming lost. Memory test performance, however, is typically inefficient, and impairments arise secondary to patients' frontal regulatory disturbances (inattention, lack of active strategies for learning and retrieval) rather than to a primary amnesia. Executive deficits are typically more evident in inert, avolitional patients than in overactive, disinhibited patients, although even in the latter, abnormalities can be elicited on tests of selective attention.

Two other prototypic clinical syndromes occur in FTLD: progressive nonfluent aphasia (PA)[5-9] and semantic dementia (SD).[5,10,11] PA is a disorder of expressive language, characterized by effortful speech production, phonologic and grammatical errors, and word retrieval difficulties. Difficulties in reading and writing also occur. Understanding of word meaning is relatively well preserved. The disorder of language occurs in the absence of impairment in other cognitive domains, although behavioral changes of FTD may emerge late in the disease course. In SD a severe naming and word comprehension impairment

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occurs in the context of fluent, effortless, and grammatical speech output; relative preservation of repetition; and the ability to read aloud and write orthographically regular words. Also there is an inability to recognize the meaning of visual percepts (associative agnosia). This loss of meaning for both verbal and nonverbal concepts (semantics) contrasts with the preservation of visuospatial skills and day-to-day memory.

The generic term FTLD refers to the circumscribed progressive degeneration of the frontotemporal lobes. The associated clinical syndromes are determined by the distribution of the pathology. In FTD there is prominent bilateral and usually symmetric involvement of the frontal lobes. In PA, atrophy is asymmetric, involving chiefly the left frontotemporal lobes. In SD, atrophy is typically bilateral and is most marked in the anterior temporal neocortex, with inferior and middle temporal gyri being predominantly affected. Asymmetries in the involvement of the left and right temporal lobes in SD mirror the relative severity of impairment for verbal and visual concepts (word meaning versus object recognition). Evidence that the different clinical manifestations may occur within the same family and that there may be an overlap in symptom pattern over the course of disease[5] reinforces the link between the syndromes. Moreover, the distinct clinical syndromes are associated with the same underlying histopathologies. There are two main histologic types: prominent microvacuolar change without specific histologic features (frontal lobe degeneration type) or severe astrocytic gliosis with or without ballooned cells and inclusion bodies (Pick type).[1] The disease etiology is not known but it has a high familial incidence and is likely to be under genetic influence. Molecular studies have shown mutations on chromosome 17[12,13] or linkage to chromosome 3[14] in some families.

The clinical syndromes have a predominantly presenile onset, unlike AD and vascular dementia, which are more common in the elderly. The severe amnesia and visuospatial impairment and myoclonus characteristic of AD are not features of FTD, PA, and SD. Although EEGs show progressive slowing of waveforms in AD, the standard EEG is strikingly normal during the course of FTD, PA, and SD. Functional imaging using SPECT and PET reveal characteristic biparietal posterior abnormalities in the initial stages of AD, whereas in the clinical syndromes of FTLD the salient abnormality lies in the anterior hemispheres.

The course of FTD, PA, and SD is one of gradual evolution without the occurrence of ictal events, which are more characteristic of vascular dementia. The "bradyphrenia" of subcortical vascular disease is not a feature of the clinical syndromes of FTLD. Indeed, in FTLD, although striatal signs may develop late in the disease course, in the early and middle stages neurologic signs are absent or confined to the presence of primitive reflexes. Patients' physical well-being contrasts with the wealth of neurologic symptoms and signs common in vascular dementia. Although MRI frequently discloses extensive lesions in subcortical white matter in vascular dementia, this is not a pronounced feature of FTD, PA, or SD.

There are comprehensive descriptions in the literature of the clinical features and neuroradiologic manifestations of FTD, PA, and SD[1-32] that enable the general and nonspecialist reader to appreciate the nature of historic evolution of the three syndromes. The types of underlying pathologic change have also been described extensively[1,5,33-41] and an empiric nosologic taxonomy proposed prior to ultimate molecular biological definition. The purpose of this article is to present formalized diagnostic criteria for FTD, PA, and SD to enable researchers to perform further work into the neuropsychology, neuropathology, genetics, molecular biology, and epidemiology of these disorders. It is anticipated that usage in different fields of inquiry will lead to modification and improvements in the utility of these clinical criteria.

Criteria. The clinical criteria are set out in lists 1 through 4. The criteria for each of the three major clinical syndromes are divided into sections. The clinical profile statement together with the core clinical inclusion and exclusion features provide the necessary foundation for diagnosis. Additional clinical features, neuropsychological investigation, and brain imaging support the clinical diagnosis. Operational definitions of specific features are outlined later.

Clinical profile. This statement (seen in lists 1 through 3) summarizes the neurobehavioral profile necessary to fulfill criteria for diagnosis.

Core diagnostic features. These are features (see lists 1 through 3) integral to the clinical syndrome. All features must be present to fulfill the criteria for diagnosis.

Supportive diagnostic features. Clinical. These are features (see lists 1 through 3) that are not present in all patients, or they may be noted only during one phase of the disease. They are therefore not necessary conditions for diagnosis. Supportive features are characteristic, often with high diagnostic specificity, and their presence adds substantial weight to the clinical diagnosis. The diagnosis becomes more likely when more supportive features are present.

Physical. In each of the clinical syndromes physical signs are few in contrast to the prominent mental changes. Parkinsonian signs typically emerge only during late disease. The physical features outlined should be regarded as "supportive" rather than as necessary conditions for diagnosis.

Investigations. Formal neuropsychological assessment, EEG, and brain imaging each can provide support for and strengthen the clinical diagnosis. Such investigatory techniques are not available universally, and ought not to be considered a prerequisite for diagnosis. When neuropsychological assessment is per-

List 1 *The clinical diagnostic features of FTD: Clinical profile*

Character change and disordered social conduct are the dominant features initially and throughout the disease course. Instrumental functions of perception, spatial skills, praxis, and memory are intact or relatively well preserved.

I. Core diagnostic features
  A. Insidious onset and gradual progression
  B. Early decline in social interpersonal conduct
  C. Early impairment in regulation of personal conduct
  D. Early emotional blunting
  E. Early loss of insight

II. Supportive diagnostic features
  A. Behavioral disorder
    1. Decline in personal hygiene and grooming
    2. Mental rigidity and inflexibility
    3. Distractibility and impersistence
    4. Hyperorality and dietary changes
    5. Perseverative and stereotyped behavior
    6. Utilization behavior
  B. Speech and language
    1. Altered speech output
      a. Aspontaneity and economy of speech
      b. Press of speech
    2. Stereotypy of speech
    3. Echolalia
    4. Perseveration
    5. Mutism
  C. Physical signs
    1. Primitive reflexes
    2. Incontinence
    3. Akinesia, rigidity, and tremor
    4. Low and labile blood pressure
  D. Investigations
    1. Neuropsychology: significant impairment on frontal lobe tests in the absence of severe amnesia, aphasia, or perceptuospatial disorder
    2. Electroencephalography: normal on conventional EEG despite clinically evident dementia
    3. Brain imaging (structural and/or functional): predominant frontal and/or anterior temporal abnormality

List 2 *The clinical diagnostic features of progressive nonfluent aphasia: Clinical profile*

Disorder of expressive language is the dominant feature initially and throughout the disease course. Other aspects of cognition are intact or relatively well preserved.

I. Core diagnostic features
  A. Insidious onset and gradual progression
  B. Nonfluent spontaneous speech with at least one of the following: agrammatism, phonemic paraphasias, anomia

II. Supportive diagnostic features
  A. Speech and language
    1. Stuttering or oral apraxia
    2. Impaired repetition
    3. Alexia, agraphia
    4. Early preservation of word meaning
    5. Late mutism
  B. Behavior
    1. Early preservation of social skills
    2. Late behavioral changes similar to FTD
  C. Physical signs: late contralateral primitive reflexes, akinesia, rigidity, and tremor
  D. Investigations
    1. Neuropsychology: nonfluent aphasia in the absence of severe amnesia or perceptuospatial disorder
    2. Electroencephalography: normal or minor asymmetric slowing
    3. Brain imaging (structural and/or functional): asymmetric abnormality predominantly affecting dominant (usually left) hemisphere

formed, the profile of deficits must demonstrate disproportionate executive dysfunction in FTD or disproportionate language/semantic breakdown in PA and SD. With regard to brain imaging, the patterns of abnormality are characteristic, but not seen invariably. For example, prominent atrophy of the temporal lobes is well visualized by high-resolution MRI, but may be undetected by CT. Failure to demonstrate the prototypic appearances on imaging need not result in diagnostic exclusion.

Supportive features common to each of the clinical syndromes. These features (see list 4) support but are not a necessary condition for FTLD. Onset of disease is most commonly before the age of 65 years, although rare examples of onset in the very elderly have been reported. A positive family history of a similar disorder in a first-degree relative has been reported[2,4] in as many as 50% of patients: Some families have shown mutations on chromosome 17 or linkage to chromosome 3. Motor neuron disease is a recognized albeit uncommon accompaniment to the clinical syndromes of lobar degeneration.[42-47] The development of motor neuron disease in patients presenting with a progressive behavioral or language disorder would strongly support a clinical diagnosis of FTD or PA respectively.

Exclusion features common to each clinical syndrome. Clinical. All features (see list 4) must be absent. Early severe amnesia, early spatial disorientation, logoclonic speech with loss of train of thought, and myoclonus are features designed to exclude AD.

Investigations. All features should be absent (when the relevant information is available).

Relative diagnostic exclusion features. These are features (see list 4) that caution against but do not firmly exclude a diagnosis of FTLD. A history of alcohol abuse raises the possibility of an alcohol-related basis for a frontal lobe syndrome. However, excessive alcohol intake may also occur in FTD patients as a secondary manifestation of social disinhibition or hy-

List 3 *The clinical diagnostic features of semantic aphasia and associative agnosia (SD): Clinical profile*

Semantic disorder (impaired understanding of word meaning and/or object identity) is the dominant feature initially and throughout the disease course. Other aspects of cognition, including autobiographic memory, are intact or relatively well preserved.

I. Core diagnostic features
   A. Insidious onset and gradual progression
   B. Language Disorder characterized by
      1. Progressive, fluent, empty spontaneous speech
      2. Loss of word meaning, manifest by impaired naming *and* comprehension
      3. Semantic paraphasias *and/or*
   C. Perceptual disorder characterized by
      1. Prosopagnosia: impaired recognition of identity of familiar faces *and/or*
      2. Associative agnosia: impaired recognition of object identity
   C. Preserved perceptual matching and drawing reproduction
   D. Preserved single-word repetition
   E. Preserved ability to read aloud and write to dictation orthographically regular words

II. Supportive diagnostic features
   A. Speech and language
      1. Press of speech
      2. Idiosyncratic word usage
      3. Absence of phonemic paraphasias
      4. Surface dyslexia and dysgraphia
      5. Preserved calculation
   B. Behavior
      1. Loss of sympathy and empathy
      2. Narrowed preoccupations
      3. Parsimony
   C. Physical signs
      1. Absent or late primitive reflexes
      2. Akinesia, rigidity, and tremor
   D. Investigations
   E. Neuropsychology
      1. Profound semantic loss, manifest in failure of word comprehension and naming and/or face and object recognition
      2. Preserved phonology and syntax, and elementary perceptual processing, spatial skills, and day-to-day memorizing
   F. Electroencephalography: normal
   G. Brain imaging (structural and/or functional): predominant anterior temporal abnormality (symmetric or asymmetric)

List 4 *Features common to clinical syndromes of FTLD (extension of lists 1 through 3)*

III. Supportive features
   A. Onset before 65 years: positive family history of similar disorder in first-degree relative
   B. Bulbar palsy, muscular weakness and wasting, fasciculations (associated motor neuron disease present in a minority of patients)

IV. Diagnostic exclusion features
   A. Historical and clinical
      1. Abrupt onset with ictal events
      2. Head trauma related to onset
      3. Early, severe amnesia
      4. Spatial disorientation
      5. Logoclonic, festinant speech with loss of train of thought
      6. Myoclonus
      7. Corticospinal weakness
      8. Cerebellar ataxia
      9. Choreoathetosis
   B. Investigations
      1. Brain imaging: predominant postcentral structural or functional deficit; multifocal lesions on CT or MRI
      2. Laboratory tests indicating brain involvement of metabolic or inflammatory disorder such as MS, syphilis, AIDS, and herpes simplex encephalitis

V. Relative diagnostic exclusion features
   A. Typical history of chronic alcoholism
   B. Sustained hypertension
   C. History of vascular disease (e.g., angina, claudication)

peroral tendencies. The presence of vascular risk factors such as hypertension ought to alert investigators to a possible vascular etiology. Nevertheless, such risk factors are common in the general population and may be present coincidentally in some patients with FTLD, particularly in those of more advanced age.

Definitions of clinical features. This information assists in the use of the diagnostic lists.

Frontotemporal dementia. See list 1.

Core features. *Insidious onset and gradual progression.* There should be no evidence of an acute medical or traumatic event precipitating symptoms. Evidence for a gradually progressive course should be based on historic evidence of altered functional capacity (e.g., inability to work) over a period of at least 6 months, and may be supported by a decline in neuropsychological test performance. The degree of anticipated change is not specified because it is highly variable. In some patients change is dramatic over a 12-month period, whereas in others it is manifest only over a period of several years. Dramatic social and domestic events leading to perturbations in the patient's behavior must be distinguished from ictal occurrences of a neurologic or psychological nature. Only the latter are grounds for exclusion.

Early decline in social interpersonal conduct. This refers to qualitative breaches of interpersonal

etiquette that are incongruent with the patient's premorbid behavior. This includes decline in manners, social graces, and decorum (e.g., disinhibited speech and gestures, and violation of interpersonal space) as well as active antisocial and disinhibited verbal, physical, and sexual behavior (e.g., criminal acts, incontinence, sexual exposure, tactlessness, and offensiveness). "Early" for this and other features implies that the abnormality should be present at initial presentation of the patient.

Early impaired regulation of personal conduct. This refers to departures from customary behavior of a quantitative type, ranging from passivity, inertia, and inactivity to overactivity, pacing, and wandering; and increased talking, laughing, singing, sexuality, and aggression.

Early emotional blunting. This refers to an inappropriate emotional shallowness with unconcern and a loss of emotional warmth, empathy, and sympathy, and an indifference to others.

Early loss of insight. This 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.

Supportive features: behavioral disorder. *Decline in personal hygiene and grooming.* The caregivers' accounts of failure to wash, bathe, groom, apply makeup, and dress appropriately as before are reinforced by clinical observations of unkemptness, body odor, clothing stains, garish makeup, and inappropriate clothing combinations.

Mental rigidity and inflexibility. This refers to egocentricity and loss of mental adaptability, evidenced by reports of any one of the following: the patient has to have his or her own way, is unable to see another person's point of view, adheres to routine, and is unable to adapt to novel circumstances.

Distractibility and impersistence. These are reflected in failure to complete tasks and inappropriate digressions of attention to nonrelevant stimuli.

Hyperorality and dietary changes. This refers to overeating; bingeing; altered food preferences and food fads; excessive consumption of liquids, alcohol, and cigarettes; and the oral exploration of inanimate objects.

Perseverative and stereotyped behavior. This encompasses simple repetitive behaviors such as hand rubbing and clapping, counting aloud, tune humming, giggling, and dancing, as well as complex behavioral routines such as wandering a fixed route, collecting and hoarding objects, and rituals involving toileting and dressing.

Utilization behavior. This is stimulus-bound behavior[48] during which patients grasp and repeatedly use objects in their visual field, despite the objects' irrelevance to the task at hand (e.g., patients repeatedly switch lights on and off, open and close doors, or continue eating if unlimited supplies of food are within reach). During clinical interview they may drink repeatedly from an empty cup or use scissors placed before them.

Speech and language. *Altered speech output.* There are two types of altered speech output: aspontaneity and economy of utterance, and press of speech. In aspontaneity and economy of utterance, the patient either does not initiate conversation or else output is limited to short phrases or stereotyped utterances. Responses to questions involve single-word replies or short, unelaborated phrases such as "don't know." Encouragement to amplify responses are unsuccessful. In press of speech, the patient speaks interruptedly, monopolizing a conversational interchange.

Stereotypy of speech. These are single words, phrases, or entire themes that the patient produces repeatedly and habitually either spontaneously or in response to questions, replacing appropriate conversational discourse.

Echolalia. Echolalia refers to a repetition of the utterances of others, either completely or in part, sometimes with change of syntax (e.g., Interviewer: "Did you go out yesterday?" Patient: "Did I go out yesterday") when this is a substitute for and not a precursor to an appropriate elaborated response.

Perseveration. Perseveration is defined as a repetition of a patient's own responses. It is a word or phrase that, once uttered, intrudes into the patient's subsequent utterances. It differs from a stereotypy in that the repeated word or phrase is not habitual. Perseverations may occur spontaneously in conversation or are elicited in naming tasks (e.g., the patient names scissors as "scissors" and later names a clock as "scissors"). Perseveration includes palilalia, in which there is immediate repetition of a word, phrase, or sentence (e.g., "I went down town, down town, down town").

Mutism. This is an absence of speech or speech sounds. Patients may pass through a transitional phase of "virtual mutism," during which they generate no propositional speech, yet echolalic responses and some automatic speech (e.g., "three" when prompted with "one, two") may still be present.

Physical signs. *Primitive reflexes.* At least one of the following is present: grasp, snout, and sucking reflexes.

Incontinence. This refers to voiding of urine or feces without concern.

Neuropsychology. *Significant impairment on frontal lobe tests, in the absence of severe amnesia, aphasia, or perceptuospatial disorder.* Impairment on frontal lobe tests is defined operationally as failures (scores below the fifth percentile) on conventional tests of frontal lobe function (e.g., Wisconsin/Nelson card sort, Stroop, Trail Making) in which a qualitative pattern of performance typically associated with frontal lobe dysfunction is demonstrated: concreteness, poor set shifting, perseveration, failure to use information from one trial to guide subsequent responses, inability to inhibit overlearned responses, and poor organization and temporal sequencing.

Abnormal scores that arise secondary to memory, language, or perceptuospatial disorder (such as forgetting instructions or the inability to recognize or locate test stimuli) would not be accepted as evidence of impairment on frontal lobe tests as operationally defined.

FTD patients may perform inefficiently on formal memory, language, perceptual, and spatial tests as a secondary consequence of deficits associated with frontal lobe dysfunction, such as inattention, poor self-monitoring and checking, and a lack of concern for accuracy. Poor test scores per se would not therefore exclude a diagnosis of FTD. An absence of severe amnesia, aphasia, or perceptuospatial disorder would be demonstrated by patchiness or inconsistency in performance (e.g., failure on easy items and pass on more difficult items) or demonstration that correct responses can be elicited by cuing or by directing the patient's attention to test stimuli.

Electroencephalography. *Normal despite clinically evident dementia.* Conventional EEG reveals frequencies within the normal range for the patient's age (minimal theta would be considered within normal limits). There are no features of focal epileptiform activity.

Brain imaging (structural or functional). *Predominant frontal or anterior temporal abnormality.* Atrophy, in the case of structural imaging (CT or MRI), and tracer uptake abnormality, in the case of functional brain imaging (PET or SPECT), is more marked in the frontal or anterior temporal lobes. Anterior hemisphere abnormalities may be bilaterally symmetric or asymmetric, affecting the left or right hemisphere disproportionately.

Progressive nonfluent aphasia. Definitions are for features (see list 2) that differ from or are in addition to those of FTD.

Core features. *Nonfluent spontaneous speech with at least one of the following: agrammatism, phonemic paraphasias, and anomia.* Nonfluent speech is defined as hesitant, effortful production, with reduced rate of output. Agrammatism refers to the omission or incorrect use of grammatical terms, including articles, prepositions, auxiliary verbs, inflexions, and derivations (e.g., "man went town"; "he comed yesterday").

Phonemic paraphasias are sound-based errors that include incorrect phoneme use (e.g., "gat" for "cat") and phoneme transposition (e.g., "aminal" for "animal"). The frequency of such errors should exceed that reasonably attributed to normal slips of the tongue.

Anomia is defined as a difficulty in naming manifest by an inability to find the correct word, by prolonged word retrieval latencies relative to the norm, or by incorrect word production. The availability of partial knowledge of a word, such as the initial letter, would be consistent with anomia, as would several attempts to produce a word, each yielding a close approximation (e.g., "scinners . . . sivvers . . . scivvers . . . scissors").Supportive diagnostic features: speech and language. *Stuttering or oral apraxia.* Articulation is effortful, and repetition of parts of a word, particularly the first consonant, occurs in the patient's effort to produce a complete utterance. (Developmental stuttering is excluded.)

Impaired repetition. The patient has a reduced repetition span (less than five digits forward; less than four monosyllabic words) or makes phonemic paraphasias when attempting to repeat polysyllabic words, word sequences, or short phrases.

Alexia and agraphia. Reading is nonfluent and effortful. Sound-based errors are produced (phonemic paralexias). Writing is effortful, contains spelling errors, and may show features of agrammatism.

Early preservation of word meaning (understanding preserved at single-word level). Patients should show an understanding of the nominal terms employed during a routine clinical examination. There should be a demonstrable discrepancy between word comprehension and naming: Patients should show understanding of words that they have difficulty retrieving.

Behavior. *Early preservation of social skills.* The language disorder should be the presenting symptom. At the time of onset of language disorder, patients should demonstrate preserved interpersonal and personal conduct.

Late behavioral changes in FTD. The changes outlined for FTD in conduct, if they occur, should not be presenting symptoms. There should be a clear, documented period of circumscribed language disorder before their development.

Neuropsychology. *Nonfluent aphasia in the absence of severe amnesia or perceptuospatial disorder.* There is difficulty in verbal expression. The language impairment may compromise performance on verbal memory tasks, so that poor scores on memory tests per se would not exclude a diagnosis of progressive aphasia. The presence of normal scores on one or more tests of visual memory, or a demonstration of normal rates of forgetting (i.e., no abnormal loss of information from immediate to delayed recall/recognition), would provide evidence for an absence of severe amnesia. An absence of a severe perceptual disorder would be demonstrated by accurate recognition of the line drawings employed during routine naming tasks, as determined by the patient's ability to produce a correct name, an approximation to the name, a functional description of the object's use, or a pertinent gesture or action pantomime. An absence of severe spatial disorder is demonstrated by normal performance on two or more spatial tasks, such as dot counting, line orientation, and drawing copying.

Semantic aphasia and associative agnosia (SD). Core features. *Fluent, empty spontaneous speech.* Speech production is effortless, without hesitancies, and the patient does not search for words. However, little information is conveyed, reflecting reduced use of precise nominal terms, and increased use of broad generic terms such as "thing." In the early stages of

the disorder the "empty" nature of the speech output may become apparent only on successive interviews, which reveal a limited and repetitive conversational repertoire.

Loss of word meaning. There must be evidence of a disorder both of single-word comprehension and naming. A semantic deficit may be alerted by patients' remarks of the type, "What's a **? I don't know what that is." However, impairment may not be immediately apparent in conversation because the patient's effortless speech gives an impression of facility with language. Word comprehension impairment needs to be established by word definition and object-pointing tasks. A range of stimuli needs to be tested, both animate and inanimate, because meaning may be differentially affected for different material types.

Semantic paraphasias. Semantically related words replace correct nominal terms. Although these may include superordinate category substitutions (e.g., "animal" for camel), coordinate category errors (e.g., "dog" for elephant; "sock" for glove) must be present to meet operational criteria.

Prosopagnosia. This is impaired recognition of familiar face identity, not attributable to anomia. It is demonstrated by the patient's inability to provide defining or contextual information about faces of acquaintances or well-known celebrities.

Associative agnosia. This is an impairment of object identity, present both on visual and tactile presentation, that cannot be explained in terms of nominal difficulties. It is indicated historically by reports of misuse of objects or loss of knowledge of their function. It is demonstrated clinically by patients' reports of lack of recognition and by their inability to convey the use of an object either verbally or by action pantomime.

Preserved perceptual matching and drawing reproduction. There should be some demonstration that the patient's inability to recognize faces or objects does not arise at the level of elementary visual processing. Demonstration of an ability to match for identity (to identify identical object pairs, shapes, or letters) or to reproduce simple line drawings (e.g., of a clock face, a flower, or a simple abstract design) would provide the minimum requirement to fulfill criteria for diagnosis.

Preserved single-word repetition. The relative preservation of repetition skills is a central feature of the disorder. This typically includes the ability to repeat short phrases and sequences of words, although for such complex material, errors may emerge ultimately in advanced disease in the context of severe semantic loss. Demonstration of accurate repetition at least at the level of a single polysyllabic word is required to fulfill criteria for diagnosis.

Preserved ability to read aloud and to write to dictation orthographically regular words. The ability to read without comprehension is central to the disorder. However, reading performance is not entirely error free. Orthographically irregular words commonly elicit "surface dyslexic"-type errors (e.g., "pint" read to rhyme with "mint"; "glove" to rhyme with "rove" and "strove"). Patients should demonstrate the ability to read aloud accurately at least one-syllable words with regular spelling-to-sound correspondence. Writing of orthographically irregular words also typically reveals regularization errors (e.g., "caught" written as "cort"). Patients should demonstrate accurate writing to dictation at least of one-syllable orthographically regular words.

Supportive diagnostic features: speech and language. *Press of speech.* The patient speaks without interruption. This occurs in many but not all patients.

Idiosyncratic word usage. Vocabulary is used consistently but idiosyncratically. For example, the word "container" applied to small objects regardless of their facility to contain, and "on the side" applied to spatial locations, both near (e.g., on the table) and distant (e.g., in Australia). The semantic link between the adopted word or phrase and its referent may be tenuous or absent.

Absence of phonemic paraphasias in spontaneous speech. Sound-based errors are absent in conversational speech. The feature, although characteristic, is not included as a core feature because occasional phonemic errors may emerge in advanced disease in the context of a profound disorder of meaning.

Surface dyslexia/dysgraphia. The presence of surface dyslexic errors (described earlier) in reading and writing is a strong supportive feature.

Preserved calculation. The preserved ability of patients to calculate (to carry out accurately two-digit written addition and subtraction) is characteristic. It is not included as a core feature because calculation skills may break down in advanced disease as a consequence of failure to recognize the identity of Arabic numerals.

Behavior. *Loss of sympathy and empathy.* Patients are regarded by relatives as self-centered, lacking in emotional warmth, and lacking awareness of the needs of others.

Narrowed preoccupations. Patients are reported to have a narrowed range of interests that they pursue at the expense of routine daily activities (e.g., doing jigsaw puzzles all day and neglecting the housework).

Parsimony. Patients show an abnormal preoccupation with money or financial economy. This may be demonstrated by hoarding or constant counting of money, by patients' avoidance of spending their own money, by their purchase of the cheapest items regardless of quality, or by their attempts to restrain usage by other family members of household utilities (e.g., electricity and water).

Neuropsychology. *Profound semantic loss, manifest in failure of word comprehension and naming, or face and object recognition; preserved phonology and syntax, and elementary perceptual processing, spatial skills, and day-to-day memorizing.* Significant impairment should be demonstrated on word compre-

hension and naming or famous face identification or object recognition tasks. It should be shown that poor scores arise at a semantic level and not at a more elementary level of verbal or visual processing by demonstrating that the patient can repeat words that are not understood, can match for identity, and can copy drawings of objects. Patients should demonstrate normal performance on two or more spatial tasks, such as dot counting and line orientation. Performance on formal memory tests (e.g., involving remembering words or faces) is compromised by patients' semantic disorder. Nevertheless, patients retain the ability to remember autobiographically relevant day-to-day events (e.g., that a grandchild visits on Saturdays). Such preservation is striking clinically but may be difficult to capture on formal tests, which by definition are divorced from daily life.

Features common to each clinical syndrome. Diagnostic exclusion features. Early, severe amnesia. Symptoms of poor memory may be present and inefficient performance demonstrated on memory tests; these may occur secondary to executive or language impairments. However, memory failures are patchy and inconsistent, and patients do not present a picture of classic amnesia. Demonstration that a patient is disoriented in both time and place and shows a consistent, pervasive amnesia for salient contemporary autobiographic events would be incompatible with the clinical syndromes of FTLD.

Spatial disorientation. Patients with FTD who wander from a familiar environment may become lost because of failure of self-regulation of behavior (i.e., for reasons that are not primarily spatial). They do not exhibit spatial disorientation in familiar surroundings such as their own home. They negotiate their surroundings with ease, and localize objects in the environment with accurate reaching actions. Preservation of primary spatial skills is demonstrable even in patients with advanced disease by their capacity, for example, to align objects and to fold paper accurately. Evidence of poor spatial localization and disorientation in highly familiar surroundings would exclude clinical diagnoses of FTD, PA, or SD.

Logoclonic, festinant speech with rapid loss of train of thought. Logoclonia is defined as the effortless repetition of the final syllable of a word (e.g., Washington . . . ton . . . ton . . . ton). Festinant speech refers to a rapid, effortless reiteration of individual phonemes. Logoclonic and festinant speech need to be distinguished from stuttering, which has an effortful quality and usually involves repetition of the first consonant or syllable. They need to be distinguished from palilalia, during which there is repetition of complete words and phrases. Loss of train of thought is a common feature of AD: patients begin sentences that they fail to complete, not only because of word-finding difficulty but also because of rapid forgetting of the intended proposition. A demonstration in conversation that patients are rapidly losing track would be contrary to a diagnosis of FTLD.

Conclusion. These criteria provide a mechanism for diagnosis and differentiation of dementias associated with FTLD. The core diagnostic criteria indicate the consensus of the group in identifying the key clinical aspects that differentiate FTD, PA, and SD.

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