CLINICAL STUDY

Clinical accuracy of the distinction between Alzheimer's disease and frontotemporal lobar degeneration

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Abstract: Alzheimer's disease (AD) is the most common cause of dementia. Frontotemporal lobar degeneration (FTLD), although less prevalent overall, is almost as common as AD in patients under the age of 65. AD and FTLD are histopathologically distinct, with AD being characterised by extracellular amyloid plaques and intraneuronal neurofibrillary tangles, and FTLD by the presence of non-AD histological pathology, most commonly either tau-positive inclusions or ubiquitin-positive or TDP 43 positive inclusions. Clinically, AD and FTLD may occur with overlapping symptoms, especially in the early stages of the disease. In the case of Alzheimer's disease, it is represented by isolated decline of recent episodic memory; later on, by the impairment of time and space orientation, whereby the alteration of social behaviour and amnesic aphasia occur predominantly in the advanced phases of the disease. Frontotemporal lobar degeneration is demonstrated in three clinical sub-units: 1) The behavioural-dysexecutive variant of FTLD (frontotemporal dementia, the frontal variant of FTLD, {fvFTLD}), 2) Progressive non-fluent aphasia, 3) Semantic dementia (SD) with the profound impairment of social conduct (fvFTLD) or with severe speech impairment (PNFA, SD). Considering the different clinical symptomatology with FTLD diagnostics, it is necessary to use different psychometric tests than in the case of Alzheimer's disease. Therapy and the degree of dependence of the affected person are also different. All three diseases within the FTLD category, mainly the behavioural-dysexecutive variant, require a higher level of nursing care on the part of other persons or institutions in comparison with Alzheimer's disease. The goal of our publication is to point to the differences in clinical manifestation and the findings of auxiliary examinations that are helpful in the clinical accuracy of the distinction between these two types of dementia *(Tab. 1, Fig. 3, Ref. 18)*. Text in PDF *www.elis.sk.*
Key words: Alzheimer's disease, frontotemporal lobar degeneration, dementia, clinical accuracy, behavioural disorders.

Accuracy in the clinical diagnosis of dementia is increasingly important for therapeutic and scientific investigation. Frontotemporal lobar degeneration is one of the neurodegenerative disorders commonly mistaken for Alzheimer's disease, mainly in the early stages. Because it often affects people in midlife, it is also mistaken for primary psychiatric disorders. In recent years, it has become clear that there are distinct dementia profiles, which reflect the distribution of pathological changes within the brain and which, by interference, are predictive of the underlying pathology. For example, dominant problems in memory combined with problems in word retrieval, perceptuospatial and constructional difficulties, occurring alongside preserved social skills, strongly suggest Alzheimer's disease (1). In contrast, the breakdown of social behaviour, affect and executive functions occurring alongside preserved perceptuospatial skills favour a diagnosis of frontotemporal dementia (2). On the other hand, differences can be blurred in the early stage of both diseases.

Alzheimer's disease

Progressive memory impairment is the single most prominent feature of Alzheimer's disease (1). This memory dysfunction especially involves the ability to learn new information, typically characterised as a loss of episodic memory. The recall of memories stored in long-term memory is preserved until the advanced stage of the disorder. At onset, the patient may be aware of his or her learning and memory problems, but typical anosognosia will soon develop. Disorientation in time and space occurs early on, accompanied by disturbances in executive functioning. Focal cortical symptoms, such as aphasia (paraphasias, the use of automatic phrases and clichés and anomia are frequently encountered), apraxia and agnosia will develop during the course of the disease. Of those, aphasia is most frequently seen usually in the form of Wernicke's type or the transcortical sensory type (2). Rarely, aphasia may be the presenting sign and then differential diagnosis with progressive aphasia or semantic dementia becomes crucial. Other focal defects include left-right discrimi-

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nation and acalculia. Behavioural and personality changes become more obvious as the disease progresses. Patients may be agitated, emotionally unstable, irritable, apathetic, depressed, and often develop paranoid delusions. At a later stage, visual hallucinations may develop. Abnormal motoric behaviour deepens – aimless walking around the house, browsing the drawers, constant aimless motor activity of the hands (aimless object sorting, aimless loading of used dishes etc.). Urgent attitudes dominate in behaviour (patients do not recognise their partners and banish them from the house), which often leads to aggressiveness. During the last years of the disease, they wane physically as well as psychically;they tend to neglect hygiene. They speak only learned phrases, and are generally directable only with difficulty. At the onset of the disease and in the early phase, neurological examination is normal. Later on, extrapyramidal signs, in particular rigidity, followed by myoclonus and overt epilepsy may develop. The disease's total duration from the detection of the first symptoms of memory disorder to complete cognitive degradation takes on average 10 years (3).

Main symptoms

Memory
  Disturbances in recent episodic and semantic memory
  The inability to learn new knowledge or skills (using a cell phone, remote control, etc.)
  Long-term memory is well preserved at the beginning
  Repeated repetitions in conversation, the inability to lead meaningful conversation

Orientation
  Difficulties with everyday time orientation
  Time orientation generally fades in the form of date →day of the week → month → season → year
  Spatial orientation (also tends to fade from details to everything)

Speech
  Difficulty finding words
  Difficulty remembering people's names
  The descriptive naming of objects
  Difficulty following group conversation
  General speech expression, non-specific (clichés)
  Impaired repetition with phonemic errors
  Impaired sentence comprehension

Calculation
  Impaired mental and written arithmetic – especially subtractions involving holding and manipulating numbers, carrying across columns

Perception, visual-spatial skills, praxis
  Disrupted spatial perception
  The loss of spatial perception while drawing
  Difficulties with remembering the placing of objects in space

  Disorientation in well-known places
  Difficulties with driving (the inability to judge the distance and speed of oncoming cars)
  Difficulties with manual actions requiring logic and spatial perception (folding clothes, laying the table, etc.)

Executive functions
  Difficulties with the realisation of multi-stage commands and tasks
  Difficulties with the organisation of household duties
  Uncertainty, perseveration with most activities

Behaviour
  Socially appropriate until the advanced stages
  Irritability, anxiety
  Mental rigidity (accented stubbornness, incompliance)
  Abnormal motoric behaviour (aimless walking around the house, browsing the drawers, etc.)
  Aggressiveness (in the case of some people in advanced stages, in connection with the accent of personal features and pathologic deliberation within the disease)

Frontotemporal lobar degeneration (FTLD)

Classification from the clinical point of view (4)
  1) The frontal variant, the newer behavioural-dysexecutive variant of FTLD (frontotemporal dementia in the strict meaning of the word)
  2) Non-fluent progressive aphasia (PNFA)
  3) Semantic dementia (SD)

  Frontotemporal lobar degeneration (FTLD) has recently become known as a heterogeneous clinical syndrome caused by the progressive degeneration of the frontal and temporal brain lobes. Its occurrence makes up on average 10 % of all dementia with an onset between the ages of 45 and 65. The clinical manifestation of individual subtypes differs. The common denominators are behavioural disturbances, speech disorder and the impairment of executive functions leading to severe dementia. Memory and visuospatial functions remain relatively well-preserved until the advanced stages of the disease (5).

The behavioural-dysexecutive variant of FTLD (also frontal variant; fvFTLD)

  The behavioural-dysexecutive variant of FTLD comprises the severe alteration of personality immediately in the initial stages, behavioural and speech disturbances, the impairment of executive functions and progressive dementia.
  The most common manifestation of fvFTLD is an early change in social and personal conduct, characterised by difficulty in modulating behaviour to the social demands of a situation. This is often associated with a lack of inhibition, resulting in impulsive or inappropriate behaviour; for example, swearing at inappropriate times, outbursts of frustration, or a lack of social

tact. The progression of the disease may lead to poor financial judgement or impulsive acts (such as grabbing food from someone else's plate, shoplifting or impulsive buying). At the extreme, impulsivity can be self-destructive; for example, patients try to get out of a moving car because something of interest has caught their attention. In some individuals, inappropriate sexual behaviour occurs. There may also be repetitive or compulsive behaviour; this may include a preoccupation with repeating specific personal acts (e.g. rereading the same book) or repeating specific physical actions (e.g. repeatedly walking to the same locations). Dietary habits and personal hygiene may also change. Overeating is common, as well as food fads in which only certain foods are eaten. There is a loss of concern for one's personal appearance (patients can be increasingly unkempt early in the disease). As the disease progresses, the callosity and clumsiness of motions and expression also deepens. In later stages, affective disturbances worsen (5). Patients often shout madly due to a minimal impulse, they swear crudely, etc. As the disease progresses, apathy and aboulia also escalate. Patients generally sit at the same place without any movement for long hours; when attempting to move them, they react in a rough, inadequate, almost brachial, aggressive manner.

The behavioural-dysexecutive variant of FTLD (also frontal variant; fvFTLD) (4)

Core diagnostic features:
- Insidious onset and gradual progression
- Early deterioration of social activities
- Early change of social behaviour and the inability to regulate it (severe and specific answers to questions, a loss of empathy, rare hypersexual behaviour, inadequate reactions, hyperactivity or passivity)
- Early emotional blunting
- The early loss of insight (unconsciousness or negation of clinical symptoms)

Supportive diagnostic features:
- Loss of hygiene habits
- Mental rigidity (egocentrism, the inability to adapt to situations and to learn something new)
- Distractibility and instability (the inability to finish a given task under the influence of another disturbing impulse, paying too much attention to the disturbing impulse)
- Inadequate reactions to impulses (intense verbal or brachial reactions, groundless aggressiveness)
- Changes in food intake (increased intake, the preference of sweets)
- In some cases, symptoms of motor neuron disease (FTLD/MND)

Disorders of speech production:
- A decrease of spontaneity
- A decrease of speech production and telegraphic speech
- Stereotyped speech (the repetition of individual words and phrases or topics of interest for adequate conversation)

- Echolalia (the repetition of words or whole sentences; e.g. repeating after an examiner instead of giving an answer)
- Perseverations (the repetition of one's own answers, i.e. words or sentences)
- Talking without pause
- Mutism (the patient does not speak or produce any sounds; in some cases,echophrasia is present or automatic speech; i.e. if we say e.g. "one, two", the patient adds "three")

Progressive non-fluent aphasia (PNFA)

Progressive non-fluent aphasia is a disorder of expressive language, characterised by effortful speech production, phonologic and grammatical errors and word retrieval difficulties. The first symptoms of the disease are represented by discrete speech disorders in the sense of aphatic stuttering, anomia, sporadic agramatisms and phonemic paraphasias. As the disease progresses, the anomia and agramatisms also progress, vocabulary is reduced, speech becomes non-fluent and the frequency of neologisms increases. Difficulties in reading and writing also occur. The understanding of word meaning is relatively well preserved. The disorders of language occur in the absence of impairment in other cognitive domains, although behavioural changes similar to fvFTLD may emerge late in the disease (signs of pre-frontal syndrome, irritability, agitation that may alternate with apathy). Depression is very frequent.

Core diagnostic features (4, 6):

- Insidious onset and gradual progression
- Non-fluent spontaneous speech (speech loses its fluency, is produced only with great effort, aphatic stuttering is present)with the presence of at least one of following symptoms:
- Anomia (the inability to find the right word)
- Agramatisms (grammatically incorrect words, sentences)
- Phonemic paraphasias (the mutilation of words that sound like the correct words but the phoneme is changed, e.g. "clown" – "crown")

Supportive diagnostic features

- Speech disorder: symptoms include aphasic stuttering, sometimes jointly with the apraxia of muscle groups involved with speech production, difficulties with repetition, alexia, agraphia. In the early phase, the preserved recognition of word meaning; in the later phase, mutism.
- Behaviour disorders:preservation of social skills present in the early phase; in the later phase, behavioural changes similar to fvFTLD – the enforcement of one's own rituals, obsessional behaviour, non-diversibility, aggressiveness at any attempts to provide direction
- Somatic symptoms: Primitive reflexes (grasp, suction and glabellar reflex), sometimes in later stages Parkinson-like symptoms (hypokinesia, rigidity, rarely tremor), symptoms of motor neurone disorder

Semantic dementia (SD; semantic aphasia and visual agnosia)

In semantic dementia, a severe naming and word comprehension impairment occurs alongside fluent, effortless, and grammatical speech output. Speech is fluent at the beginning, but anomia (the inability to denominate subjects) and semantic paraphasia (the exchange of words of the same category) are present. Speech production is effortless without hesitancies, and the patient does not search for words. However, little information is conveyed, reflected in the reduced use of precise nominal terms, and the increased use of broad generic terms such as "thing". In the early stages of the disease, the "empty" nature of the speech output may become apparent only in successive interviews, which reveal a limited and repetitive conversational repertoire. Loss of meaning follows a hierarchical model. Patients first lose the ability to distinguish between members of one unit (e.g. kinds of apples); later, they are unable to distinguish a difference between members of one group (e.g. apples and oranges) and in the end they are unable to distinguish individual hypergroups (e.g. fruit and vegetables). First, "a poodle" is called "a dog", later on all dogs are called "animals" and at the end all animals are called "things" (7). Word meaning fades, despite a preserved ability to read and write. As the disease progresses, speech is fluent without any effort, but the content is empty. Visual associative agnosia is also present (the inability to denominate objects seen). Elementary visual-constructive and practical functions are relatively well-preserved (the ability to draw a simple picture, to pair similar objects). In advanced phases of disease, the patient gradually stops speaking and the occurrence of symptoms similar to the dysexecutive variant with apathic symptoms to the fore is possible.

Core diagnostic features (4)
• Insidious onset and gradual progression
• Progressive, fluent, empty spontaneous speech
• The loss of word meaning, manifested by impaired naming and comprehension – difficulties with the denomination of objects
• Semantic paraphasias (a word from the same semantic category replaces the correct term, e.g. "fruit" instead of "orange" or "apple" instead of "pear", etc.)
• Visual agnosia (prosopagnosia) – a disorder of the recognition of well-known faces or individual kinds of fruit
• The preserved ability to draw a simple picture, intact elementary perception (the affected person is able to pair the same figures, letters, objects)
• The preserved ability to repeat individual words
• The preserved ability to read aloud and to write simple words as dictated

Supportive diagnostic features
• *Speech disorders:* talking without pause, the choice of idiosyncratic words (the expression "small box" for all small objects, no matter what their function or shape is), the absence of phonemic paraphasias (the misrepresentation of words that sound alike or similar to the correct word), the preserved ability to count
• *Behavioural disorders:* loss of empathy, the narrowing of in-

terest counter to routine daily activities (e.g. doing puzzles all day instead of taking care of the household), parsimonia (an abnormal care of money, e.g. the continuous counting of money, an aversion to spending money and buying the cheapest things regardless of their quality)
• *Somatic symptoms:* the absence or late development of primitive frontal reflexes, akinesis, rigidity, tremor

Psychometric tests helping to distinguish Alzheimer's disease and FTLD disease

Psychometric tests are designed to review disorders of cognitive abilities from a quantitative and qualitative point of view. Through their use, we set the extent and seriousness of cognitive deficit as well as the subtype of dementia. The basic screening test focused on the examination of memory disorder is MMSE (8). MMSE is set for screening and the ambulant identification of cognitive disorder, mainly of an Alzheimer's type. Its content and administration are generally well-known, so it is not necessary to proceed with it in detail. For a more precise examination of cognitive disorder we use ADAS-Cog (9), the MOCA test (10, 11) the Addenbrook cognitive test (12) or Wechsler's memory test (13). In suspected cases of a syndrome within the FTLD, or in the case of a need to distinguish between Alzheimer's disease and FTLD in clinically ambiguous cases, we prefer the Addenbrook cognitive test (ACE-R). Within ACE-R we examine five domains: 1) attention and orientation, 2) memory, 3) verbal fluency, 4) speech ability and 5) visuospatial abilities. Worse performance in the field of verbal fluency and speech, in comparison with performance in the field of orientation and memory, points to some of the FTLD syndromes. In the case of such a suspicion, we consequently carry out the FAB test (14) or Stroop test (15), which enable a more detailed examination of the extent of specific cognitive impairment and its subclassification within the framework of FTLD (Tab. 1).

The Frontal Assessment Battery (FAB test) is the first-choice test for the evaluation of syndromes within FTLD, and mainly the dysexecutive FTLD variant. The FAB test consists of six subtests:
1) Conceptualisation and abstract reasoning (similarities test); Patients have to find the superior term for objects within a given category, e.g. "banana" and "apple"or "chair" and "table". Patients with FTLD have difficulties with abstraction and are unable to identify summarily the terms as fruit or furniture.
2) Verbal fluency test; Patients have to name as many words starting with a given consonant as possible, e.g. "s". Tasks focused on phonemic fluency require planning as well as controlled searching within semantic memory. A disturbed ability to search for words starting with the same letter mainly indicate left-side

Tab. 1. Scheme for setting the subtype of dementia and distinguishing between AD and FTLD by means of the Addenbrook cognitive test.

verbal fluency (subscore)	+	speech (subscore)	if ≤ 2,2 = FTLD
orientation (subscore)	+	memory (subscore)	if ≥ 3,2= AD

frontal disorder. Patients with FTLD display a decreased verbal production of such words.

3) Motoric programming – Luria motoric sequences; Patients are asked to hit a pad with their hand in a given order: the fist, the edge of the hand, the palm, whereby the examiner demonstrates it to them. In the case of frontal dysfunctions, the time order is disordered as well as the permanency of the required movement. Patients with FTLD find it difficult to abide by the required order; the occurrence of a limited sequence for two actions only is possible or preservations may occur.

4) Conflicting instructions; Patients are asked to clap their hands twice when the examiner claps once and to clap once when the examiner claps twice. In this task, a conflict between verbal instruction and sensorial stimulus occurs. Patients with FTLD (mainly fvFTLD) tend to react automatically to sensorial impulse, whereby the response to verbal direction is suppressed (patients clap their hands as the examiner does).

5) Inhibitory control "go-no go test"; Patients are asked to clap their hands once if the examiner claps once and not to clap their hands at all if the examiner claps twice. This task requires the detection of reaction implicit from sensorial stimulus. The test mainly determines the dysfunction of the ventral area of the frontal lobe. Patients with FTLD (mainly with fvFTLD) have difficulties not to clap their hands if the examiner claps his or her hands twice, which points to a disorder of inhibition control.

6) Environmental autonomy (prehension behaviour); Patients have their hands lying free on the table or on their knees. The examiner approaches them with his or her hands towards theirs and touches their palms softly. The examiner waits for patients to grasp his or her hands spontaneously. If they do, on the second attempt, patients are asked to not grasp his or her hands. Patients with fvFTLD have deliberated grasp reflex and grasp the hands of the examiner even if being told not to do so. Every subtest is scored with 0–3 points. 3 points are granted for exact performance and 0 points are granted for a total failure of the test. The maximum score is 18 points. Each of the items of the FAB scale is associated with the functionality of a specific area of the frontal lobe on the basis of correlation with neuropsychological, electrophysiological and functional display methods: Conceptualisation with dorsolateral, lexical fluency with medial and inhibition control with medial and orbitofrontal areas. There is a significant correlation between the FAB total score and perfusion in the medial and dorsolateral frontal cortex (BA9, BA10) bilaterally, but no correlations with other cortical or subcortical regions (16). However, the FAB scale does not contain enough items to follow up FTD. The main scale used to follow up the disease is the Neuropsychiatric Inventory (NPI). The Frontal Behavioural Inventory (Kertesz) seems to be interesting, but did not enter into widespread usage. The Mattis Dementia Rating Scale, not specific for FTD, is used to assess the cognitive rate. The activities of daily living scales and the caregiver burden are not well known in FTD.

Imaging methods

Medial temporal lobe atrophy (MTA) is a recognised marker of Alzheimer's disease. MTA comprises gyrusparahippokampalis that contains entorhinal, transenthorinal cortex and subiculum and hippocampal formation. According to the latest revised criteria for Alzheimer's disease diagnosis (1), the specific memory decline and MTA satisfactory criteria are enough for stating the diagnosis of the prodromal stage of Alzheimer's disease. Mediotemporal atrophy correlates best with progressive memory decline. The given criteria refer to typical Alzheimer's disease. Among a special group of patients, the disease does not start with disorders of episodic and semantic memory; It either starts with disorders of visuospatial orientation, speech disorders, acalculia or with behaviour disorders. In these cases, we talk about atypical Alzheimer's disease. Through MR examination, we detect the atrophy in the posterior areas of the brain, mainly in the area of the parieto-occipital sulcus, posterior cingulate sulcus, precuneus and parietal lobe (17). Atypical Alzheimer's disease with posterior atrophy is more prevalent in patients with early onset AD (17).

Through MR examination of the brains of FTLD patients, we detect the atrophy of the frontal and temporal lobes. Generally, infvFTLD, they are symmetrically affected by the atrophy of the frontal lobes and the frontal pole of the temporal lobes. In the case of progressive non-fluent aphasia, the atrophy is asymmetric with prevalence in the dominant (most frequently the left) hemisphere; the first locality affected by atrophy is the left perisilvian area. In the case of semantic dementia, we detect the atrophy of the frontal pole of the temporal lobe, with prevalence in the dominant hemisphere. Several studies have dealt with the rate of hippocampal atrophy by AD and FTLD. Scheltens et al (2006) (18) discovered that the atrophy of the hippocampus by AD is comparable with the atrophy infvFTLD; the atrophy of the left hippocampus by SD is more apparent than by AD (in compliance with the predominant impairment of the left temporal lobe by SD). With PNFA, hippocampal atrophy was not consistently present and in the event of its occurrence, it was milder than with AD. It is obvious that MTA and atrophy of the hippocampus also occur in FTLD syndromes and we have to evaluate its detection in accordance with the clinical manifestation of the diagnosed disease (Figs 1, 2, 3).

Mutual similarities and differences between AD and FTLD

Behavioural symptoms, mainly loss of the sociable and social codex, hyperorality, stereotypical and perseverative behaviour, reduced speech performance and preserved spatial orientation best fitfvFTLD and serve as a sign of differentiation from Alzheimer's disease. Lack of social feelings and social behaviour stand for most. Emotional numbness and loss of affective answers may even occur in prodormal phases, when the affected person does not show any symptoms of the disease. Other symptoms may be utterances of anxiety, obsessive-compulsive behaviour, apathy, a total lack of interest in one's surroundings and excessive irritability. On the other hand, patients with Alzheimer's disease show, in the early as well as intermediate phase, nearly intact social behaviour. In these phases, we see only sporadic signs of irritability in Alzheimer's disease patients in repeated attempts at direction. Irritability and anxiety may occur at the onset of all neurodegenerative diseases, thus it is impossible to recommend them as differentiation signs.
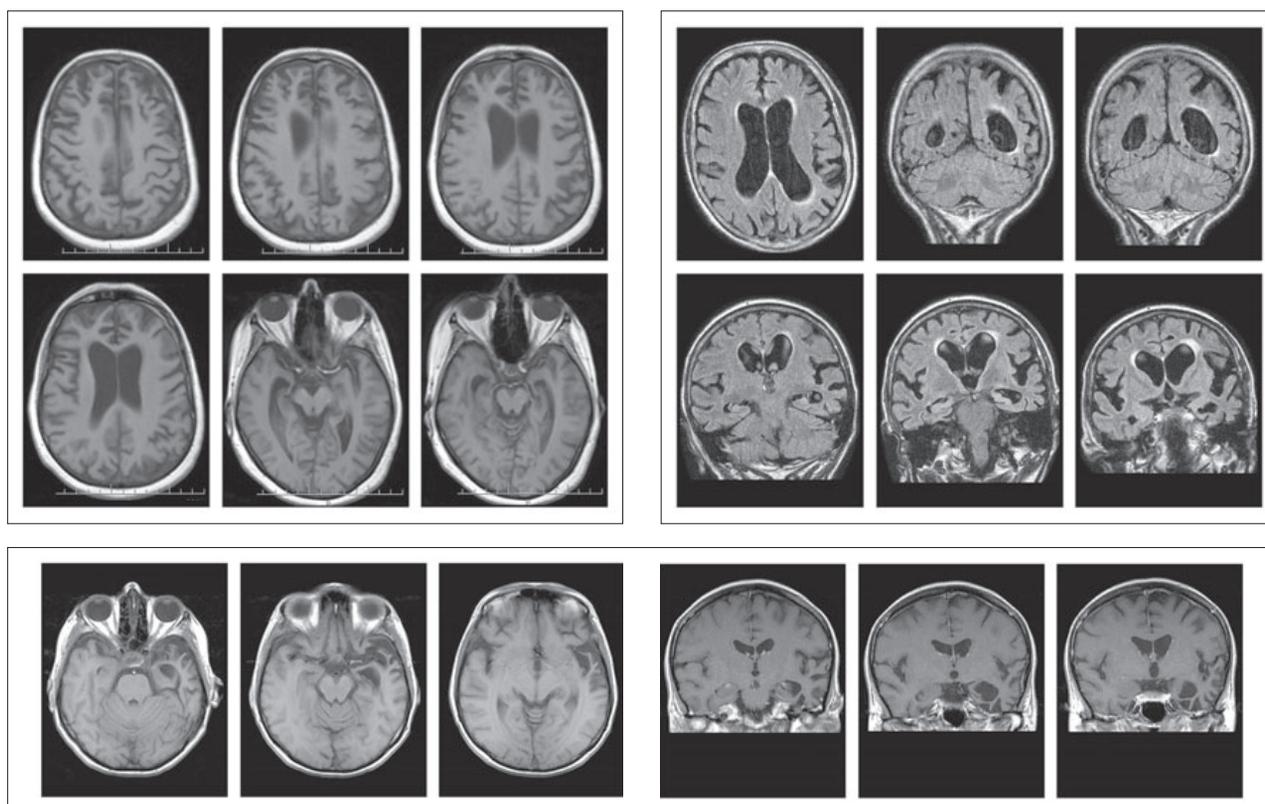
Figs 1–3. MTA and atrophy of the hippocampus also occur in FTLD syndromes and we have to evaluate its detection in accordance with the clinical manifestation of the diagnosed disease.

Speech disorders are a significant differentiation sign between AD and FTLD, as well as between individual syndromes of FTLD. In Alzheimer's disease, the speech disorder starts with difficulties when searching for words, by forgetting surnames and first names; later on, in the reduction of common vocabulary. As the disease progresses, speech becomes descriptive, less comprehensive, nonsensical, without a main idea. Affected people lose the determinative axis of conversation but their predication (not in advanced phases) is not a mess of words. Patients with fvFTLD have significantly reduced speech, very strict and specific without any emotional and affective tone. In advanced phases of the disease, the speech is stereotyped, monotonous with increasing echolalia. In late and terminal phases, affected people do not speak at all. In progressive non-fluent aphasia, the speech disorder is the first and leading sign. Immediately in the early phases, striking anomia and anomic stuttering are present. Agramatisms and phonemic paraphasia combine, speech loses its fluency and is produced only with great effort. Over the course of the disease, speech becomes reduced only to a few words that the affected person keeps on repeating and in terminal phases, the ability to speak fades completely. In semantic dementia, the speech preserves its fluency. At the beginning, the affected person stops understanding the meaning of words and semantic paraphrases start to grow (e.g. "dog" instead of "horse", patients get an order in a shop to bring an apple and bring a banana instead). In advanced phases (still with preserved speech fluency), the examiner asks patients to point to their eyes and they point to their noses; when they are asked to point to something red they point to a different colour. Gradually, patients stop understanding any basic prompts and lose the ability to understand human speech as such. Social behaviour is preserved in the long term; they are able to understand the situation partially through gestures. However, they are generally uncertain and hesitant (they will sit only after they are shown a chair with a gesture; after a while, they stand up helplessly or want to move themselves). Generally, they have a tendency to mimic other people's gestures and words. In the long term, patients with semantic dementia have relatively well-preserved logical operations (the ability to solve Sudoku or to find a way out of a labyrinth). Nevertheless, in common situations these patients behave purposelessly (when going shopping they put useless things into their basket, in their house they move things aimlessly from once place to another, etc.)

Memory and visuospatial orientation are other significant differentiation signs of AD and FTLD. In the case of Alzheimer's disease, the memory is the first of the affected cognitive domains. Even in the prodormal stage of Alzheimer's disease, the affected person loses the ability to learn new knowledge and skills; later, episodic and semantic memory decline. Time orientation is disrupted at the end of the prodormal stage and generally after this stage (or simultaneously with it) a disorder of visual-spatial orientation occurs. Patients stop orientating themselves in less well-known surroundings (in a different ward to the one they live in) and later on,

also in well-known spaces (their own houses). Patients are unable to find things of daily use and put them in a different place than they normally would. InfvFTLD, episodic and semantic memory is relatively well-preserved; however, procedural memory becomes disrupted as the disease progresses. The disruption of procedural memory (the sequence of actions in a multi-phase task, e.g. the assembly of any tool) is caused by the impairment of several cognitive domains. Generally, patients' visuospatial abilities are well-preserved until the late stages of the disease. Episodic memory is affected less, while time and space orientation are relatively well-preserved; however, it is often impossible to examine them with respect to speech disorder. In the case of semantic dementia, the situation is similar; memory as such is not significantly disrupted. Affected persons do not understand the meaning of words, which means that memory examinations are significantly limited.

Conclusion

The common denominator of Alzheimer's disease and frontotemporal lobar degeneration is the gradual onset and slow progression of the decline of specific cognitive domains. The character of cognitive and behavioural impairment is indeed specific for every clinical entity. On its basis we can already in early stages distinguish the individual clinical units and over time we can follow if the cognitive degeneration fulfils the criteria of the expected disease. The evaluation of the atrophy pattern in MR completes the diagnostic process. Histopathologic examination post mortem should be a standard part of diagnostics and will be discussed elsewhere. In our publication, we put emphasis mainly on the clinical diagnostics of neurodegenerations and on their mutual distinction in ambulant or institutional conditions. Therapeutic possibilities and prognosis are based on correct diagnosis. Even though the therapeutic possibilities are currently limited, especially with regard to Alzheimer's disease, the accurate diagnosis of individual types of neurodegeneration is a precondition for the progression of clinical research and the clinical trials of new medicaments.

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