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Differential diagnosis of behavioral variant of fronto-temporal dementia (bvFTD)

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- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
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Summary

Background:

The aim of the paper is the differential diagnosis of various types of Fronto-Temporal Dementia (FTD), with the focus on its behavioural variant (bvFTD).

Material/Method:

Material and Method. Screening was done in order to assess the depth of dementia with the short version of MMSE, while evaluation of various variants of FTD was performed with the use of such neuropsychological tests as Newcomb and Chicago Fluency Tests, Wechsler Memory Scale - III (WMS-III), Western Aphasia Battery (WAB-R), and the Boston Naming Test (BNT). Behaviour was evaluated with a Polish version of the Frontal Behavioral Inventory (FBIInv). The inventory consists of 24 questions which enable an evaluation of social behaviour disorders. The study included 112 patients - 68 men and 46 women treated in the Reintegrative -Training Centre of the Foundation for Persons with Brain Dysfunctions in Kraków and in the Clinic for Developmental Psychiatry, Psychotic Disorders and Old Age Psychiatry, of the Medical University at Gdańsk, who were suffering from various types of dementia.

Results:

It was found that FTD patients scored the highest, while the VAD patients scored somewhat lower in the FBIInv. At the same time the scores obtained by PPA patients were higher in comparison to the control groups, but not as high as in the case of patients with FTD. In the process of the neurotherapy of FTD patients we found a reduction of the behavioral disturbances, despite the progression of the illness.

Conclusions:

The results obtained in the present study confirmed the diagnostic value of FBIInv in the differential diagnosis of various types of FTD and in the evaluation of neurotherapy efficacy.

key words:

frontal cortex dysfunctions • impairments of cognitive functions • executive functions disorders • disinhibition

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BACKGROUND

Diagnosis of Fronto-temporal dementia (FTD) requires – beside brain-imaging – a careful evaluation of genetic and neuropathological, cognitive processes disorders, and behaviour problems. The complexity of the symptoms observed after frontal lobe damage creates the necessity for a very careful neuropsychological examination [1,2]. Gustafson and Nielsen [3] already in the last century proposed a way of evaluating the behaviour of patients with frontal dementia enabling a differentiation of Pick's and Alzheimer Disease. The Manchester group evaluated also the symptoms of FTD in retrospective studies in order to compare the clinical diagnosis with post mortem examination [4,5]. This made possible a differential diagnosis of Dementia and of Alzheimer Type (DAT) [6]. Lopez et al. [7] stated more symptoms of depression, anxiety, irritability, mood lability, disinhibition, inertia as well as social withdrawal in FTD patients in comparison to DAT patients, in whom paranoic symptoms were more often observed. Gregory and Hodges [8] conducted a review of psychotic symptoms in FTD patients with at least 5 basic diagnostic features. In a half of the patients a diagnosis of FTD already established, 1/3 had been diagnosed with schizophrenia, psychosis, depression with obsessive-compulsive traits, alcohol addiction, and psychogenic memory disorders.

The course of illness in FTD is similar to DAT and it includes three stages. The nature of the stages including disorders of cognitive, emotional processes as well as disorders of behaviour were described in many works [9]. Lebert [10] applied an Inventory of Symptoms to discriminate FTD, Alzheimer disease, and vascular dementia. The inventory took into account the following disorders:

1. lack of self-control,
2. self neglect,
3. egocentric behaviours,
4. mood disorders.

Miller et al. [11] performed a retrospective evaluation of occurrence and the lack of symptoms of the Lund-Manchester scale in 30 patients with FTD. Patients were selected on the basis of a SPECT examination. The following differences between patients with FTD and were noted:

1. personal neglect,
2. hyperorality,
3. stereotyped behaviours and perseveration,
4. logopenia with preserved spatial orientation.

Kertesz et al. [12] developed a Frontal Behavioural Inventory (FBIInv) in order to delineate specific behaviours, which would make possible a reliable diagnosis of frontal dementia. The inventory may be used both for the purpose of an introductory evaluation and to perform retrospective diagnosis. The items of the inventory were selected from the elementary diagnostic of the Lund-Manchester group and out of the most common syndromes of FTD observed in the patients examined by Kertesz et al. [13]. The test was administered to 12 FTD patients, 16 DAT patients at the early stage of illness, and 11 patients with dementia caused by depression diagnosed by a psychiatrist and the Beck Depression Test during a pilot study. DAT patients were found to meet the criteria of NINCDS-ADRD. The depth of dementia was defined on the basis of scores gained on the Mattis Dementia

Rating Scale (MDRS). FTD patients were selected taking into account clear cut behavioural symptoms, yet several developed logopenia at the later state of illness, and a typical Motor Neuron Disorder (MND) was stated in one of them. Frontal lobes atrophy was observed in 10 of those 12 patients with neuroimaging techniques. Pick disease was confirmed in 3 patients post-mortem, while in one cortico-basal symptoms were noted, while in two tau-negative ubiquitin inclusions as well as clinical symptoms of MND were stated. Results of the pilot study revealed that patients with frontal lobe lesions obtained much higher scores in the FBIInventory than did the two control groups, something which was confirmed with ANOVA. No significant differences between the scores of patients with Alzheimer dementia and dementia following depression were noted. Patients with Alzheimer dementia were older, than patients with FTD and depression with one exception – all FTD patients were 65 years old at the onset of illness (which is a common time for falling ill in such cases). An analysis of the mean scores gained at FBIInv revealed that the most common behavior disorders were: lack of insight, thinking rigidity, concreteness, personal neglect, inappropriate remarks due to disinhibition. A significant difference, however, was stated between the scores of FTD patients, and the control groups. The results made it possible to define a **cutting point**, and to operationalize the behavioural diagnosis of FTD. The point consists of 27 out of 72 points, which can be gained in FBIInv, and includes all the FTD patients. Only one patient from amongst those with depressive dementia behaviour disorders was observed. Symptoms of depression were confirmed by vegetative symptoms as well as by scores recorded on the Beck Depression Inventory. All DAT patients, and most depressive patients scored below 24 points. Kertesz [14] notes, that the cutting points of FBIInv may enable a grouping of the patients in order to perform a further examination. There are many inventories of behaviour evaluation that aim at screening deviant behaviours in geriatric, psychiatric or dementive patients [15–22]. Geriatric scales frequently combine cognition, behaviour, and everyday activities in order to measure global functional deterioration but they do not discriminate particular behavioural syndromes. Psychiatric behavioural scales also do not discriminate frontal and psychiatric symptoms. A direct evaluation of behaviour of FTD patients takes into account items measuring motor or cognitive perseverations, verbal inclusions, disinhibition, as spontaneity, and utilization behaviours. There were attempts to make the evaluation of symptoms of frontal lobe injuries more formal with the use of executive interviews [23]. Such direct tests often are a part of neurological examination and supplement FBIInv. Logopenia appears at the later stages of FTD, and is sometimes connected with verbal and oral apraxia. Frequent hesitations in speech, prozodic disorders, the leaving out of initial consonants, and stuttering was also noted. Yet the scores of items evaluating those disorders were as a rule lower as they appear at a later stage of the illness in FTD patients. Those symptoms used to be called a Primary Progressive Aphasia (PPA) [24]. At the later phases of PPA personality disorders are quite common [26].

Some modification including new items were introduced to FBIInv with time. The new version consists of a series of 24 items enabling an evaluation of social behaviour disorders as well as motor behaviours and the syndrome of alien hand. The last 5 items apply to behaviours appearing at the

Table 1. Demographic data of examined patients.

Variables	DAT	VAD	FTD	DD	PPA
Age (mean; SD)	69.84±9.7	65.73±8.4	56.41±9.8	56.18±12.3	61.36±6.9
Education* (mean; SD)	2.4±3.2	2.4±3.2	2.1±2.3	2.9±3.8	2.6±3.2
Onset of illness (mean; SD)	4.3±5.8	4.4±5.8	3.4±6.7	6.9±5.3	3.9±5.8
Duration of neurotherapy (mean; SD)	6.4±3.5	8.4±3.5	4.2±1.2	7.8±1.2	8.4±3.5

* Years of education after finishing primary school.

late stage of FTD. They create a lot of anxiety in family members who are reluctant to speak about them. The author believe that the inventory discussed may be of use in the case of PPA if administered along with specific language tests.

The aim of our research was to show the diagnostic value of FBIInv [12–14, in distinguishing FTD from such syndromes as VAD or depression as well as in evaluating the efficacy of neurotherapy.

MATERIAL AND METHOD

The examination included 112 patients, 68 men and 46 women, who were diagnosed and treated at the Reintegrative-Training Centre of the Foundation for Brain Damaged Persons in Kraków, and in Clinic for Developmental Psychiatry, Psychotic Disorders and the Old Age Psychiatry at the Medical University of Gdańsk, suffering from various types of dementia including depression. The demographic characteristics of the patients are presented in Table 1.

The group consisted of 41 patients with Alzheimer dementia including 25 men and 16 women; the mean age was 69.84 (SD 9.7), 14 patients with vascular dementia including 9 men and 5 women; the mean age was 65.73 (SD 8.4), 18 FTD patients including 11 men and 9 women; with a mean age of 56.41 (SD 9.8), 27 DD patients including 16 men and 11 women; mean age 56.18 (SD 12.3), 12 PPA patients including 7 men and 5 women; mean age 61.36 (SD 6.9).

The following tasks were applied:

1. clinical interview,
2. neuropsychological tests [Wechsler Intelligence Scale-Revised – WAIS-R [26]; Wechsler Memory Scale-Revised – WMS-R [27]; Western Aphasia Battery – Revised – WAB-R [28]; Lines Evaluation Test [29], Face Recognition Test [30,31],
3. screening with MMSE to evaluate the depth and progression of dementia and with the Polish version of the Boston Naming Test (BNTvPL) [32] which aimed at discrimination of language and behavioural variants of Frontotemporal Dementia,
4. Frontal Behaviour Inventory (FBIInv) adapted for Polish [9]. The inventory was filled out by the patients caregivers. The final version of the FBIInv consists of questions that include both correct as well as incorrect, negative aspects of behaviour – out of which the carer selects those he thinks describe the patient best. The particular questions can be put in other words if the carer has problems with understanding them. The particular items are grouped into two types of behaviour. They are:

- a. *negative behaviours*, such as apathy, asponaneity, indifference, thinking rigidity, concreteness, personal neglect, distractibility, inattention, loss of insight, logopenia, verbal apraxia, and alien hand syndrome [the last 3 items were included to evaluate the specific motor and linguistic behaviours that might occur in FTD].
- b. *positive behaviours*, connected with disinhibition, such as perseveration, irritability, excessive jocularity, unpredictability, irresponsibility, inappropriateness, impulsivity, restlessness, aggression, hyperorality, hypersexuality, utilization behaviour, and incontinence.

Procedure

The inventory was given to a patient caregiver, and the examiner provided explanations of the meaning of particular questions in the case of such a need.

RESULTS

The scores gained by the examined patients with FTD did not differ in as far as sex is concerned, therefore, further analysis will be conducted for both men and women together in each group.

Evaluation of cognitive functions

The screening of cognitive functions taking into account intellectual abilities, memory, visual functions, language functions, and general features of dementia in individual groups is presented in Table 2.

Intellectual functions

An analysis of WAIS-R scores shows that the lowest global I.Q. was noted in patients with Alzheimer dementia, fvFTD patients, and PPA patients. Therefore, it does not discriminate the examined groups. Yet, it may be observed that the distribution of results in nonverbal I.Q. and verbal I.Q. is different in the groups. Thus, patients with Alzheimer dementia gained significantly lower scores in nonverbal I.Q. when compared with their verbal I.Q. On the other hand, the proportions are reversed in fvFTD and PPA patients as their nonverbal I.Q. is much higher than nonverbal I.Q.

The above is most probably connected with the different profile of disorders in Alzheimer dementia, in which visual-spatial deficits connected with a performance part of WAIS-R are more pronounced, while language disorders dominate in PPA and FTD patients (five patients with

Table 2. Scores of examined patients in individual tests assessing cognitive processes.

Index	Scale	Variables				
		DAT	VAD	fvFTD	DD	PPA
WAIS – R [1]						
I.Q. Full	100	73.5	87.8	79.3	88.35	78.1
I.Q. Verbal	100	79.6	87.2	67.1	89.4	66.8
I.Q. Nonverbal	100	67.5	88.3	91.5	87.3	89.3
WMS – R [2]						
Instant logical memory	24	13.4	15.7	19.1	21.6	16.7
Delayed logical memory	24	3.8	7.4	11.3	16.5	10.4
Instant visual reproduction	41	9.5	15.3	32.6	34.7	30.2
Delayed visual reproduction	41	2.6	6.7	11.9	26.8	21.7
Visual-spatial orientation						
Lines Evaluation Test	30	13.1	19.2	26.7	28.7	26.7
Face Recognition Test	54	13.3	24.5	51.3	52.8	50.3
Language Functions – WAB [3]						
Aphasia Quotient – AQ	100	87.3	92.7	85.1	97.3	64.3
Cortex Quotient – CQ	100	68.6	81.5	89.3	94.5	81.2
General intellectual functions						
MMSE	30	19.0	20.8	19.3	23.9	21.9

[1] WAIS – R Wechsler Adult Intelligence Scale; [2] WMS-R – Wechsler Memory Scale – Revisited; [3] WAB – Western Aphasia Battery.

Semantic Dementia – SD were included in that group, and this might have influenced the results).

Memory

WMS-III test revealed disorders of logical memory in all examined patients, yet the depth of those disorders is different. Most severely impaired were DAT patients, less PPA and VAD patients, and the least DD patients. All of them presented difficulties in performing tasks with delay. It should be noted that DAT patients, as might be expected, exhibit more clear cut impairments in visual memory than other groups. In fact they practically do not accomplish any delay tasks whatsoever. On the other hand, FTD and PPA patients score much worse in auditory memory than in the visual memory. On reproduction with delay they score worse but they are able to remember considerable amounts of information.

Visual-spatial functions

The most pronounced disorders of visual-spatial functions occurred as was expected for DAT patients both in the Benton Test as well as in the Face Recognition Test, the disorders were less pronounced in VAD patients. FTD and PPA patients revealed non-significant disorders, while DD patients stayed within a norm. Those results can be explained due to the observation of patients performance. It can be noticed that FTD and PPA patients tend to abandon the tasks, which

may be the cause of a lower scoring. Visual-spatial dysfunctions may be also connected with deficits in memory selectivity, as the patients spare much less time to individual tasks.

Language functions

Western Aphasia Battery (WAB) showed the occurrence of aphasic disorder in all examined patients with the exception of patients with depression. As expected most pronounced disorders were observed in PPA patients – with Aphasia Quotient =64.3, slightly lower in AD patients – with AQ=87.3, and in FTD patients – with AQ=85.1. The least pronounced disorders were stated in VAD patients – with AQ=92.7. Depressive patients were on the borderline of the norm.

Slightly surprising are the profiles of the cortical quotients as they show the reverse tendency. The worst scores were gained by DAT patients – with a Cortical Quotient =68.6. It was probably due to the fact that Picture recognition scores are included in the CQ, and as we know this is frequently impaired in Alzheimer dementia.

General traits of dementia

Comparison of the scores of the examined groups in the MMSE Test did not reveal statistically significant differences among the examined groups. The lowest mean, however, was gained by patients with DAT, and the lowest patients

Table 3. FBIInv scores of patients with various types of dementia.

Type of dementia	N	Sex		Age		Scores of FBIInv	
		M	K	X	SD	X	SD
AD	41	25	16	69.8	9.7	10.8	7.8
VAD	14	9	5	69.3	8.6	25.1	8.4
FTD	18	11	9	56.8	9.8	38.1	6.7
DD	27	16	11	56.1	12.3	9.1	8.3
PPA	12	7	5	67.5	6.9	15.3	12.5
Total	112	68	46	63.9	9.46	19.68	8.74

Table 4. Frequency of occurrence of individual frontal lobe symptoms in 18 patients with bvFTD.

Symptoms	%	Symptoms	%
Loss of insight	86	Hyperorality	35
Inappropriate remarks	76	Irritability	34
Perseveration	75	Restlessness	34
Logopenia, anomia	75	Puissance	31
Personal neglect	69	Impulsivity	29
Apathy	65	Careless driving*	29
Forgetfulness**	61	Incontinence	26
Inattention, distractibility	59	Aspontaneity	19
Indifference, emotional flatness	57	Excessive touching of objects (compulsiveness)	19
Disorganization, inability to plan	52	Hypersexuality	18
Social withdrawal***	51	Excessive Jocularly (moria)	18
Financial errors	47	Kleptomania	17
Thinking rigidity, concreteness	44	Emotional lability	12
Loss of insight	43	Childish behaviour	11
Verbal mistakes	41	Paranoia	9
Aggression	39	Echolalia	9

* This is not specific as a result of the overlap in symptoms with the loss of impulsivity and the ability to evaluate; ** As a result of the lack of specificity the following have been erased: forgetfulness and wandering off; *** As a result of the overlapping of symptoms with apathy social withdrawal is not specific.

with depression and PPA, which was in agreement with expectations.

Behavioural changes

The FBIInv scores of patients with various types of dementia are presented in Table 3. It may be observed that the highest scores (much above the cutting point) were obtained by FTD patients. The scores of PPA patients were higher than in the control groups, but not as high as in the case of patients with FTD. The scores of VAD patients were similar to the scores of FTD patients. It confirms the observations of other authors that the so called frontal type occurs within VAD – which must be connected with dissociation of the

frontal subcortical structures taking place in VAD [33,34]. It was stated that disinhibition symptoms, which prevail over apathy and withdrawal, are helpful in distinguishing FTD patients from VAD or DD patients [35].

Frequency of the occurrence of individual frontal lobe symptoms in 18 patients with bvFTD, correlated with the data gathered from the structured interview is shown in Table 4. This will enable the reader to better see the spectrum of behaviour disorders that appear in bvFTD patients.

In our study bvFTD patients were given a half-a-year neuropsychotherapy aimed at a reduction of frontal symptoms in accordance with a program elaborated by Pačalska

Table 5. Scores of bvFTD patients in individual traits of FBIInv in I and II examination.

No.	TRAIT	Mean evaluation		▲*
		Exam. 1	Exam. 2	
1	Apathy	2.67	2.13	-20.22%
2	Spontaneity	1.93	2.29	18.81%
3	Indifference, Emotional Flatness	2.85	1.25	-56.14%
4	Inflexibility	1.96	2.35	19.64%
5	Concreteness	1.92	2.36	22.92%
6	Personal neglect	2.11	2.51	19.15%
7	Disorganization	2.26	2.98	31.81%
8	Inattention	2.36	2.91	23.18%
9	Loss of insight	2.63	2.89	9.89%
10	Logopenia	1.74	2.78	59.77%
11	Verbal apraxia	0.53	2.31	335.85%
12	Perseveration	2.95	1.69	-42.85%
13	Irritability	2.49	1.32	-46.99%
14	Excessive Jocularly	0.98	1.98	102.04%
15	Utilization Behaviour	2.43	2.41	-1.03%
16	Inappropriateness	2.56	2.49	-2.81%
17	Impulsivity	2.13	2.89	35.68%
18	Restlessness	1.95	2.67	36.92%
19	Aggression	1.93	2.89	49.74%
20	Hyperorality	1.35	1.76	30.67%
21	Hypersexuality	1.13	0.98	-13.27%
22	Compulsiveness	1.34	0.31	-76.87%
23	Incontinence	0.34	1.86	447.06%
24	Alien hand	0.02	0.23	1050.00%

* The difference between the mean of the CHI group, and the mean of the FTD group divided by the mean FTD group, in percentage.

[36]. The patients behaviour was then evaluated with FBIInv. The results of the study are shown in Table 5, and in Figure 1A, B. It may be observed that rehabilitation resulted in an improvement of some deviant behaviours. Thus, a significant decrease of indifference and emotional flatness as well as of apathy was observed. Yet, some disorders, mainly the behaviours connected with disinhibition did increase along with the progression of the illness despite neurotherapy. Those behaviours such as impulsivity, restlessness, aggressiveness, and excessive jocularity. Behaviours resulting from difficulties in passing from an idea to action as well as apathy also increased. Those were apraxia of speech, concreteness, disorganization, and inattention.

As might have been expected alien hand symptoms as well as incontinence also increased.

Mean scores of patients with bvFTD in I and II examination in the first 12 traits of the inventory, i.e. negative behaviours resulting from difficulty in passing from an idea to action as well as apathy is shown in Figure 1A.

Mean scores of bvFTD patients in I and II examination in the other 12 trait of the inventory, which measure positive behaviours connected with disinhibition are shown in Figure 1B.

To sum up, it is worth pointing out that the above results are in agreement with the results obtained in the studies of other authors that, however, were performed much later than our study [34].

DISCUSSION

In the course of diseases following degeneration of the brain a number of behaviour disorders and other psychopathological symptoms occur, beside the classical cognitive deficits. Such symptoms as psychotic disorders, restlessness, mood disorders, sleep disorders, journeying and many others, which accompany degenerative processes are called behavioural and psychological symptoms [37].

In Table 6, a differential analysis of FTD and DAT was presented on the basis of both our own research [9] and other studies [33,38-43].

It can be noticed that executive functions disorders are more pronounced than memory disorders in Fronto-Temporal Dementia, while the reverse pattern of disorders occurs in Alzheimer Dementia.

It is worth pointing out, however, that the intensity of those symptoms as well as the clinical picture varies in accordance with the degree of degenerative changes [44,45], and with so called cognitive reserve [46]. The behavioural manifestation of the process depends both upon neurobiological factors, such as the localization of changes, as well as the dynamics of the process of dementia [9].

Clear cut differences in behavioural manifestations evaluated with FBIInv were noted in our study. The most pronounced behavioural disruptions were observed in the bvFTD group. Both *negative behaviours* connected with passing from thought to action and apathy as well as *positive behaviours* following disinhibition were noted. The results confirm the usefulness of FBIInv for description and the distinguishing of bvFTD from other types of dementia as well as an evaluation of neurotherapy results.

It should stressed here that classic descriptions of the frontal syndrome pointed to the appearance of a number of early behavioural symptoms before clinical disorders of memory [34].

Behaviours and symptoms most frequent in FTD as observed in our study (Table 3) are in agreement with the typical clinical picture of that disease [47]. The possibility of noting differences and similarities among the examined groups was increased by including groups of patients with a

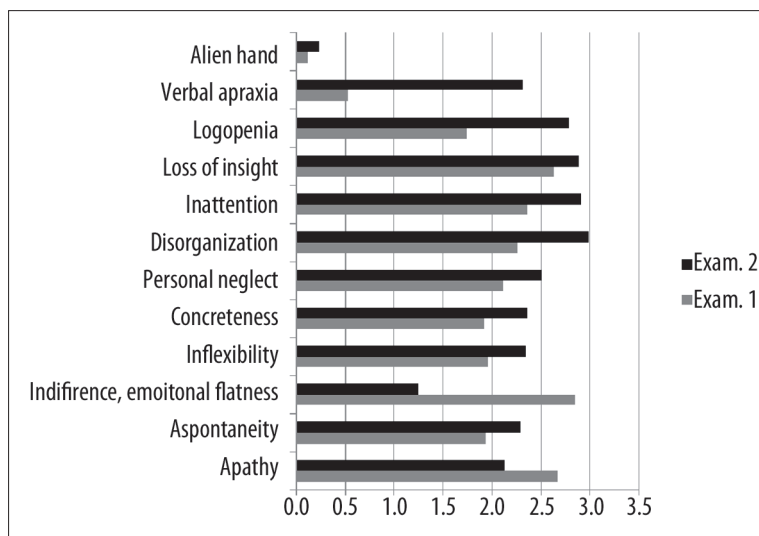


Figure 1A. Mean scores of bvFTD patients (the first 12 traits of the Inventory in I and II examination).

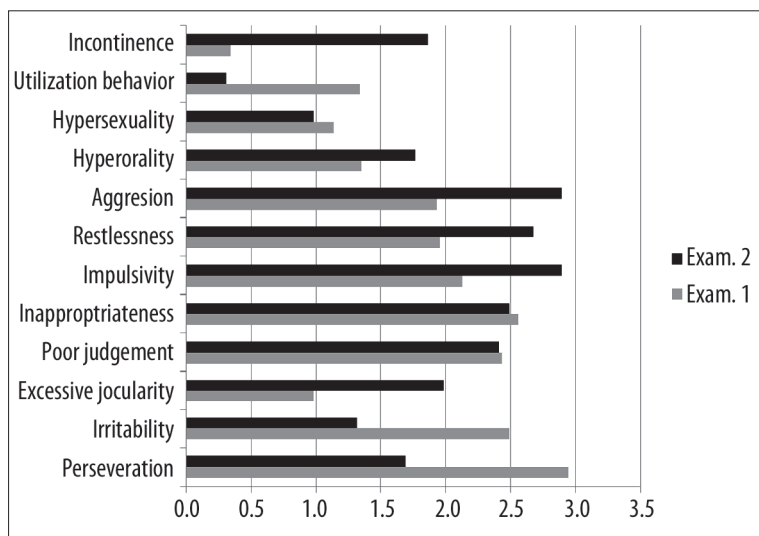


Figure 1B. Mean scores of patients with bvFTD (the other 12 traits of the Inventory in I and II examination).

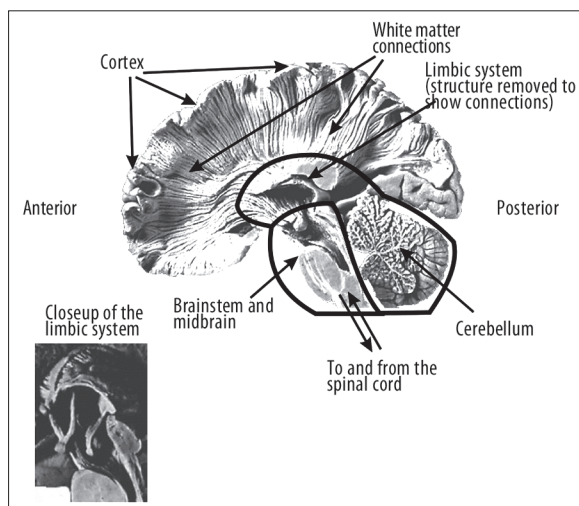


Figure 2. Medial cross-section of the human brain and white matter connections (From: Pachalska and MacQueen [75]).

decrease in cognitive functions following various degenerative processes. Biochemical aspects were taken into account by the inclusion of one group with tauopathy (FTD) and amyloidopathy (Alzheimer disease), forms conditioned by the primary vascular process, and functional disorders of cognitive functions following depression. The neuroanatomic discrimination is reflected in our results.

Since speech disorders are quite frequent in FTD Semantic Dementia as well as Primary Progressive Aphasia treated as a clinical variant of FTD, this is distinguished by some authors alongside with the temporal and frontal form [35]. Such symptoms as: stereotyped utterances, echolalia, perseveration, mutism, semantic aphasia, semantic deficit, and spontaneous speech reduction are considered to belong to the prodromal symptoms of FTD [48].

It seems questionable whether processes at the basis of progressive aphasia and FTD are identical or close to each other. Those nosographic doubts follow from the fact that the level of behavioural disorders registered in FBInV was significantly different in both groups. Thus, a high behavioural

Table 6. Differential analysis of characteristics of Fronto-Temporal Dementia [FTD] and Dementia of Alzheimer Type [DAT]* [Source: Pachalska [9]].

Function	FTD	DAT
Clinical characteristics		
Deficit pattern	Predominance of disorders of executive functions over memory deficits	Predominance of memory deficits over disorders of executive functions
Controlling and monitoring behavior	<i>Behavioral variant (frontal):</i> Hyperorality, disinhibition, inappropriateness and uncontrollable eating. Language abilities are well preserved <i>Linguistic variant:</i> lack of behavior disorders at the initial stage.	Wandering, indifference
Initial symptoms	Disorders of language or personality as well as social behaviors disorders	Memory deficits connected with visual-spatial disorders
Age at the onset of illness	Typically before 65 years of age	80 years on average
Sex of the patient	Men mainly	No sex preference (both men and women fall ill)
Course	Progression to decease 8.7 ± 1.2 years. Years of outlive shorter for frontal variant (behavioural) bvFTD	Progression to decease 11.8 ± 0.7 years
Progression of illness	<i>Early stage:</i> loss of insight, disorders of personality/behaviour or language <i>Late stage:</i> memory loss, decrease of cognitive abilities, possible mutism	<i>Early stage:</i> memory disorders, general decrease of cognitive abilities <i>Late stage:</i> disorders of personality/behaviour, disorders of functional communication
Brain damage	Massive atrophy of frontal lobes and anterior temporal lobes often including limbic structures, hypoperfusion and hypometabolism	Cortical atrophy, mainly of posterior cortex and hippocampus
Memory	Episodic memory and general orientation is preserved; deficit of semantic memory, inability to remember past events	Episodic memory and general orientation is disturbed; semantic memory is preserved at the early stage of illness, ability to remember past events is preserved at the early stage of illness
Language	Depending upon variant subtype: <i>Behavioural variant (frontal):</i> Well preserved linguistic abilities <i>Linguistic variant:</i> Progressive non-fluent aphasia: Errors in content and structure of utterances, possible logopenia Semantic dementia: Wrong meanings of utterances. Difficulties with differentiation of meaning of utterances (connected mainly with the loss of word-image relationships)	Depending upon progression of illness: <i>I (early deterioration) stage:</i> Errors in content of utterances. Difficulties with distinguishing meanings (connected with auditory discrimination and difficulties with recognizing objects). <i>II (mean deterioration) stage:</i> Errors in content and structure of utterances. Difficulties with differentiation of meaning and structure of utterances <i>III (deep deterioration) stage:</i> Errors in content and structure of utterances including phonemic paraphasia
Naming	Symptoms depend upon the subtype of FTD	Paraphrasing. Changing semantics /phonetic indications. Loss of basic concepts.
Writing	Symptoms depend upon the subtype of FTD	Spelling mistakes, coping abilities worse than spontaneous writing

*Information summing up our own studies; Pachalska [9] and studies of other authors: Kertesz and Munoz [33]; Hornberger et al. [34]; Neary et al. [35]; Harciarek and Jodzio [38]; O'Keefe et al. [39]; Barcikowska [40]; Bidzan et al. [41]; Grochmal-Bach et al. [42] Kertesz [43]; Cummings & Bathgate [47]; Rasmuson et al. [51]; Geerlings et al. [57]; Diehl [73]; Cardarelli [79].

manifestation was noted in the case of vascular dementia. Vascular dementia may follow many vascular degenerations of varied localization. It should be also borne in mind that a clinical picture caused by vascular factors varies to a considerable degree, and thus does not fit a classic description of dementia [49].

It is true that diagnostic criteria contrast vascular dementia with primary degenerative diseases of the brain. Yet, the

border line may be not clear, Since vascular factors are present also in primary degenerative processes such as Alzheimer Disease for example. Such vascular changes were observed in about 1/3 of Alzheimer patients [50].

Some of the vascular degenerations (amyloid angiopathy, leukoencephalopathy) are observed in almost all the examined cases of Alzheimer Disease [51]. Those changes increase the impairment of cognitive functions [52].

It is generally accepted that behavioural disorders are more frequent in vascular dementias than in Alzheimer Disease, at least at the early stages of the illness. This concerns mainly disorders of affect [53,54] something that was also confirmed in the present study.

A similar level of deviations was noted in the study of persons with DAT and with depression, which may suggest some connections between those diseases. It might seem surprising if we realize that two different disorders are being compared there: one following the slow degeneration of brain tissue, and the other that passes sometimes even without treatment. Yet, the connection between Alzheimer Disease, or dementia in its broader sense, and depression have much in common.

The more frequent occurrence of mood disorders (particularly of a depressive type) in DAT has already been mentioned. Yet, the present study makes it necessary to point out that depressive disorders are connected with a decrease of cognitive ability, which sometimes remind one of dementia due to their degree [55,56]. Quite often depression appears at the early phases of dementia, even in the preclinical stages. And it masks the development of dementia [57]. Hence, episodes of depression are treated as a significant factor pointing to the possibility of the occurrence of dementia, and of the Alzheimer type in particular [58].

Those complex relations may be, at least in part, explained on a neurobiological basis. The structure which unites those processes is hippocampus. Degenerative changes in Alzheimer Disease start in the hippocampus and olfactory cortex, and then expand to the frontal, temporal, and parietal associative cortex [59]. Moreover, the loss of subcortical neurons in the basal nucleus and bluish nucleus occurs quite often [34,60].

In the case of the relation between Alzheimer Dementia and depression the basic role seems to be played by the damage of the hippocampus, which leads to impairment of the mechanisms of control of the corticosteroids level. In DAT both an increase in the level of basic cortisol, and a lack of decrease of its level after the application of deksametason was observed [61–63].

The damage to the hippocampus causing an increase in the CRH level leads to an excessive activity of the hypothalamic-pituitary-adrenal pivot, which is often observed in depression too. Disruptions of the control of the corticosteroids level in depressions may also be connected with disorders of intellectual functions [64,65]. For our studies it is of importance that a hippocampus lesion occurs at the early or even preclinical stages of DAT [37,66].

Not only biological mechanisms indicating the connection of depression with Alzheimer Disease are taken under consideration. Some studies point to a significant loss of neurons in the bluish nucleus in Alzheimer patients, in whom depression was diagnosed at the same time [67,68]. Forstl et al. [69] noted also a more marked degeneration of neurons in the bluish nucleus in patients with Alzheimer Dementia, in whom depression was stated before the clinical development of dementia.

We should also take into account some other factors, while discussing the possible neurobiological mechanisms of

creating psychological and behavioural symptoms of the diseases examined here. It is worth pointing out that the pathogenesis of psychological and behavioural symptoms is very complex. It is possible that morphological degenerations observed in dementias predestine some behaviours, which, however, are determined by premorbid personality traits as well as environmental factors [70].

Psychological and behavioural symptoms depend also upon the stage of dementia progression. Hence, aggressive behaviours appear more often in periods preceding faster progression [71,72]. At this present stage of the analysis of the results an evaluation of the process dynamics was not performed.

Better knowledge of the psychological picture, and of behavioural symptoms in particular is of great practical value. It should be borne in mind that dementive processes are preceded by an signalling period, during which behaviour disorders may dominate over cognitive disorders, which at that time are difficult to distinguish during a clinical examination. Especially in the case of FTD, the symptoms of dementia may be neglected for a long time [34,73]. In consequence, such persons are often given the wrong diagnosis, which often results in a delay of proper treatment.

How can this be explained?

Naturally, the limbic structures, which play an essential role in basic drives and their affective correlates, may not be damaged at the early stage of FTD. The lesions may be noted after cutting of the ways leading from the frontal lobes to the limbic system or if that system is destroyed as a consequence of neurodegenerative changes.

Ablation of the frontal part of the temporal lobe connected with the bilateral ablation of the amygdalia body in animals is followed by dramatic changes in sexual and aggressive behaviours [30]. Klüver-Bucy syndrome, including hypersexuality, lack of fear reaction and visual agnosia, show how dramatic the results of lesions of the limbic structures for emotional-motivational functions can be. FTD patients often exhibit Klüver-Bucy Syndrome. They exhibit various deviant social behaviors, such as disinhibition, verbal or physical aggression, and executive functions disorders connected with apathy [36]. Lesions leading to the above mentioned pathological behaviours are difficult to grasp. Dysfunctions observed in those patients remind one of the behaviours of animals with lesions disrupting the activity of the limbic system. Microgenetic theory of a symptom [74] developed on the basis of an evolutionary, four-dimensional model of brain work [75] may be of help in understanding those disorders. Damage to the limbic system or of one of its connections with other brain structure including the frontal lobes (Figure 2) disrupts the normal activity of the brain, and due to that basic limbic-cortical dysfunction many patients with dementia exhibit difficulties with “adult” or “civilized” behaviours [36,75].

Behaviour disorders are often the first symptom of an illness, which may enable putting an early by a well trained evaluator [36]. The microgenetic model of brain work makes us aware that in Fronto-Temporal Dementia the whole of the brain systems become disrupted and not only specific cognitive functions as in the case of local brain injuries. The

function of those systems are at first disorganized only in part, but then undergo global disruption, after the destabilization reaches a level, which causes a loss of integrity. It needs to be stressed that even in the case of the linguistic variant of FTD (lvFTD), neither the course nor the nature of the disorders observed, speech and language disorders, recalls aphasia [9,76,77]. There is a difference in reaction of the dynamic system that receives one strong and localized blow as is the case in a brain stroke; and of the system, which loses its energy and undergoes entropy as in the case of dementia. In such case the changes are vertical: the upper levels of complex brain processes lose energy, become disorganized, and finally disintegrate, in contradistinction to the "horizontal" effects of focal lesions, when one part of the system is damaged, and others remain untouched.

As cortical dementia traits grow, which occurs both in Alzheimer disease as well as in FTD, the process of neurodegeneration runs counter to microgenesis, that is: from the upper areas to the lower (deeper) areas of the brain. The deeper the neurodegenerative changes in the brain are, the less specific will be the symptoms. And after the illness assaults the lowest level (brain stem and midbrain), basic life functions will also undergo entropy: will lose energy and disintegrate, which results in decease. Therefore, at the final stage of any neurodegenerative dementive disease differences in the clinical picture, which might be clear at the very beginning, become difficult to distinguish [78,79]. In other words, each dementia:

1. starts with an upset of one's own identity, due to the arising disturbances,
2. runs in a way specific for the basic pathomechanism of a given type of dementia,
3. with time its specific traits are lost and each ends in a similar way.

CONCLUSIONS

To sum up, it should be stressed that the scores of the present study enable differentiation due to the specific behavioural profiles of the various dementive syndromes and are of significance for the course of therapy. At the same time they enable evaluation of the efficacy of neurotherapy, and hence they make possible a raising in the quality of life of persons with various types of dementia.

The results obtained in the present study confirmed the diagnostic value of FBIInv in the differential diagnosis of various types of FTD and in the evaluation of neurotherapy efficacy.

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