LEWY-TESTES ÉS FRONTOTEMPORALIS NEUROKOGNITÍV ZAVAR

ZÁDORI DÉNES

SZTE ÁOK SZAKK NEUROLÓGIAI KLINIKA

SZTE-SZAB 221. NEUROLÓGIAI KEREKASZTALA

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NEUROKOGNITÍV ZAVAROK CSOPORTOSÍTÁSA (DSM-V)

Delírium

Enyhe (≈MCI)

Major (≈dementia)

Neurokognitív zavar
(a kórkép meghatározó jellegzetessége)

A. Mérsékelt Kifejezett
hanyatlás 1 v. több kognitív doménben

B. Nem zavarja Zavarja
az önellátást a mindennapi tevékenységek során

C. A kognitív zavar nem kizárólag deliriumhoz köthető

D. A kognitív deficit nem magyarázható jobban egyéb mentális zavarral (pl. depressio, schizophrenia)

Dementia (DSM-IV): memóriazavar és további 1 v. több kognitív domén funkciózavara

KOGNITÍV ZAVAROK LEGGYAKORIBB KEZELHETŐ ÉS NEM KEZELHETŐ OKAI

Tünetileg vagy okilag többnyire jól kezelhető kórképek

- gyulladásos/autoimmun (pl. sclerosis multiplex)
- nutricionális (pl. B1 vagy B12 vitamin hiány)
- metabolikus/endokrin (pl. hepaticus encephalopathia, hypo-/hyperthyreosis)
- hydrocephalus

Mérsékelten effektív/ ineffektív tüneti terápia

- Alzheimer-kór (~70%)
- vascularis neurokognitív zavar (~20%)
- Lewy testes vagy Parkinson-kórhoz társuló neurokognitív zavar (~5%)
- Frontotemporalis neurokognitív zavar (1%)
- Prion betegséghez társuló neurokognitív zavar (0,01%)

NEUROKOGNITÍV ZAVAR KIVIZSGÁLÁSÁNAK DIAGNOSZTIKAI SORRENDISÉGE

1. Labor
2. koponya képalkotó (MR: 3D T1, FLAIR CUBE, COR T1 a hippocampus síkjára merőlegesen, SWAN, DWI)
3. Neuropszichológiai vizsgálat
4. Lumbalpunctio
5. EEG

(6. Biopsia)

7. Genetikai vizsgálat

LEWY TESTES NEUROKOGNITÍV ZAVAR DIAGNOSZTIKÁJA

Table 1 Revised[1,2] criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.

Core clinical features (*The first 3 typically occur early and may persist throughout the course.*)

Fluctuating cognition with pronounced variations in attention and alertness.
Recurrent visual hallucinations that are typically well formed and detailed.
REM sleep behavior disorder, *which may precede cognitive decline*.
One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.

Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.

Indicative biomarkers

Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET.
Abnormal (low uptake) ^{123}iodine-MIBG myocardial scintigraphy.
Polysomnographic confirmation of REM sleep without atonia.

Supportive biomarkers

Relative preservation of medial temporal lobe structures on CT/MRI scan.
Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging.
Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

Probable DLB can be diagnosed if:

a. Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers, or

b. Only one core clinical feature is present, but with one or more indicative biomarkers.

Probable DLB should not be diagnosed on the basis of biomarkers alone.

Possible DLB can be diagnosed if:

a. Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or

b. One or more indicative biomarkers is present but there are no core clinical features.

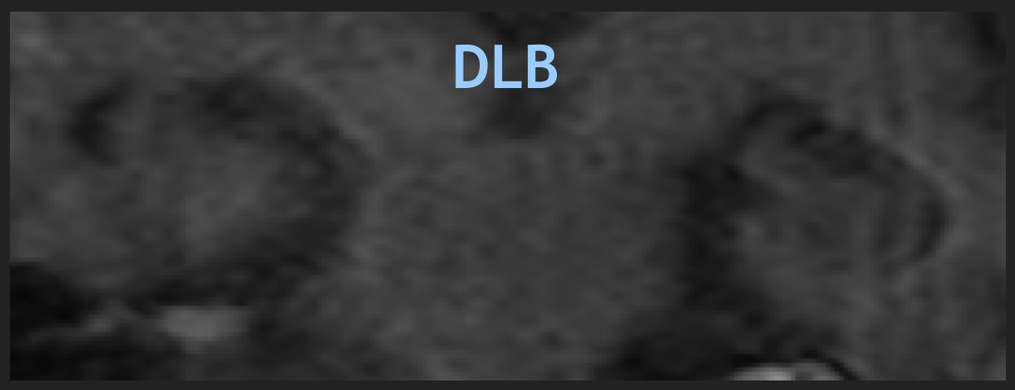
DLB is less likely:

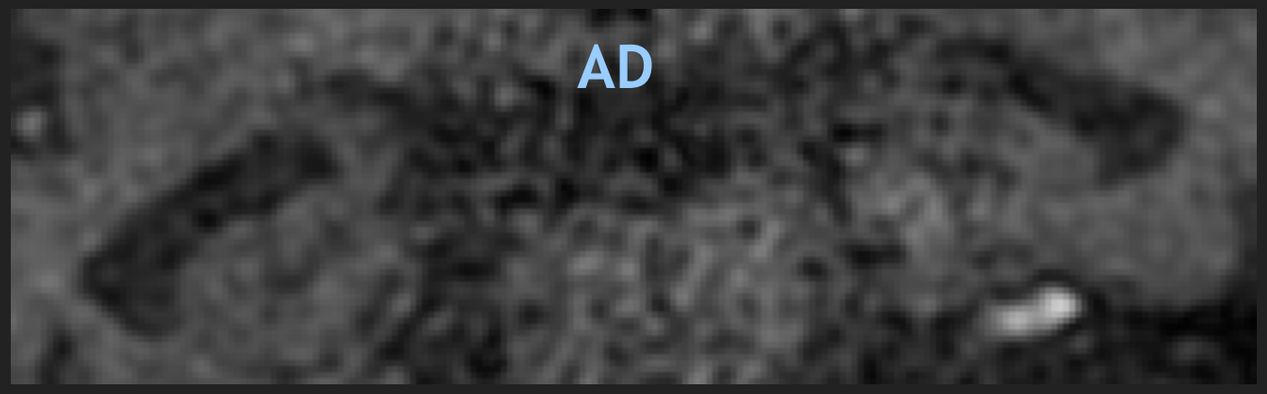
a. In the presence of any other physical illness or brain disorder including cerebrovascular disease, sufficient to account in part or in total for the clinical picture, although these do not exclude a DLB diagnosis and may serve to indicate mixed or multiple pathologies contributing to the clinical presentation, or

b. If parkinsonian features are the only core clinical feature and appear for the first time at a stage of severe dementia.

DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism. The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as Lewy body disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism continues to be recommended.

McKeith et al., Neurology, 2017





PARKINSON-KÓRHOZ TÁRSULÓ DEMENCIA

TABLE 1. *Features of dementia associated with Parkinson's disease*

I. Core features

1. Diagnosis of Parkinson's disease according to Queen Square Brain Bank criteria
2. A dementia syndrome with insidious onset and slow progression, developing within the context of established Parkinson's disease and diagnosed by history, clinical, and mental examination, defined as:
   - Impairment in more than one cognitive domain
   - Representing a decline from premorbid level
   - Deficits severe enough to impair daily life (social, occupational, or personal care), independent of the impairment ascribable to motor or autonomic symptoms

II. Associated clinical features

1. Cognitive features:
   - Attention: Impaired. Impairment in spontaneous and focused attention, poor performance in attentional tasks; performance may fluctuate during the day and from day to day
   - Executive functions: Impaired. Impairment in tasks requiring initiation, planning, concept formation, rule finding, set shifting or set maintenance; impaired mental speed (bradyphrenia)
   - Visuo-spatial functions: Impaired. Impairment in tasks requiring visual-spatial orientation, perception, or construction
   - Memory: Impaired. Impairment in free recall of recent events or in tasks requiring learning new material, memory usually improves with cueing, recognition is usually better than free recall
   - Language: Core functions largely preserved. Word finding difficulties and impaired comprehension of complex sentences may be present
2. Behavioral features:
   - Apathy: decreased spontaneity; loss of motivation, interest, and effortful behavior
   - Changes in personality and mood including depressive features and anxiety
   - Hallucinations: mostly visual, usually complex, formed visions of people, animals or objects
   - Delusions: usually paranoid, such as infidelity, or phantom boarder (unwelcome guests living in the home) delusions
   - Excessive daytime sleepiness

III. Features which do not exclude PD-D, but make the diagnosis uncertain

- Co-existence of any other abnormality which may by itself cause cognitive impairment, but judged not to be the cause of dementia, e.g. presence of relevant vascular disease in imaging
- Time interval between the development of motor and cognitive symptoms not known

IV. Features suggesting other conditions or diseases as cause of mental impairment, which, when present make it impossible to reliably diagnose PD-D

- Cognitive and behavioral symptoms appearing solely in the context of other conditions such as:

  Acute confusion due to
  a. Systemic diseases or abnormalities
  b. Drug intoxication

  Major Depression according to DSM IV
- Features compatible with "Probable Vascular dementia" criteria according to NINDS-AIREN (dementia in the context of cerebrovascular disease as indicated by focal signs in neurological exam such as hemiparesis, sensory deficits, and evidence of relevant cerebrovascular disease by brain imaging AND a relationship between the two as indicated by the presence of one or more of the following: onset of dementia within 3 months after a recognized stroke, abrupt deterioration in cognitive functions, and fluctuating, stepwise progression of cognitive deficits)

Emre et al., Mov Disord, 2007

KOGNITÍV ELTÉRÉSEK - PARKINSON-KÓR VS. LEWY TESTES NEUROKOGNITÍV ZAVAR

Parkinson-kór	Lewy testes neurokognitív zavar
a betegség kezdetén az exekutív funkciózavar (tervezés, téri-vizuális munkamemória) és a figyelemváltás nehézsége dominál	a posterior corticalis deficit már a betegség elején is kifejezett lehet (semanticus fluencia csökkenése, visuospatialis funkciók romlása)
fluktuáló kogníció, melyet a gyógyszerelés is befolyásolhat	
az azonnali és a késleltetett felidézés zavarával jellemezhető memóriazavar, melyet az irányadó segítségnyújtás javíthat	

Goldman et al., Mov Disord, 2014

GENETIKAI VIZSGÁLATOK LEWY TESTES NEUROKOGNITÍV ZAVARBAN

Table 1 Representative examples of genetic studies conducted in sporadic DLB

Study type	Gene(s) or variant analysed	Ethnicity, population	Cases	Controls	Clinically or pathologically diagnosed DLB	DLB diagnostic criteria	Main finding	Ref.
Candidate gene	*C9orf72*	Caucasian—North American	111 DLB*	0	All with pathological diagnosis—86 neocortical, 25 transitional. 66% met pathological criteria for AD	2005	No expansions > 30 repeats found	[17]
Candidate gene	*C9orf72*	Caucasian—UK	102 DLB	0	All with clinical diagnosis—probable DLB	2005	2 clinical DLB with > 30 repeats	[18]
Candidate gene	*C9orf72*	Caucasian—European, American, Australian	1524 DLB***	0	1398 pathologically, 126 clinically diagnosed	2005	*C9orf72* repeat expansions not common in pathologically diagnosed DLB	[19]
Candidate gene	*ADORA1* sequencing	Caucasian—North American	111 DLB* and 1214 PD cases	4911	All DLB pathologically diagnosed—86 neocortical, 25 transitional	2005	*ADORA1* variants not common in PD or DLB	[20]
Candidate gene	Exon 24 of *DNAJC13*	Caucasian—US, European	1938 PD, 828 LBD	0	1938 clinical PD, 828 pathologically diagnosed LBD	2005	Did not find p.Asn855Ser in any cases	[21]
Candidate gene	*TREM2* p.Arg47His	Caucasian—American	1271 total LBD	1154	442 clinical DLB cases, 829 pathologically diagnosed LBD cases: high (349), intermediate (254), and low clinical DLB likelihood (226)	2005	p.Arg47His not associated with DLB	[22]
Candidate gene	*RAB39B* sequencing	Caucasian—American	884 PD, 399 DLB and 379 LBD**	0	Clinical DLB, pathologically diagnosed LBD	Unclear, 2005 (?)	No coding variants found	[23]
Candidate gene	*MAPT* haplotype genotyping	Caucasian—American	731 DLB**	1049	431 clinically diagnosed, 347 pathologically diagnosed (high-likelihood)	Clinical 2005 1996, pathological - 2005	*MAPT* H1G haplotype suggested to be associated with DLB	[24]
Candidate gene	*MAPT* p.Ala152Thr	Caucasian —American, European	3229 PD, 442 DLB, 181 MSA and 832 LBD**	2456	All clinical DLB	2005	p.Ala152Thr suggested to be associated with DLB and LBD	[25]
Candidate gene	Certain *LRRK2* variants	Caucasian—American	725 total DLB**	1790	417 clinical DLB (384 probable DLB, 33 possible DLB), 355 pathologically diagnosed high likelihood DLB. (47 cases in both)	2005	No significantly associated *LRRK2* variants with DLB	[26]
Candidate genes (multiple)	*GBA, LRRK2, MAPT, APOE, APP, PSEN1, PSEN2, SCARB2* and *SNCA*	Caucasian—North American	111 DLB*	222 neuro normal	All pathologically diagnosed—86 neocortical, 25 transitional 69% also met pathological criteria for AD	2005	Several variants identified	[27]
Candidate genes (multiple)	PD and AD loci	Caucasian—European, American, Australian	788 DLB***	2624	667 pathologically diagnosed	2005	*SNCA, APOE* significantly associated with DLB, whilst. *SCARB2* showed	[28]
GWAS	Genome-wide genotyping	Caucasian—European, North American, Australian	1743 DLB***	4454	1324 pathologically diagnosed, intermediate to high likelihood of DLB	2005	*SNCA, APOE, GBA* were genome-wide significantly associated with DLB	[16••]

Genetic studies in DLB are limited compared to Alzheimer's and Parkinson's disease. Furthermore, most genetic studies in DLB are focused on one or more candidate genes, highlighting the need for an unbiased, genome or exome-wide view of DLB genetics. Where possible to ascertain, DLB patients that are included in multiple studies are denoted by *, **, or ***. Some DLB patients may have a family history of disease; however, the majority of analysis focused on sporadic patients and not DLB families. Genetic studies in families with DLB phenotypes have previously been reviewed [85]. Studies solely investigating *APOE* and *GBA* are not included in the table but are discussed in the main text. A mixture of clinical and pathologically diagnosed DLB patients are common in genetic studies. Some studies combine PD, PDD and DLB, or PDD and DLB patients into one study group, which negates identification of DLB specific variants

Ref reference, *GWAS* genome-wide association study, *PD* Parkinson's disease, *AD* Alzheimer's disease, *DLB* dementia with Lewy bodies, *LBD* Lewy body disease, *PDD* Parkinson's disease dementia, *FTD/ALS* frontotemporal dementia/amyotrophic lateral sclerosis, *CJD* Creutzfeldt Jakob disease, *MSA* multiple system atrophy, *CNV* copy number variation

bizonyított összefüggés:

SNCA, GBA, APOE

Orme et al.

LEWY TESTES NEUROKOGNITÍV ZAVAR KEZELÉSE

rivastigmin (PK - A szintű evidencia; LTNKZ - GCP), memantin (B szintű evidencia)

Sorbi et al., Eur J Neurol, 2012

FRONTOTEMPORALIS NEUROKOGNITÍV ZAVAR DIAGNOSZTIKÁJA I.

Table 3 International consensus criteria for behavioural variant FTD (FTDC)

I. Neurodegenerative disease

The following symptom must be present to meet criteria for bvFTD

A. Shows progressive deterioration of behaviour and/or cognition by observation or history (as provided by a knowledgeable informant).

II. Possible bvFTD

Three of the following behavioural/cognitive symptoms (A–F) must be present to meet criteria. Ascertainment requires that symptoms be persistent or recurrent, rather than single or rare events.

A. Early* behavioural disinhibition [one of the following symptoms (A.1–A.3) must be present]:
   - A.1. Socially inappropriate behaviour
   - A.2. Loss of manners or decorum
   - A.3. Impulsive, rash or careless actions

B. Early apathy or inertia [one of the following symptoms (B.1–B.2) must be present]:
   - B.1. Apathy
   - B.2. Inertia

C. Early loss of sympathy or empathy [one of the following symptoms (C.1–C.2) must be present]:
   - C.1. Diminished response to other people's needs and feelings
   - C.2. Diminished social interest, interrelatedness or personal warmth

D. Early perseverative, stereotyped or compulsive/ritualistic behaviour [one of the following symptoms (D.1–D.3) must be present]:
   - D.1. Simple repetitive movements
   - D.2. Complex, compulsive or ritualistic behaviours
   - D.3. Stereotypy of speech

E. Hyperorality and dietary changes [one of the following symptoms (E.1–E.3) must be present]:
   - E.1. Altered food preferences
   - E.2. Binge eating, increased consumption of alcohol or cigarettes
   - E.3. Oral exploration or consumption of inedible objects

F. Neuropsychological profile: executive/generation deficits with relative sparing of memory and visuospatial functions [all of the following symptoms (F.1–F.3) must be present]:
   - F.1. Deficits in executive tasks
   - F.2. Relative sparing of episodic memory
   - F.3. Relative sparing of visuospatial skills

III. Probable bvFTD

All of the following symptoms (A–C) must be present to meet criteria.

A. Meets criteria for possible bvFTD

B. Exhibits significant functional decline (by caregiver report or as evidenced by Clinical Dementia Rating Scale or Functional Activities Questionnaire scores)

C. Imaging results consistent with bvFTD [one of the following (C.1–C.2) must be present]:
   - C.1. Frontal and/or anterior temporal atrophy on MRI or CT
   - C.2. Frontal and/or anterior temporal hypoperfusion or hypometabolism on PET or SPECT

IV. Behavioural variant FTD with definite FTLD Pathology

Criterion A and either criterion B or C must be present to meet criteria.

A. Meets criteria for possible or probable bvFTD

B. Histopathological evidence of FTLD on biopsy or at post-mortem

C. Presence of a known pathogenic mutation

V. Exclusionary criteria for bvFTD

Criteria A and B must be answered negatively for any bvFTD diagnosis. Criterion C can be positive for possible bvFTD but must be negative for probable bvFTD.

A. Pattern of deficits is better accounted for by other non-degenerative nervous system or medical disorders

B. Behavioural disturbance is better accounted for by a psychiatric diagnosis

C. Biomarkers strongly indicative of Alzheimer's disease or other neurodegenerative process

*As a general guideline 'early' refers to symptom presentation within the first 3 years (for further discussion see Supplementary material, Appendix 1).
bvFTD = behavioural variant FTD.

Viselkedési variáns

Rascovsky et al., Brain, 2011

FRONTOTEMPORALIS NEUROKOGNITÍV ZAVAR DIAGNOSZTIKÁJA II.

Primer progresszív aphasia

Table 2 Diagnostic features for the nonfluent/agrammatic variant PPA

I. Clinical diagnosis of nonfluent/agrammatic variant PPA
At least one of the following core features must be present:
1. Agrammatism in language production
2. Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)
At least 2 of 3 of the following other features must be present:
1. Impaired comprehension of syntactically complex sentences
2. Spared single-word comprehension
3. Spared object knowledge
II. Imaging-supported nonfluent/agrammatic variant diagnosis
Both of the following criteria must be present:
1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Imaging must show one or more of the following results:
a. Predominant left posterior fronto-insular atrophy on MRI or
b. Predominant left posterior fronto-insular hypoperfusion or hypometabolism on SPECT or PET
III. Nonfluent/agrammatic variant PPA with definite pathology
Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia.

Table 3 Diagnostic criteria for the semantic variant PPA

I. Clinical diagnosis of semantic variant PPA
Both of the following core features must be present:
1. Impaired confrontation naming
2. Impaired single-word comprehension
At least 3 of the following other diagnostic features must be present:
1. Impaired object knowledge, particularly for low-frequency or low-familiarity items
2. Surface dyslexia or dysgraphia
3. Spared repetition
4. Spared speech production (grammar and motor speech)
II. Imaging-supported semantic variant PPA diagnosis
Both of the following criteria must be present:
1. Clinical diagnosis of semantic variant PPA
2. Imaging must show one or more of the following results:
a. Predominant anterior temporal lobe atrophy
b. Predominant anterior temporal hypoperfusion or hypometabolism on SPECT or PET
III. Semantic variant PPA with definite pathology
Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
1. Clinical diagnosis of semantic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia.

Table 4 Diagnostic criteria for logopenic variant PPA

I. Clinical diagnosis of logopenic variant PPA
Both of the following core features must be present:
1. Impaired single-word retrieval in spontaneous speech and naming
2. Impaired repetition of sentences and phrases
At least 3 of the following other features must be present:
1. Speech (phonologic) errors in spontaneous speech and naming
2. Spared single-word comprehension and object knowledge
3. Spared motor speech
4. Absence of frank agrammatism
II. Imaging-supported logopenic variant diagnosis
Both criteria must be present:
1. Clinical diagnosis of logopenic variant PPA
2. Imaging must show at least one of the following results:
a. Predominant left posterior perisylvian or parietal atrophy on MRI
b. Predominant left posterior perisylvian or parietal hypoperfusion or hypometabolism on SPECT or PET
III. Logopenic variant PPA with definite pathology
Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
1. Clinical diagnosis of logopenic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g. AD, FTLD-tau, FTLD-TDP, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia.

Gorno-Tempini et al., Neurology, 2011

FRONTOTEMPORALIS NEUROKOGNITÍV ZAVAR DIAGNOSZTIKÁJA III.

TABLE 5-3 **Diagnostic Criteria for Nonfluent Agrammatic Variant Primary Progressive Aphasia[a]**

One of the following core features must be present

1. Agrammatism in language production
2. Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)

Two of the following three ancillary features must be present

1. Impaired comprehension of syntactically complex (noncanonical) sentences
2. Spared single-word comprehension
3. Spared object knowledge

[a] Modified with permission from Gorno-Tempini ML, et al, Neurology.[20] *www.neurology.org/content/76/11/1006.full*. © 2011 American Academy of Neurology.

TABLE 5-2 **Diagnostic Criteria for Semantic Variant Primary Progressive Aphasia[a]**

Both of the following core features must be present

1. Impaired object naming
2. Impaired single-word comprehension

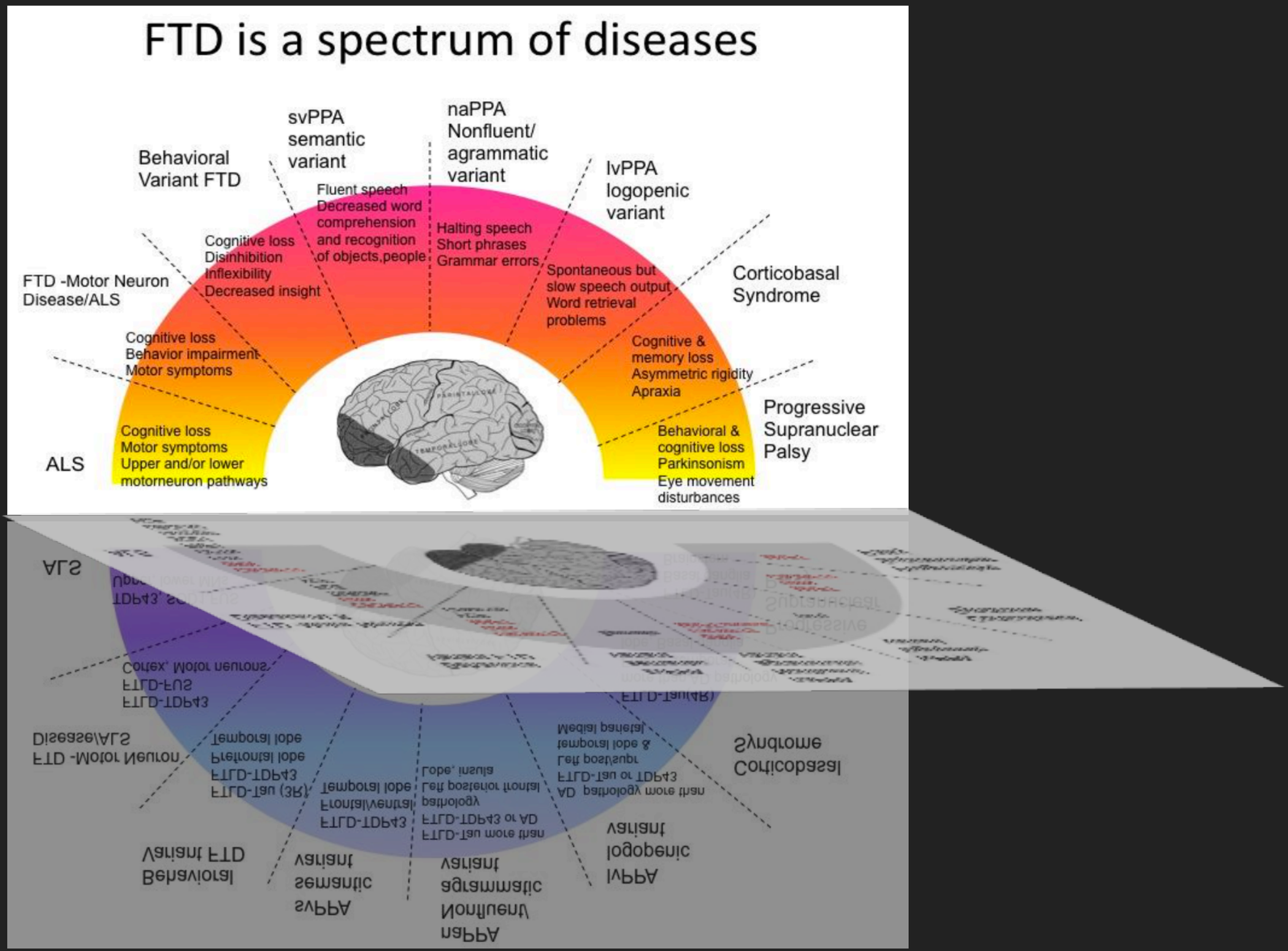
Three of the following ancillary features must be present

1. Impaired object knowledge, particularly for low-frequency or low-familiarity items
2. Surface dyslexia or dysgraphia
3. Spared repetition
4. Spared grammaticality and motor aspects of speech

[a] Modified with permission from Gorno-Tempini ML, et al, Neurology.[20] *www.neurology.org/content/76/11/1006.full*. © 2011 American Academy of Neurology.

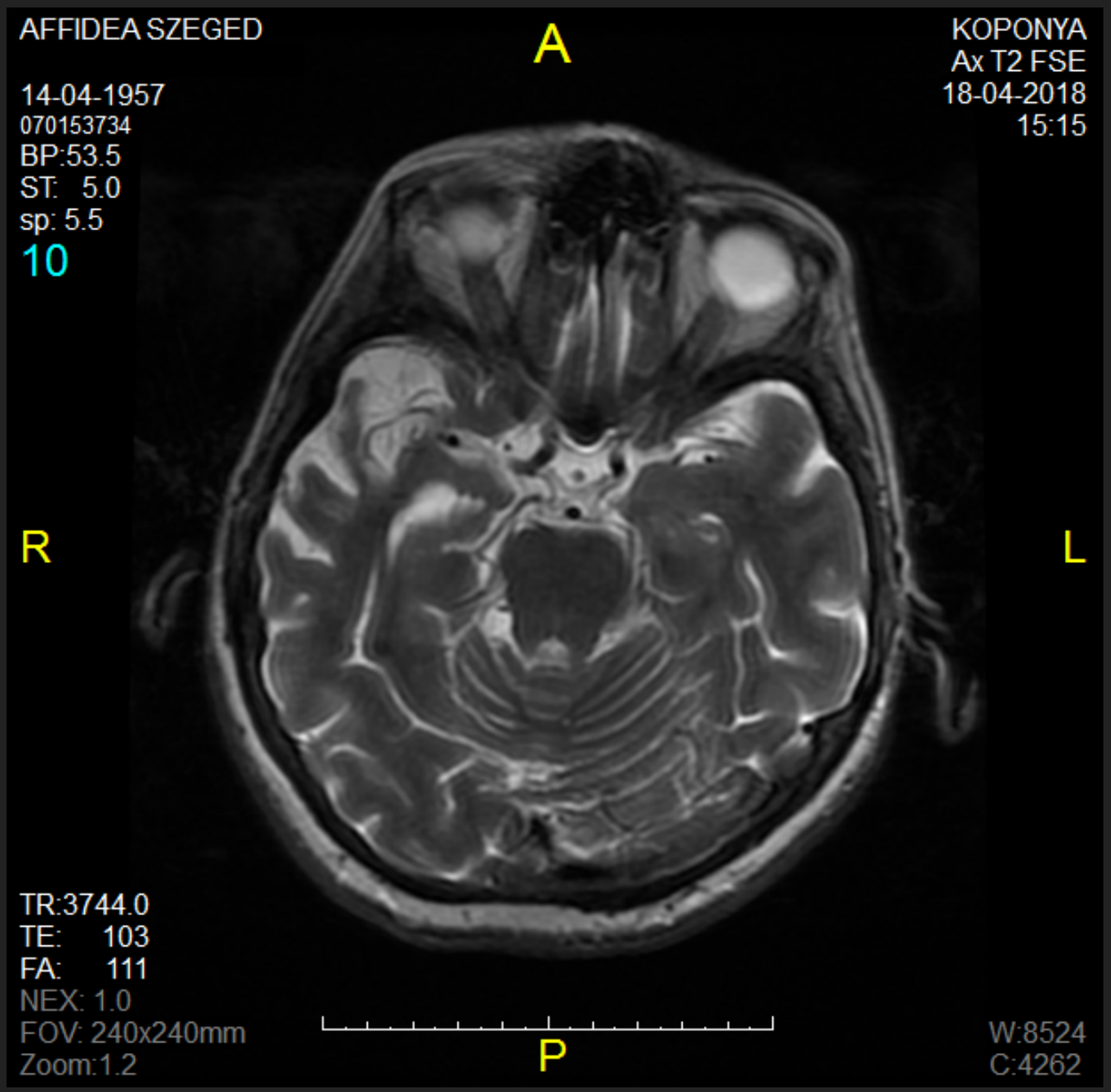
Finger, Continuum, 2016

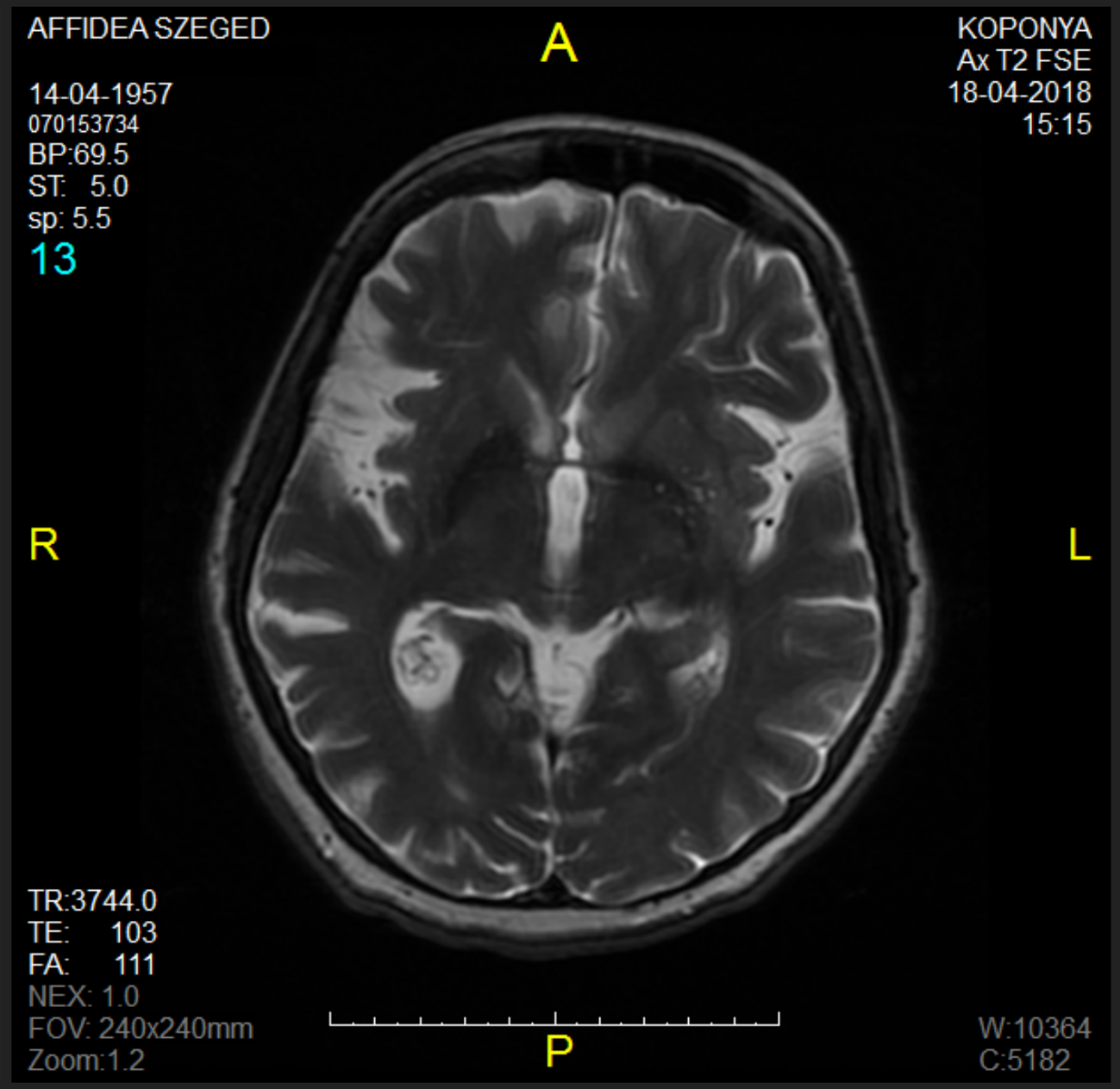
4R TAUOPATHIÁK KLINIKAI ÉS PATHOLÓGIAI SPEKTRUMA



https://www.theaftd.org/

MR ELTÉRÉSEK ÉS KEZELÉS FRONTOTEMPORALIS NEUROKOGNITÍV ZAVARBAN





GENETIKAI VIZSGÁLATOK FRONTOTEMPORALIS NEUROKOGNITÍV ZAVARBAN

Table 1 Genotype-phenotype correlation in frontotemporal dementia

Gene	Prevalence	Onset	Phenotype	MRI
MAPT	Familial 10–20% Sporadic 0–3%	Mean 55 Range 46–65	Predominant frontotemporal dementia + -parkinsonism	Frontal and temporal atrophy Symmetric
GRN	Familial 5–20% Sporadic 1–5%	Mean 65 Range 35–89	Behavioural most common, apathy, withdrawal	More widespread frontal, temporal atrophy with characteristic parietal atrophy Asymmetric
C9ORF72	25%	Mean 50 Range 27–83	Behavioural + - ALS	Frontal atrophy, less temporal involvement Symmetric
TARDNA	<20 cases described	29–77	Behavioural	
FUS FTLD-U Intermediate filament inclusion Basophilic inclusion body disease	Very rare	30 40–50 Early onset	bvFTD, Rapidly progressive bvftd + pyramidal/extrapyramidal ALS	Frontal, temporal atrophy Asymetric frontal and temporal atrophy
VCP	1.6%	Mean 40 Range 40–60	Musculoskeletal symptoms in 80% Paget's disease 45% FTD 38%	Wide spectrum No atrophy
CHMP2B	Very rare	Mean 55 Range 46–65	Behavioural	
TBK1	1.1% in Belgians	Mean 63.3% Range 56–70	Behavioural, Extrapyramidal Psychiatric	

Olszewska et al., Curr Neurol Neurosci Rep, 2016

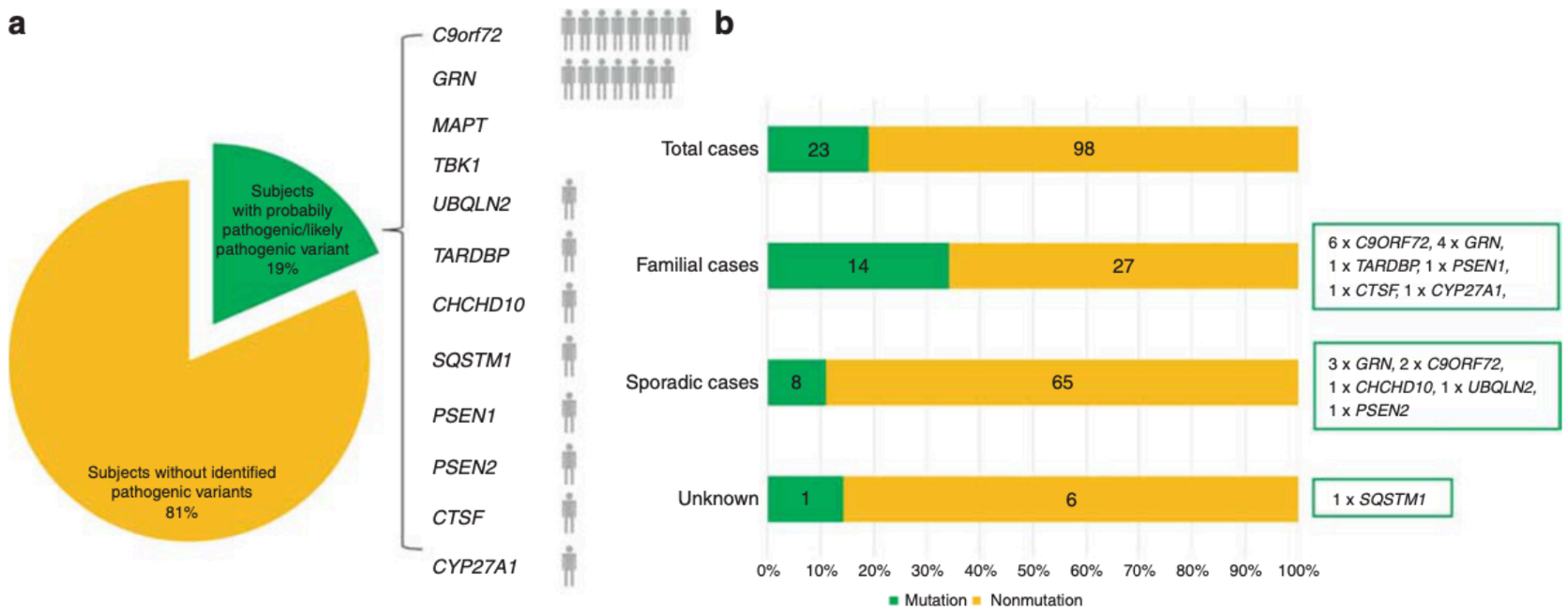


Figure 1 Relative frequencies of mutations in neurodegenerative disease (NDD) genes in a consecutive series of 121 subjects with clinical frontotemporal dementia (FTD). Twenty-three subjects carried mutations, which were distributed across common FTD genes (*C9orf72* repeat expansion, *GRN*, but surprisingly not *MAPT* or *TBK1*), less common FTD genes (*CHCHD10*, *SQSTM1*, *TARDBP*, *UBQLN2*), and also NDD genes not commonly linked to FTD (*PSEN1*, *PSEN2*, *CTSF*, *CYP27A1*) (**a**). Mutations were found not only in 34% of familial subjects, but also in 11% of sporadic subjects (**b**).

A FRONTOTEMPORALIS NEUROKOGNITÍV ZAVAR KEZELÉSE

TABLE 5-7 Treatment Approaches for Behavioral Symptoms in Frontotemporal Dementia[a]

bvFTD Symptom	Current Treatment Options	Evidence for Current Treatments	Possible Future Treatment Options
Apathy	None	NA	Dopaminergic medications
Behavioral disinhibition	SSRIs: fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram	Open-label studies supporting use of SSRIs[68–70]	
	Trazodone	Double-blind, placebo-controlled study supporting the use of trazodone[71]	
	Atypical antipsychotics: risperidone, aripiprazole, olanzapine, quetiapine	Case reports supporting use of antipsychotics[70,72,73]	
Loss of empathy	None	NA	Oxytocin
Perseverative behavior	SSRIs: fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram	Open-label studies supporting use of SSRIs[68,74,75]	
	Trazodone	Double-blind, placebo-controlled study supporting the use of trazodone[71]	
Hyperorality	SSRIs: fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram	Open-label studies supporting use of SSRIs[68,70,75]	
	Trazodone	Double-blind, placebo-controlled study supporting the use of trazodone[71]	
Executive dysfunction	None	NA	Dopaminergic medications
Neuroprotective	None	NA	Medications that prevent tau hyperphosphorylation and accumulation
			Medications that increase progranulin levels
			Medications that reduce *C9ORF72* expanded repeat dipeptide production

Finger, Continuum, 2016

bvFTD = behavioral variant of frontotemporal dementia; NA = not available; SSRIs = selective serotonin reuptake inhibitors.

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Dementia
Alzheimer's Disease
Lewy Body
Mixed Picture
Frontal Temporal
Vascular
Drug Related
Parkinson's Related
Alcohol Related
Other
Genetic Condition
MS Related
Disease Related
Infections
Aspen Senior Care