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DEMENTIA

DEMENTIA - INTRODUCTION

- De (without) - Mens (sense)

DEMENTIA - INTRODUCTION

- silent epidemic of the 21. century
- illness of the whole family – objectiv anamnesis!
- about 150.000 patients in the Czech Republic (10 million inhabitants…)

WARNING SIGNS

slowly progression,taking minimum a few months

COGNITIVE DISTURBANCE

- (memory,orientation,speech, attention, delusions, hallucination)

- BEHAVIOUR DISTURBANCE

(personality, emotion-apathy,aggression,depression)

- LOSS OF SELF-SUFFICIENCY

(employment…..take care of himselfs)

CLASSIFICATION
Swedish Consensus on Dementia and Dementia diseases

A. PRIMARY DEGENERATIVE DEMENTIA

B. VASCULAR DEMENTIA

C. SECONDARY DEMENTIA

Who diagnoses dementia in Czech Republic ?

- **Neurologist** + **psychiatrist** + **geriatrist**
- cooperation with **neuropsychologist**

NEUROPSYCHOLOGICAL EXAMINATION

TARGET:

examine all lobes of the brain

- The most exact tests are for **F lobe**
- The less exact tests are for **T lobe**
- The least exact test are for **O+P lobe**

NEUROPSYCHOLOGICAL TESTS

- Standardization (comparison of each other)
- Sensitivity (minimal deficit detection)
- Repeatable (monitoring over time)
- Quantification (score)

NEUROPSYCHOLOGICAL TESTS

- Examination takes a few hours

- Bed - side tests

Short, assessment of cognitive functions ever by general practitioner or ambulantory specialist

SIMPLE ORIENTATION RULES

The type of dominant lobe impairment helps us with differential diagnostics of dementia type

F (behavior function)	**FTD**
T+P (memory function)	**AD**
P+O (visualconstructive function)	**DLBD**
multiple impairment	**VD**

BED-SIDE TESTS
MMSE /MiniMental State Examination/

- The most used test since 1975

WHY??

ADVANTAGES:

- quick
- easy administration
- requirement of Czech insurance company
- monitoration of dementia progression

BED-SIDE TESTS
MMSE /MiniMental State Examination/

DISADVANTAGES:

Not enough sufficient for

- early stage of dementia (MMSE often normal)
- diagnosis of FTD (no examination of F lobe)
- diagnosis of DLBD (no examination of O + P lobe)

STAGE OF DEMENTIA according to MMSE (30-0 points)

- Mild 25 - 18 p.
- Moderate 17 – 6 p.
- Severe 5 – 0 p.
- Standard score 28-30 p.
- IMPORTANCE – therapeutic strategy !

BED-SIDE TESTS
ACE /Addenbrooke´s Cognitive Examination/

- SCORE

Maximum 100 points (MMSE is a part of ACE)

- Less than 82 points

: sensitivity of dementia 84%
: specificity of dementia 100%

MMSE versus ACE

MMSE

- 10-15 min
- monitoration of already developed dementia

ACE

- 25 -30 min
- early dementia
- FTD, DLBD

Which test is better to CHOOSE?

ACE:

- Suspicion of the dementia
- Expected another kind of dementia than AD or VD

MMSE:

- Already developed dementia
- Monitoration of dementia

CAUSES OF DEMENTIA

- The causes of dementia: about 60 various diseases

A/ PRIMARY NEURODEGENERATIVE Dementia

B/ VASCULAR Dementia

C/ SECONDARY Dementia

attending basic NEUROLOGICAL or INTERNAL diagnosis
(disturbance of metabolism, nutrition, endocrinopathy, toxic brain disturbance)

EXAMINATION METHODS

- Primary target: Exclude SECONDARY Dementia (TREATABLE)
- EVERY!! NEUROIMAGING (CT,MRI,PET MRI)
- Blood Tests : blood count, renal/liver biochemistry, vitamine B12, thyroid function tests, Cu + ceruloplasmin, serology HIV + syphilis
- CSF (basic, triplet, protein 14-3-3)
- (EEG)
- (genetics)

Disturbances IMITATING Dementia

- 1. Mild cognitive impairment (MCI)
  - 10-15% transformation to AD
- 2. DEPRESSION (pseudodementia)
  - therapeutic test with antidepressants
- 3. DELIRIUM
  - sudden onset, fluctuation, duration days, quantitative consciousness failure

Disturbances IMITATING Dementia

- 4. Side effects of FARMACOTREATMENT in old age

- anticholinergics (biperiden, tricyclic antidepressants)
- opioids
- hypnotics

A/ PRIMARY DEGENERATIVE DEMENTIA

HISTOLOGICAL CRITERIA:

1. AMYLOIDOPATHIES - **AD**

Amyloid plaques… deposits of beta amyloid

2. TAUOPATHIES - **FTD**, CBD, PSP

Pick bodies …. deposits of Tau protein /ubiquitin protein/

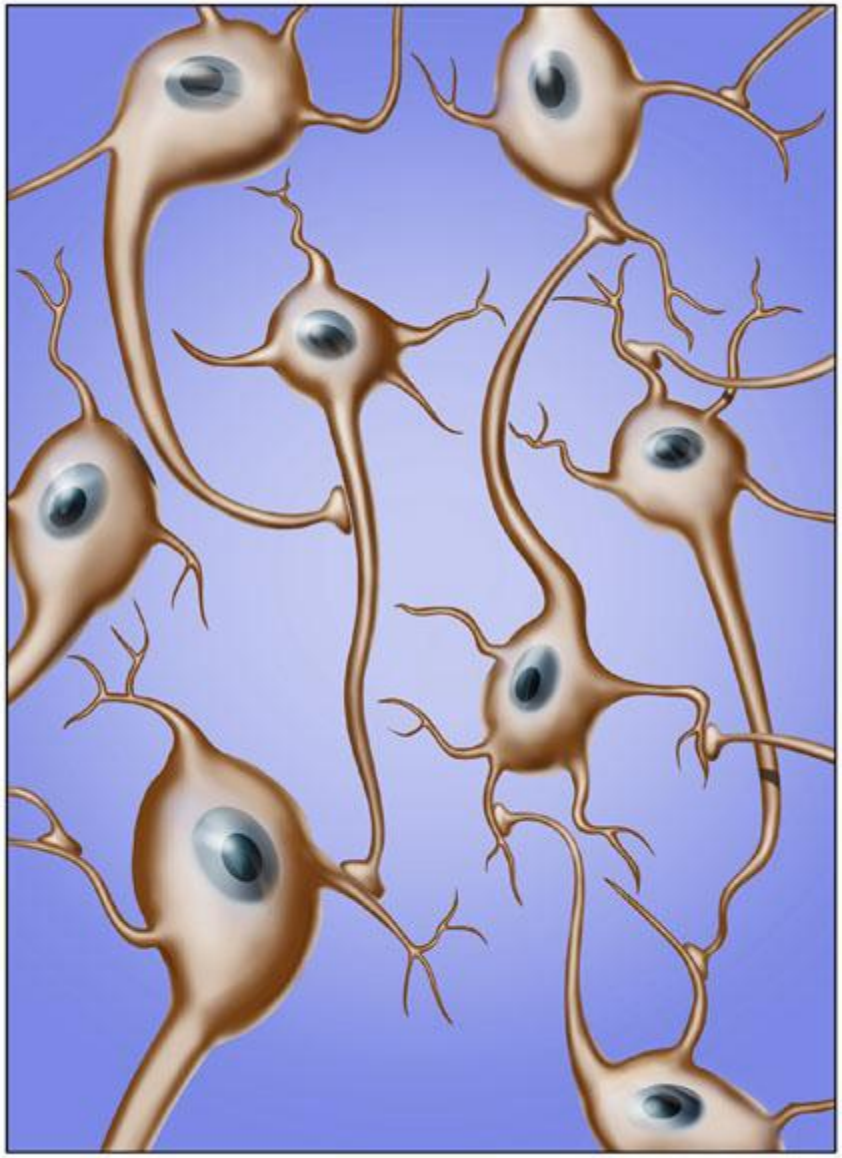
3. SYNUKLEINOPATHIES - **DLBD**, PDD

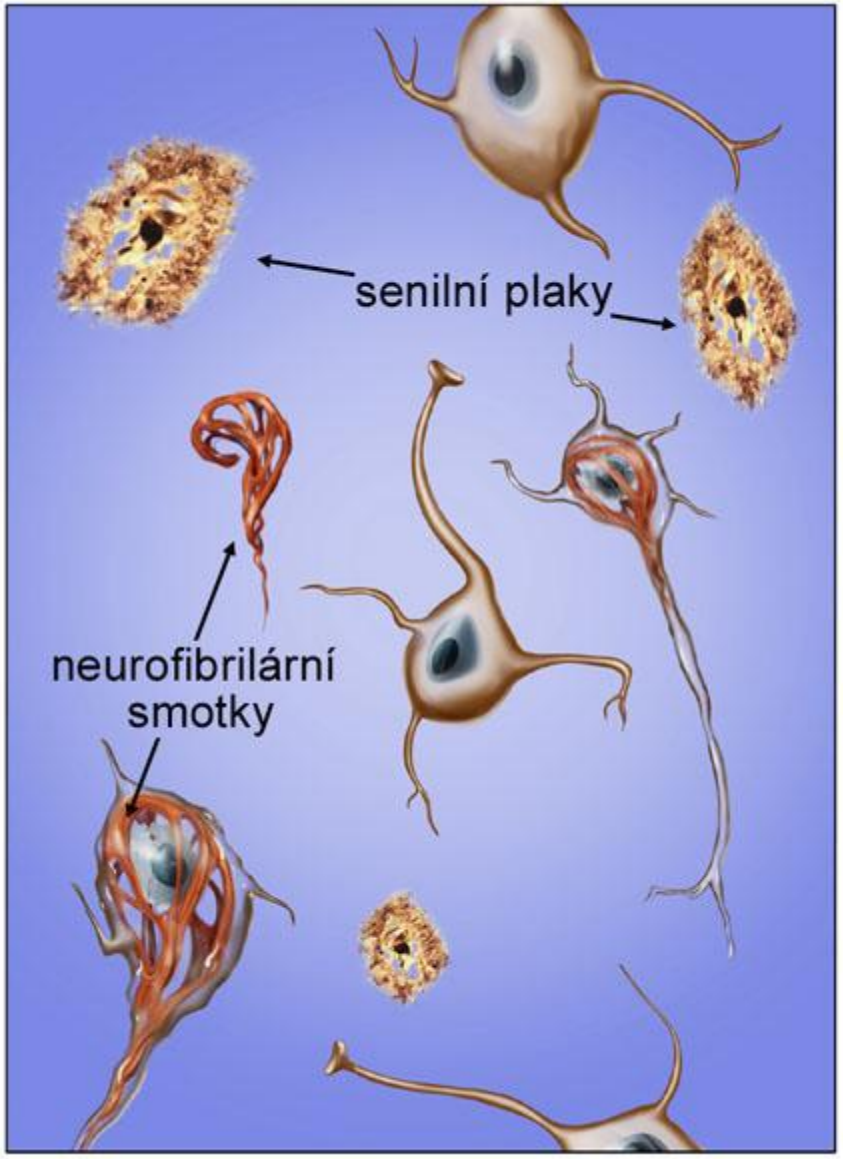
Lewy bodies … deposits of alfa synuklein

ALZHEIMER´S DISEASE

MOST OFTEN!!

- 60% of all the kinds of dementia
- Preclinical stage even 15 years
- Neuropsychological examination: The first sign - DISTURBANCE OF RECENT MEMORY
  T-P lobe
- HISTOLOGY: AMYLOIDOPATHIES




senilní plaky
neurofibrilární
smotky

RISK FACTORS

AGE !!!! 65 years - 5%
85 years - 50%

- Low education
- Low intelect and mental activity
- Low physical activity
- Social isolation
- Female gender (3,1 x)
- Genetic factors (early onset)

TYPES OF AD

- 1. AD with early onset (up to 60 years age)
  5%
  genetic risk faktors … APO E_4
  (alela E_4 for apolipoprotein E)

- 2. AD with late onset (most of the patients) !
  sporadic form

CLINICAL DIAGNOSIS OF AD

- 1. PROBABLY

Disturbance of 2 or more cognitive functions, progression between 60-90 years, depression, anxiety, delusions, hallucinations, emotion instability, incontinency.
Possible neurologic signs (epilepsy, parkinsonism)

- 2. DEFINITIVE

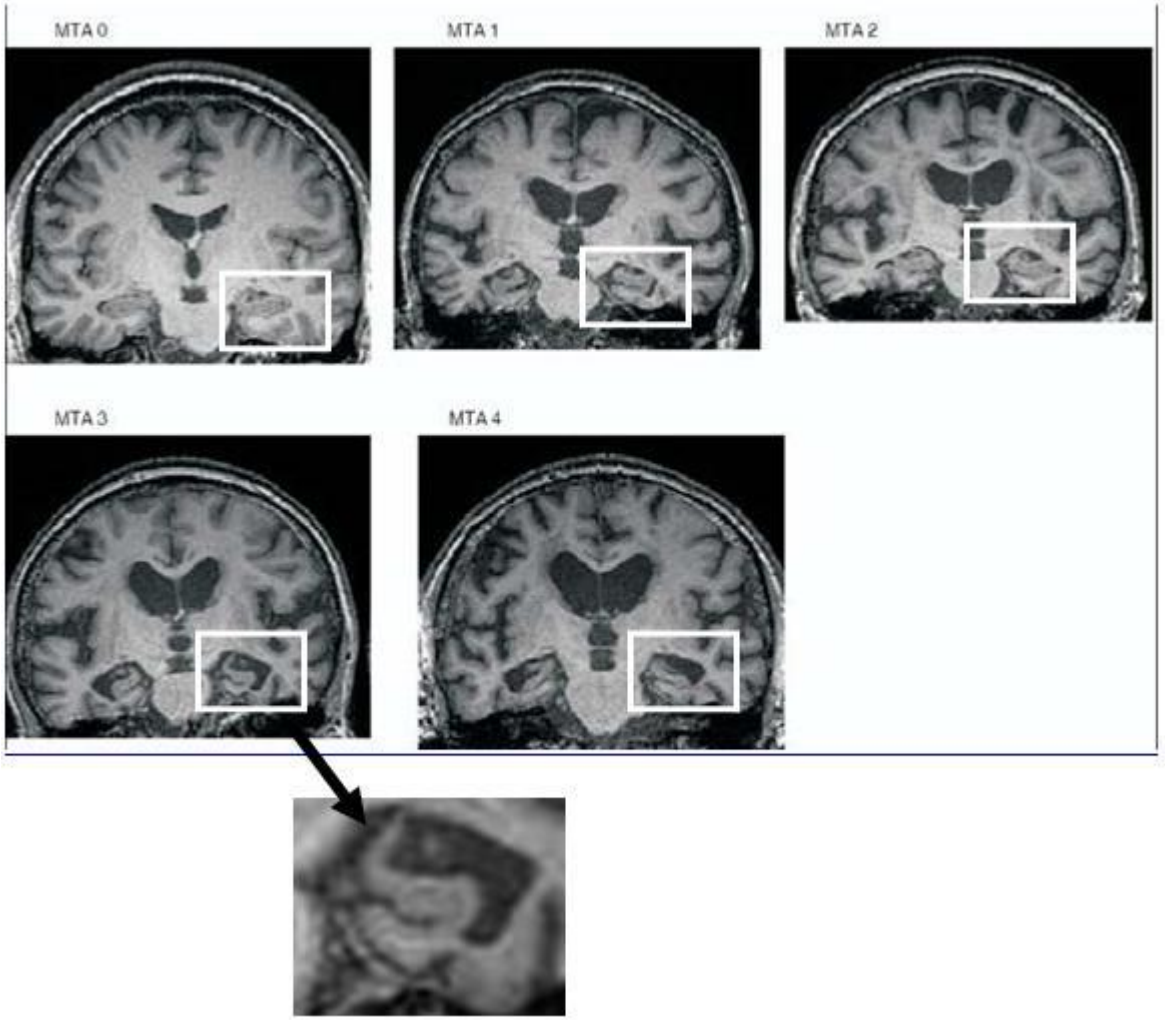
Histological verification by brain biopsy (post mortem)

NEUROIMAGING AD

- (BRAIN CT):
  - atrophy of T lobe (P), extension of lateral ventricles

- BRAIN MRI:
  - hippocampal atrophy (high specifity)

MRI - hippocampal atrophy



NEUROIMAGING AD

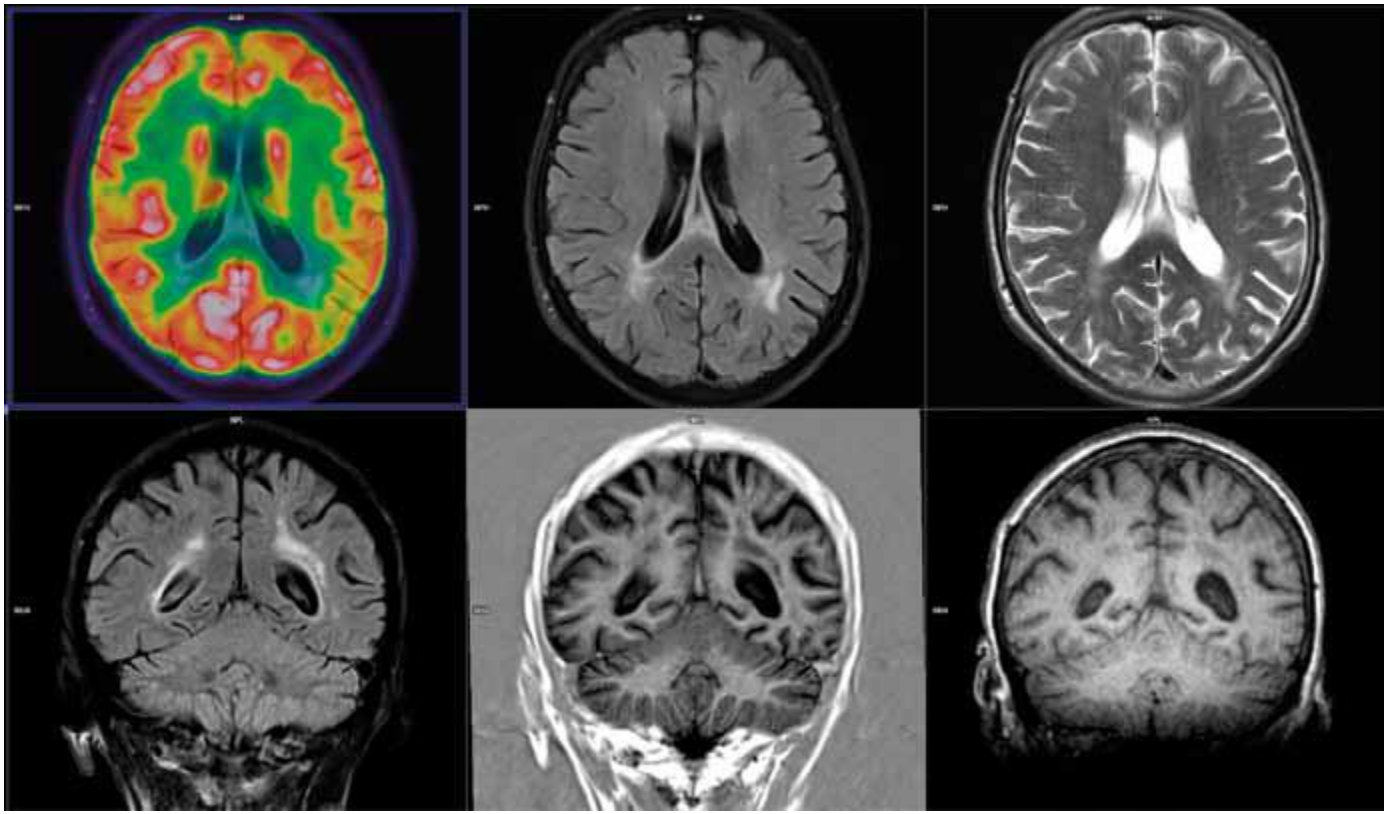
- BRAIN PET MRI

i.v. aplication of radioactive isotopes

FDG (fluorodeoxyglucose) - decreased glukose metabolism in MEDIOTemporal LOBE,
gyrus cinguli, precuneum … late T-P lobe

In University Hospital Brno since 2017

FDG PET MRI



NEUROIMAGING AD

- AMYLOID BRAIN PET MRI :

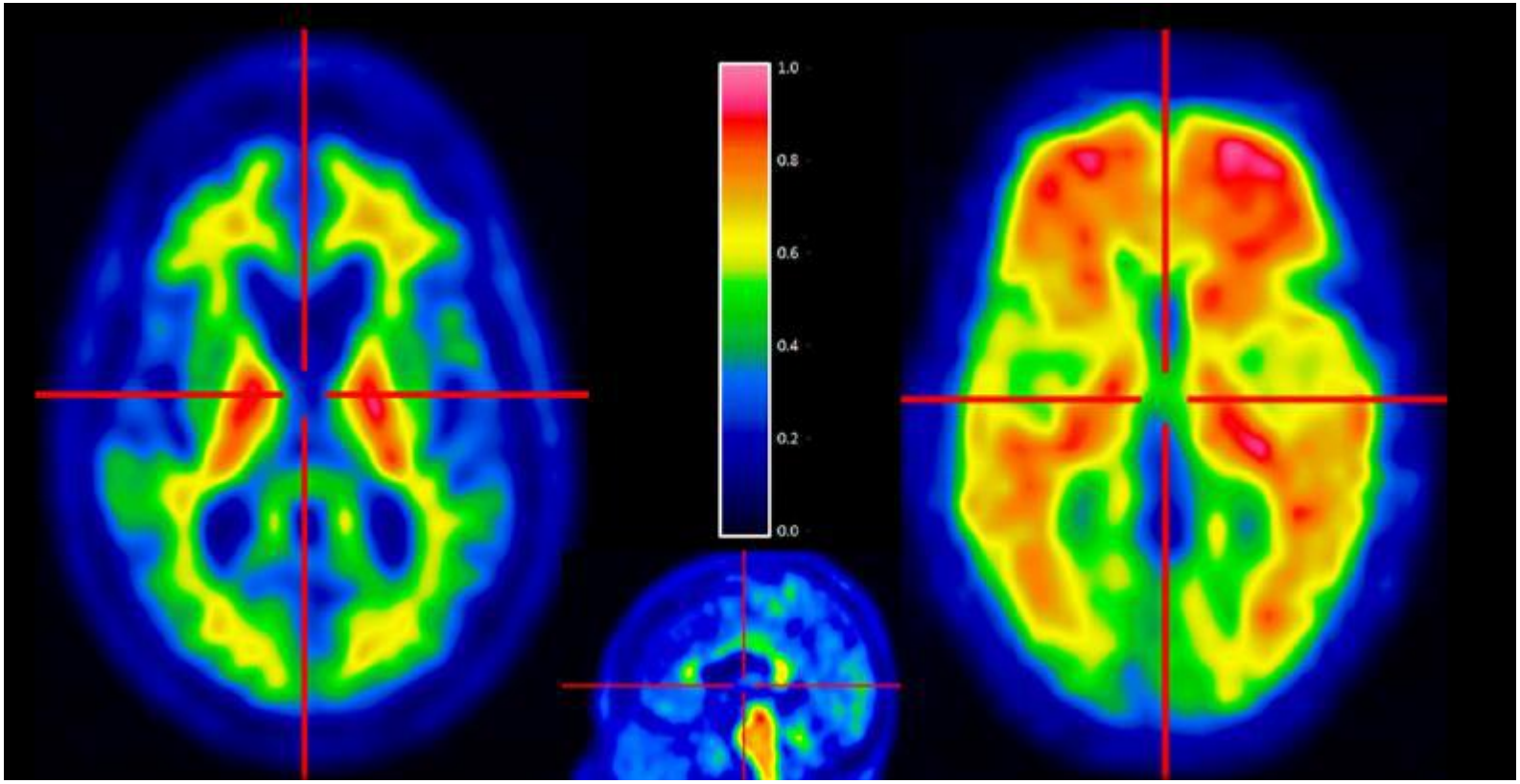
In vivo detection of amyloid plaques
Expensive /1800 dollars/

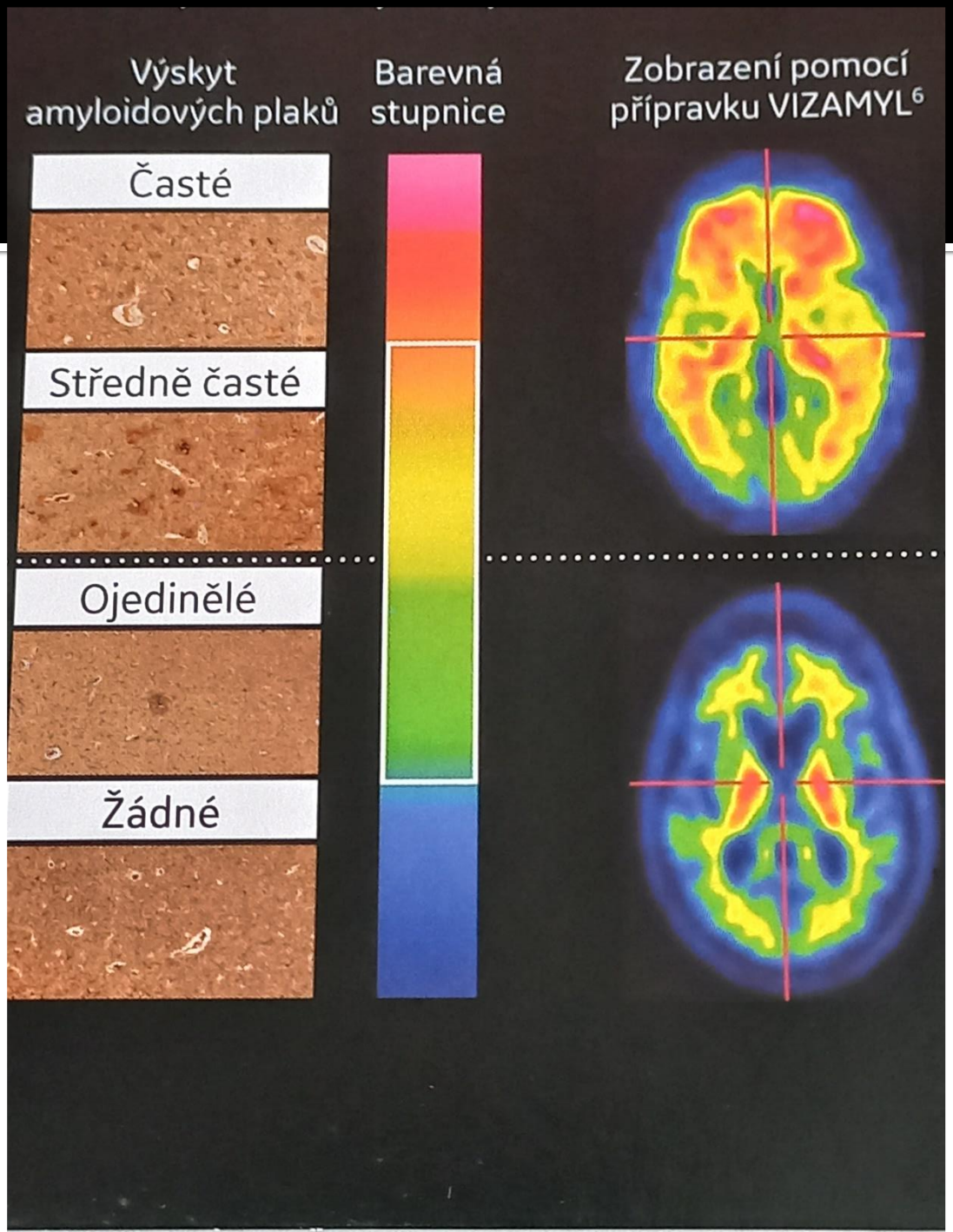
ADVANTAGE: MCI....initiation of treatment
early diagnostics
negative result exclude AD
clinical trials
NO: asymptomatic patient with family history

In University Hospital Brno since february 2023

AMYLOID PET MRI

- NORMAL PATOLOGY




Výskyt amyloidových plaků
Barevná stupnice
Zobrazení pomocí přípravku VIZAMYL[6]
Časté
Středně časté
Ojedinělé
Žádné

CSF AD

- TRIPLET: 3 biomarkers, proteins

BETA-AMYLOID decreased
TAU-PROTEIN increased
P/TAU-PROTEIN increased - most exact

- Negativ result exclude AD

- In University Hospital Brno since 2019

FARMACOTREATMENT AD

- AS SOON AS POSSIBLE
- SYMPTOMATIC : NO CURE, NO STOP, BUT SLOW DOWN

A/ ACETYLCHOLINESTERASE INHIBITORS

I: Mild and moderate stage of AD (MMSE 25-13)

- Donepezil
- Rivastigmin
- Galantamin

Side effects: impaired digestion, parkinsonism

FARMACOTREATMENT AD

B/ MEMANTIN – influence on NMDA receptors
I: Moderate stage of AD (MMSE 17-6)

A+B/ DUAL THERAPY (MMSE 17-13)

Mild stage … Memory Late stage … Behaviour

FARMACOTREATMENT AD

- TREATMENT of DEPRESSION + ANXIETY:
  SSRI, SNRI, BZD
  Cave tricyclic antidepressants - anticholinergical side effect

- TREATMENT of PSYCHOTIC SYMPTOMS:
  antipsychotics

FARMACOTREATMENT AD

- DO NOT prescribe: nootropics, vasodilatans
- Parallel therapy !!: cognitive training
  physical training

  (only to swallow a pill is insufficient)
- We have got yet no new drug since 2004
- New trials: biologic therapy - monoclonal antibodies against amyloid

DLBD - Difusse Lewy Body Disease

- HISTOLOGY: SYNUKLEINOPATHIES

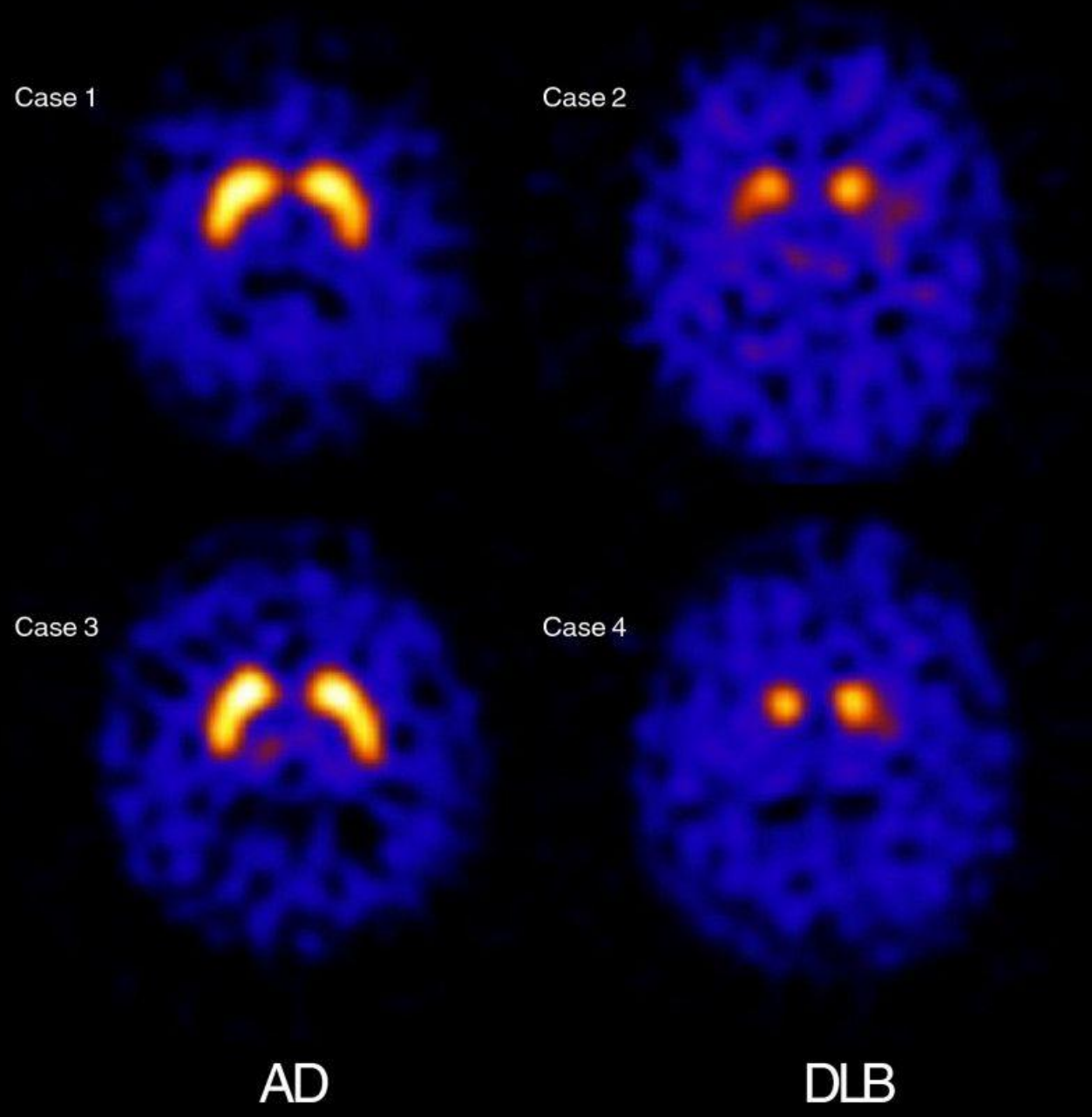
20% of dementia, underdiagnosed

HISTOPATHOLOGY: Lewy bodies (brain stem, limbic cortex, neocortex T-F)

DAT scan - asym. hypofunction in striatum
PET MRI – sym. cortical hypoperfusion T-P-O

Neuropsychological examination: visual-constructive dysfunction T-P-O

Dopaminergic FP-CIT SPECT Imaging



DLBD - Difusse Lewy Body Disease

- CLINICAL signs: fluctuating cognitive deficit
  visual hallucinations
  parkinsonism
- TREATMENT:

CAVE neuroleptic hypersensitivity (quick deterioration of parkinsonism)

- Only nontypical antipsychotics
- Acetylcholinesterase inhibitors
- L-Dopa in early stage

FTD – FRONTOTEMPORAL DEMENTIA (Pick´s disease)

- HISTOLOGY: TAUOPATHIES (ubiquitinopathies)

- Neuropsychological examination : 1. SYMPTOM BEHAVIOUR OR LANGUAGUE DISTURBANCE
F + T lobe

- EARLY onset (45 - 65 years)
- FAMILIAR OCCURENCE (30-50%)
- RAPID PROGRESSION

VARIANTS OF FTD

- 1. BEHAVIOURAL (Frontal) - 55%
- 2. LANGUAGE (PPA)
- Combination of both

1. FRONTAL VARIANT

DOMINANT symptoms:

- Early change of behaviour (perseverative, stereotypes)
- Early change of personality
- Early emotional changes (apathy, verbal or physical impulsivity)

LATE somatic signs :

- Parkinsonism, MND (10-15 %)

1. FRONTAL VARIANT

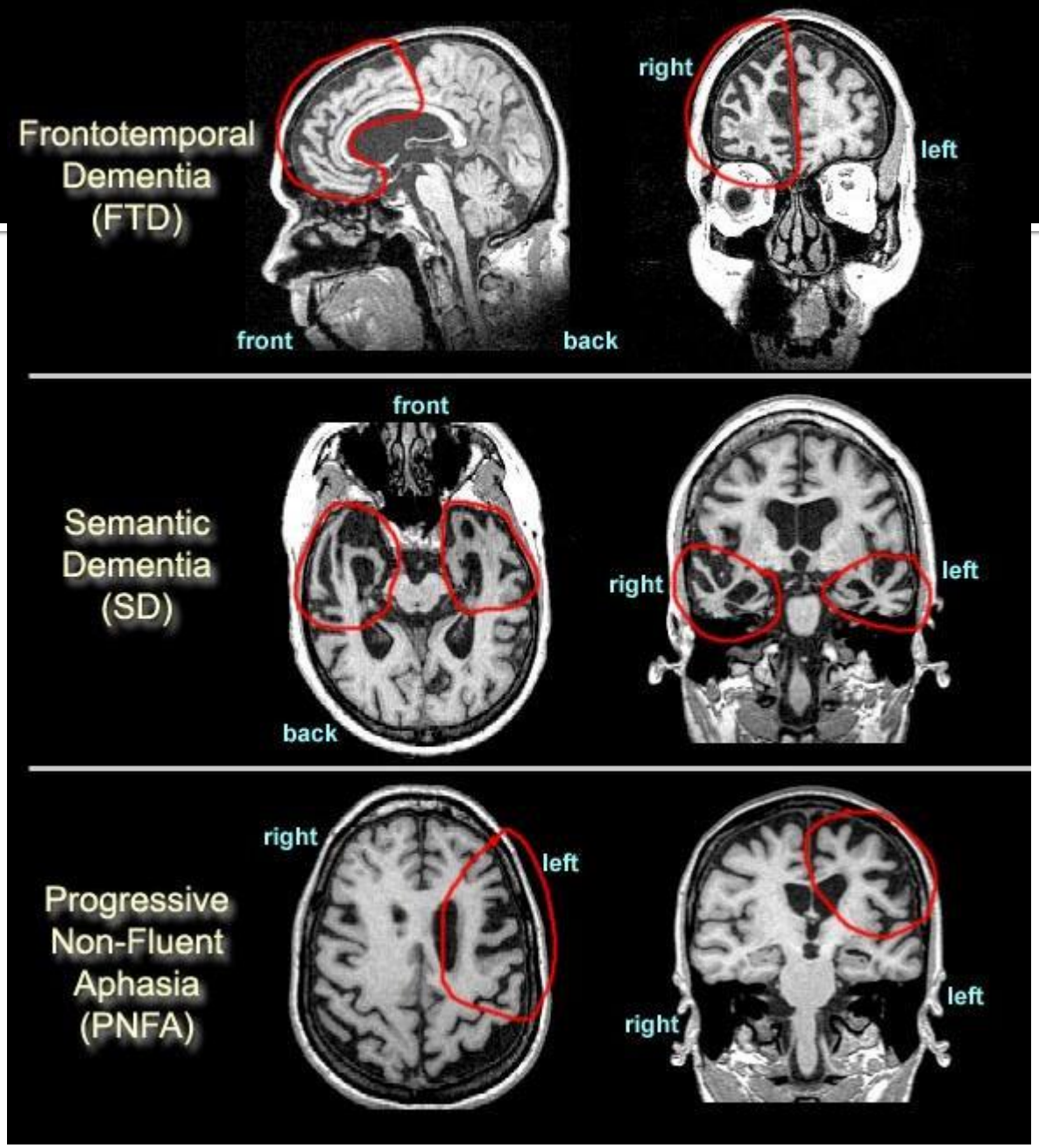
NEUROIMAGING (MRI, PET MRI):
- sym. atrophy of F + front T lobe

TREATMENT:

- Deficiency of serotonin. and dopamin. transmiter system - SSRI
- Nontypical antipsychotics
- (cognitivs rather no – minimal effect)

2. PPA primary progressive aphasia

- Subtypes: non - fluent aphasia
  semantic
  logopenic
- DOMINANT sign: APHASIA
- NEUROIMAGING: asym. atrophy of T lobe (dominant)
- TREATMENT: Speech therapy


Frontotemporal Dementia (FTD)
front
back
right
left
Semantic Dementia (SD)
front
back
right
left
Progressive Non-Fluent Aphasia (PNFA)
right
left
right
left

B/VASCULAR DEMENTIA

- 20% of dementia
- after stroke 5x higher risk of onset
- men more disabled than women

- diagnostics is problematic, differentiation of AD often only histologically, ussual is mixed dementia (AD + VD)

DIAGNOSTIC OF VD

- Brain MRI (CT)
- Neuropsychological examination: more than 1 lobe is impaired
- SONO of cerebral arteries
- CSF: biomarkers negativ

VARIANTS OF VD

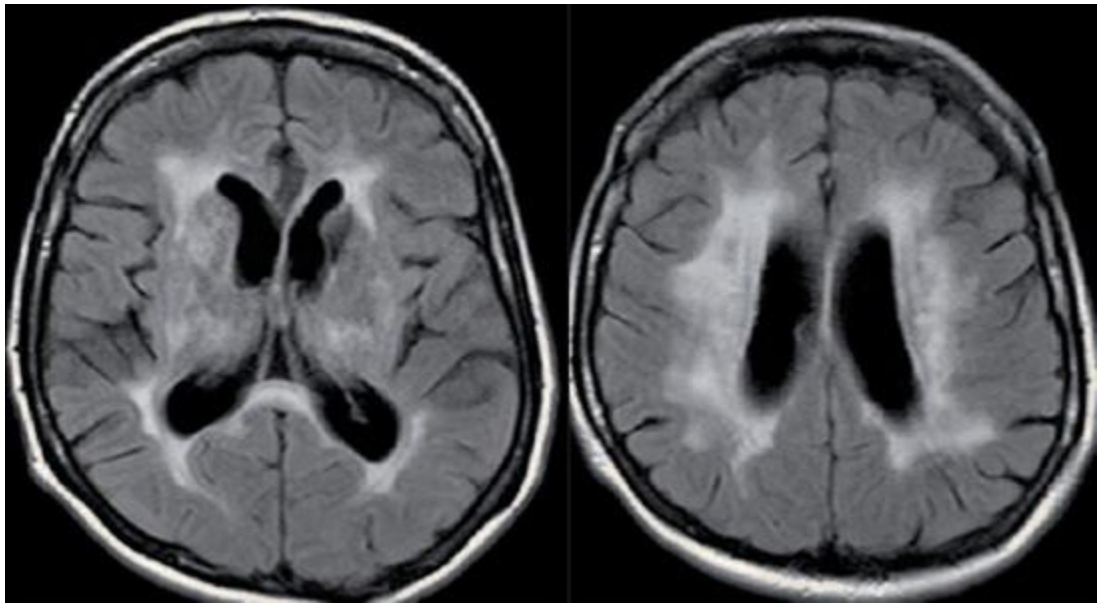
1. D. due to mikroangiopathy (90% because of HT)
   Binswanger´s disease (subcortical leukoencefalopathy)

2. D. due to strategically lokalized ischemia (F, T)

3. Multiinfarct D. (multiply small and large infarcts)

4. D. due to difusse hypoxic-ischemic encefalopathy

(5.) D. familial : AMYLOID angiopathy (frequent stroke)
CADASIL (AD, mutation of chromosome 19)
- young age, migraine, skin biopsy



TREATMENT VD

- Primary and secondary PREVENTION of cerebrovascular diseases
- Acetylcholinesterase inhibitors
- Memantin
- DO NOT Prescribe: nootropics, vasodilatant drugs

MIXED DEMENTIA

- Very common!
- Dominant AD + vascular changes
- Dominant VD + alzheimer changes

C/ SECONDARY DEMENTIA

- Symptom of basic NEUROLOGICAL DG
- Symptom of basic INTERNAL DG

C/ SECONDARY DEMENTIA

Symptom of BASIC NEUROLOGICAL DG:

- Normotense hydrocephalus
- Brain tumors
- Kraniocerebral injury - chronic SDHematoma
- Epilepsy
- Neuroinfection - JCD, neurosyphilis, AIDS
- Sclerosis multiplex - late stage
- Huntington´s disease
- Wilson´s disease

C/ SECONDARY DEMENTIA

Symptom of basic INTERNAL DG:

- Hepatal encephalopathy
- Renal (uremic) encephalopathy
- Endocrinopathy (hypothyreodism)
- Deficiency B12,B1,B6,folat acid
- Alcohol abuse

Jakob - Creutzfeldt disease (JCD)

- Prion disease
- Incidence 1-2 per million
- 100% mortality
- Incubation period more than 10 years
- The most infectious tissue: BRAIN!
  - cerebral dura, cornea, blood?

RISK:

- Transplant from affected person
  (from 2007 mandatory testing cornea donor)
- Neurosurgical operation (contaminated instruments)
- Disinfection, UV radiation – DO NOT DESTROY

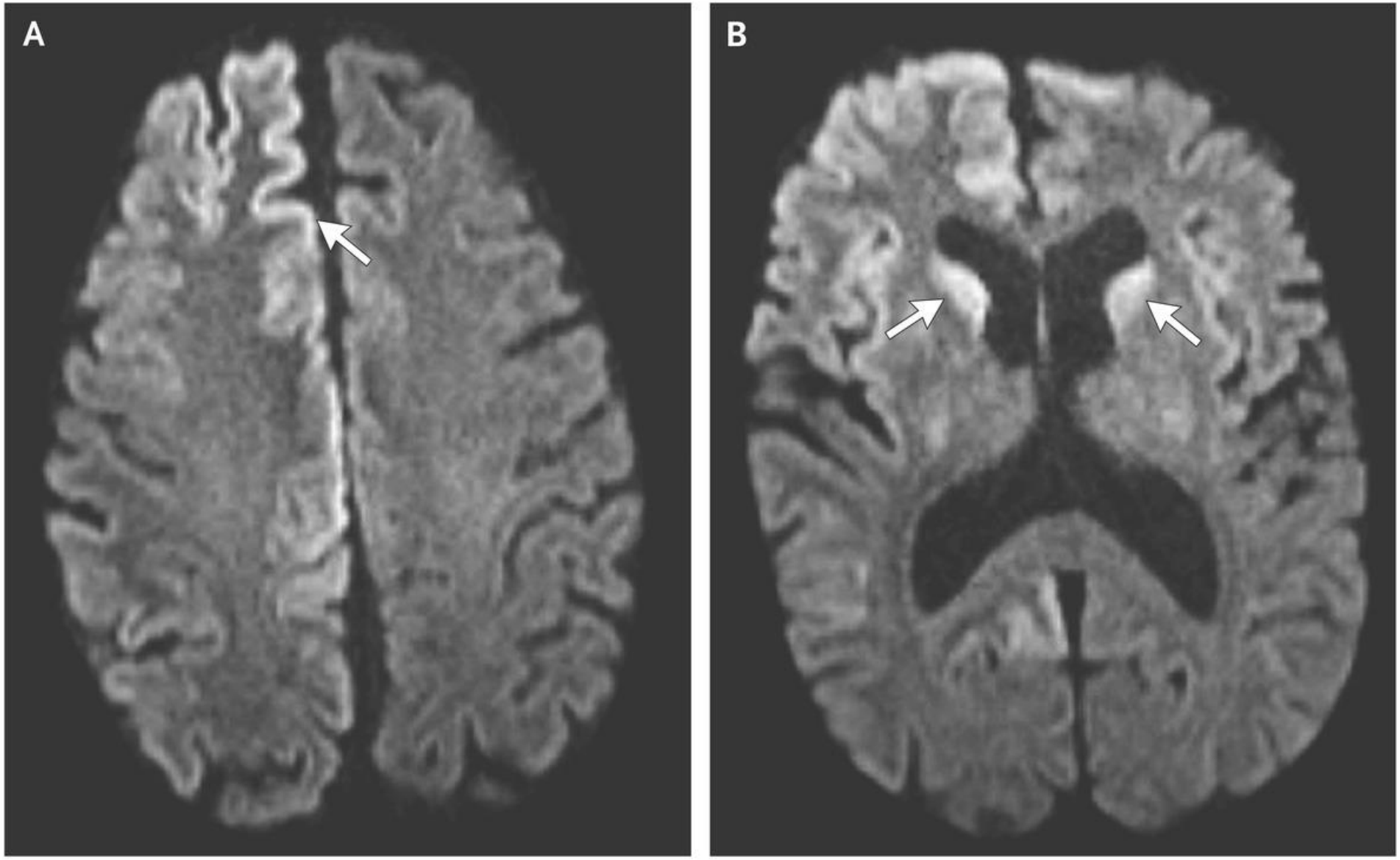
CLINICAL FEATURES JCD

- Rapidly progressive dementia
- Cerebellar or visual signs (ataxia)
- Extrapyramidal signs (myoclonus)
- Pyramidal signs
- Akinetic mutism

- AUTOPSY MANDATORY

DIAGNOSTICS JCD

- EEG: periodic sharp wave complexes
- CSF: 14-3-3 protein detection
- Brain MRI: high signal abnormalities in caudate nucleus + putamen
- INCURABLE


A
B

VARIANTS JCD

- 1. SPORADIC 85%
  50-70 years
  Duration 6 months

- 2. GENETIC (mutation) 10-15%

- 3. NEW variant (infectious) 2-3%
  19-39 years
  Duration 1-1,5 years
  Due to consumption of infectious animal (BSP)

Other (rare) prion diseases

- KURU (kanibalism, Papua N. Guinea)
- FFI Fatal familiar insomnia
- Gerstman-Straussler-Scheiner d.

Thank you for your attention