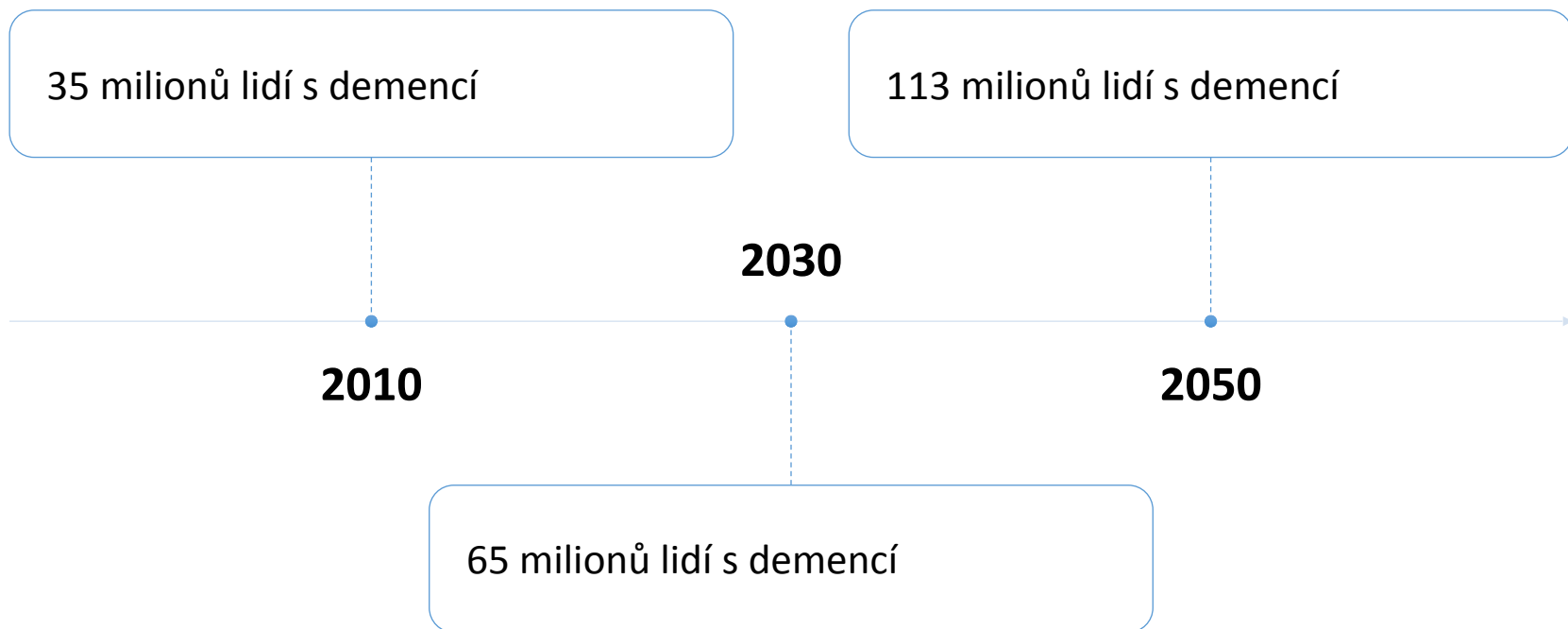


# Alzheimerova nemoc a Parkinsonova nemoc/ Demence s Lewyho tělísky

**Irena Rektorová**

**1.Neurologická klinika FNUSA a LFMU  
CEITEC MU**

# Demence



*Brodaty et al., 2011*

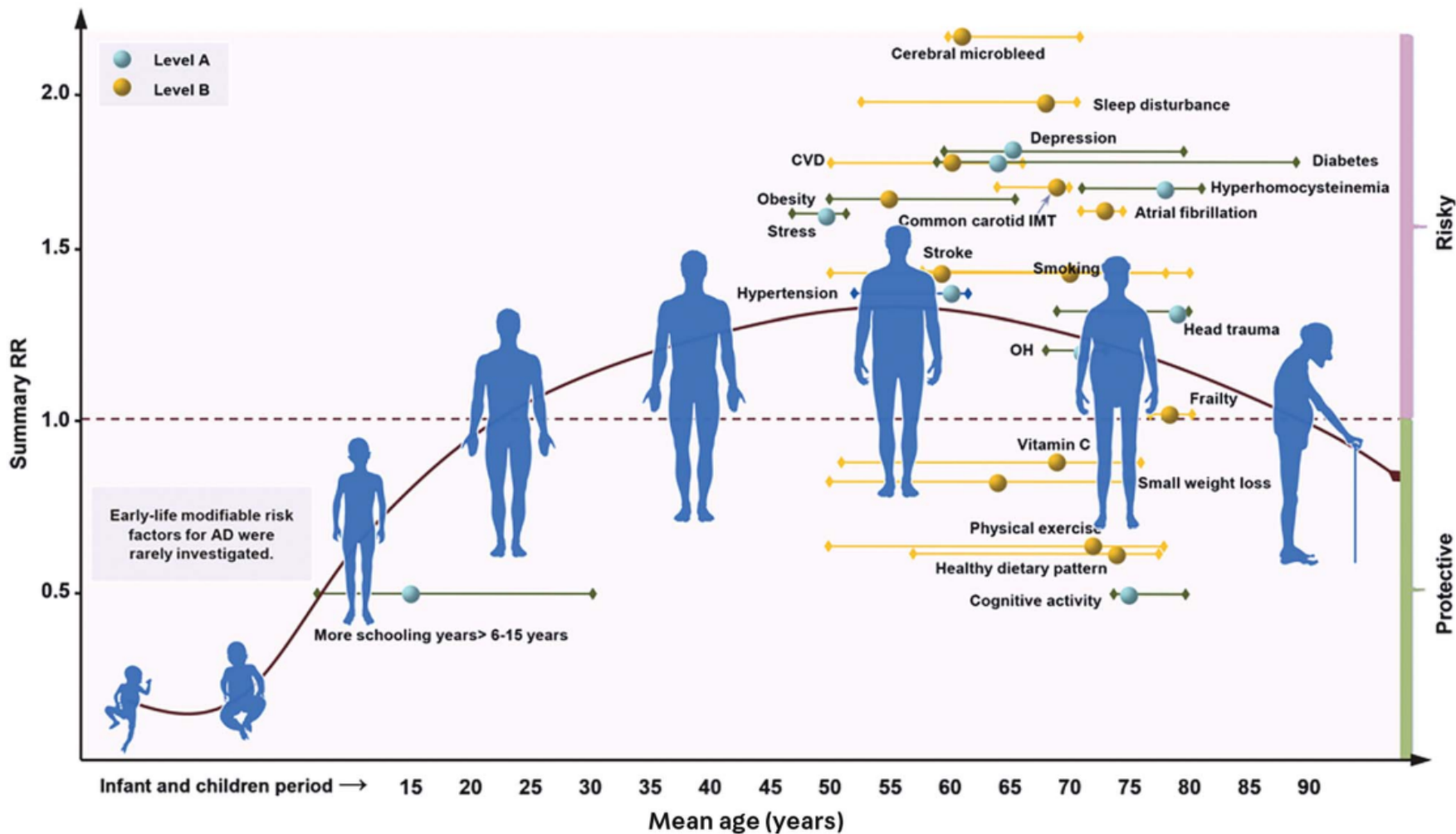
# Pravděpodobná AN, McKhan et al., 2011

- Postupný počátek a jasná progrese
- Kognitivní nebo behaviorální změny alespoň ve 2 doménách:
  - Porucha krátkodobé epizodické paměti
  - Porucha úsudku
  - Deficit zrakově-prostorových funkcí
  - Neurogenní poruchy komunikace
  - Poruchy chování

# Rizikové a protektivní faktory

- Věk
- Pohlaví
- Pozitivní RA, genetické faktory (APOE4, TREM2, SORL1, ABCA7,...)
- Nízký socio-ekonomický status, nízká úroveň vzdělání
- Úrazy mozku
- Stroke a cévní rizikové faktory!
  
- Fyzická a mentální aktivita, sociální zapojení po celou dobu života, léčba cévních RF, dieta, ne tvrdý alkohol (nebo větší množství)

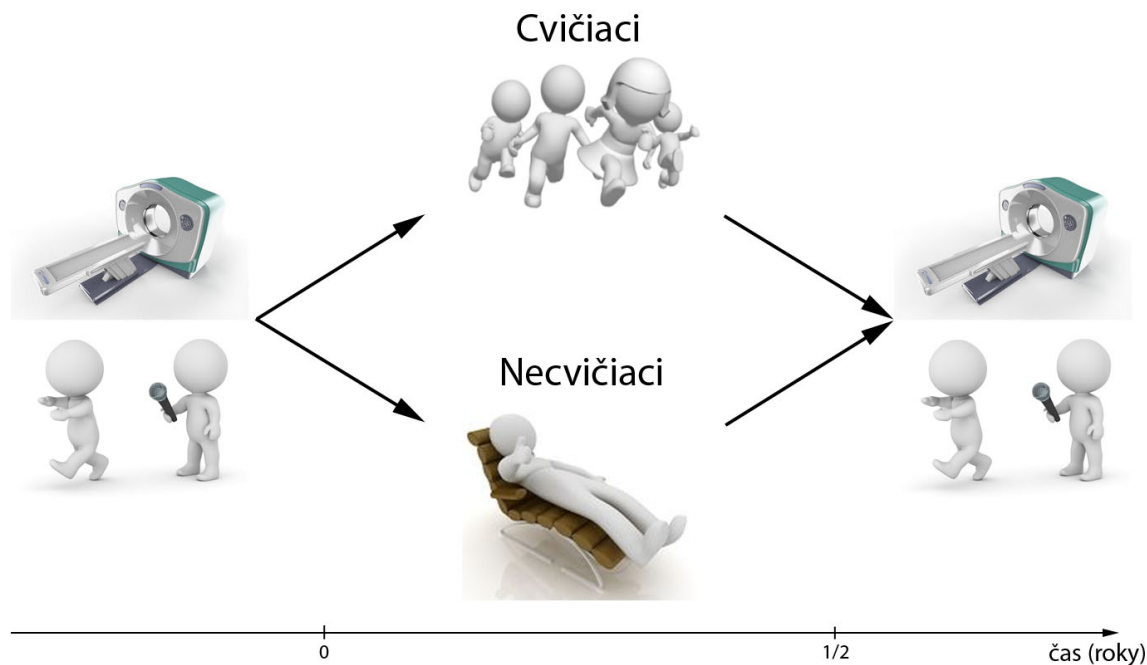
# AN: rizikové a protektivní faktory



# Tanečně pohybová intervence na kognitivní funkce, fyzickou zdatnost a změny mozku

- 4-letá RCT, celkem 120 lidí (podpořeno AZV grantem)
- Aplikované Neurovědy CEITEC MU + FSpS
- Zdraví senioři a pacienti s MCI
- Kognitivní vyšetření, vyšetření rovnováhy a fyzické zdatnosti
- MRI mozku: strukturální, funkční a strukturální konektivita

# Tanečně-pohybová intervence (DI) u zdravých seniorů a pacientů s MCI



Kropáčová et al., 2019, Rektorová et al., 2019, Šejnoha-Minsterová et al., 2020,  
 Mitterová et al., 2021a, Mitterová et al., 2021b, Balážová et al., 2021



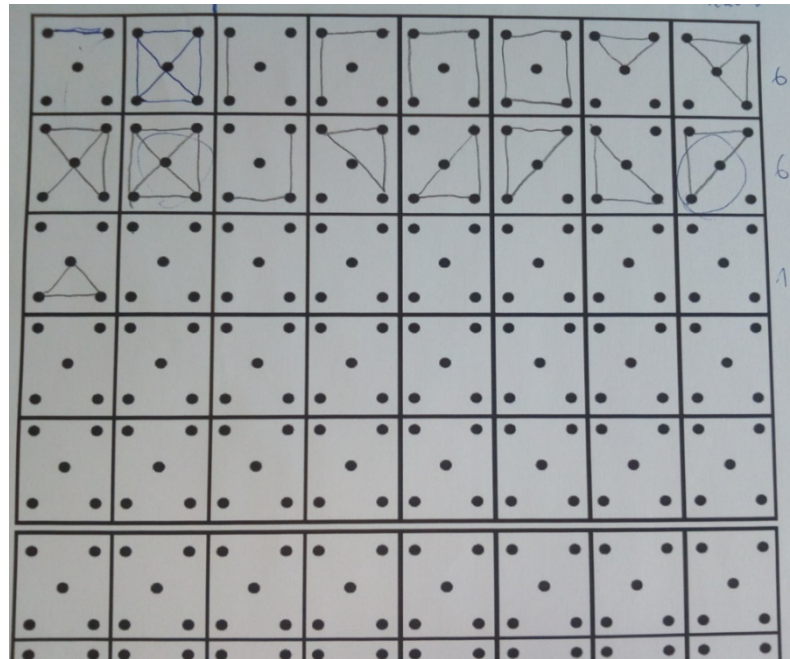
**Table 4** Change between baseline testing and cognitive assessment after 6 months

	Intervention group ( <i>n</i> = 49)					Control group ( <i>n</i> = 50)					Between groups
	<i>M</i>	<i>Sd</i>	<i>T</i>	<i>df</i>	<i>p</i>	<i>M</i>	<i>Sd</i>	<i>T</i>	<i>Df</i>	<i>p</i>	<i>p</i>
TCF 1	−0.42	1.1	−2.68	48	0.010	−3.68	0.98	−2.67	49	0.010	0.802
TCF 2	−0.57	1.1	−3.48	48	0.001	−0.49	1.05	−3.31	49	0.002	0.727
WMS III: LogPam1	−0.09	0.9	−0.70	48	0.488	−0.25	0.99	−1.76	49	0.085	0.418
WMS III: LogPam2	−0.07	0.7	−0.64	48	0.526	−0.24	0.94	−1.78	49	0.081	0.323
WAIS III: Symbols	−0.14	0.82	−1.21	48	0.234	0.08	0.80	0.67	49	0.506	0.252
WMS III: DigitSpan	−0.12	0.75	−1.12	48	0.268	0.05	0.66	0.58	49	0.562	0.22
ToH 3 time	5.04	47.8	0.73	47	0.469	19.6	59.4	2.34	49	0.024	0.185
ToH 3 movements	0.12	1.00	0.81	47	0.425	−0.13	1.2	−0.7	49	0.469	0.286
ToH 4 time	37.8	83.0	2.74	35	0.010	16.5	76.6	1.38	40	0.176	0.244
ToH 4 movements	0.09	1.61	0.35	38	0.732	0.19	1.7	0.74	43	0.462	0.466
FPT	−0.53	0.91	−4.4	48	0.000	0.02	1.1	0.16	49	0.872	
JLO	0.01	0.78	0.10	48	0.920	−0.13	0.81	−1.17	49	0.248	0.366
TCF: copy	−0.01	0.61	−0.03	48	0.974	0.06	0.48	0.95	49	0.348	0.542

**Fig. 1** Flowchart of this study

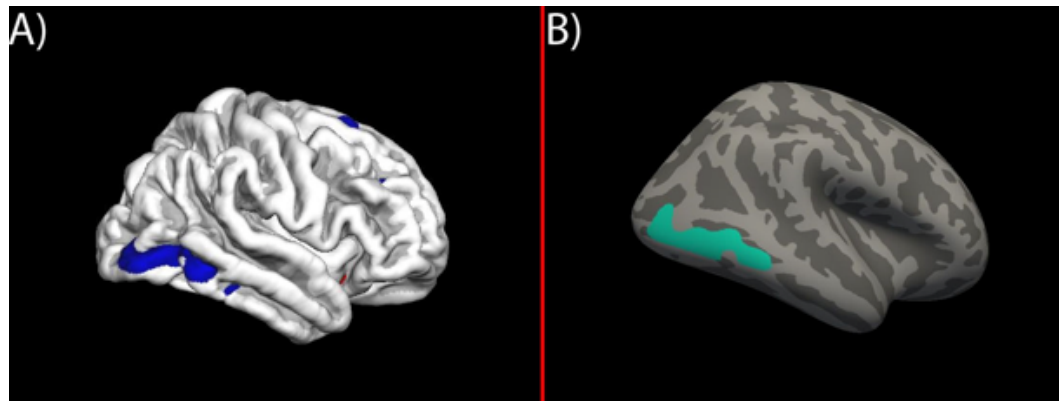


## FPT (pětibodový test): figurální fluence



Hipp/ cortex ratio: nebyl efekt indexu při vstupu na změnu v kognitivních testech

Tanečně-pohybová intervence (DI vs. kontrolní skupina – život jako doposud):  
 na změny plasticity mozku – šířka kortexu



Angiogeneze, synaptická plasticita: BDNF, IGF-1,...

Rektorova et al., Acta Neurol Scand 2019

# Zlepšení fyzické kondice zvýšením strukturální konektivity

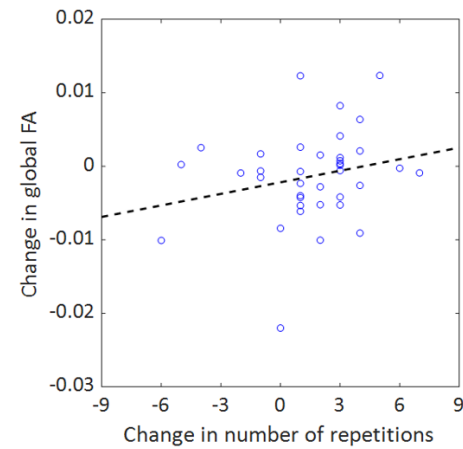
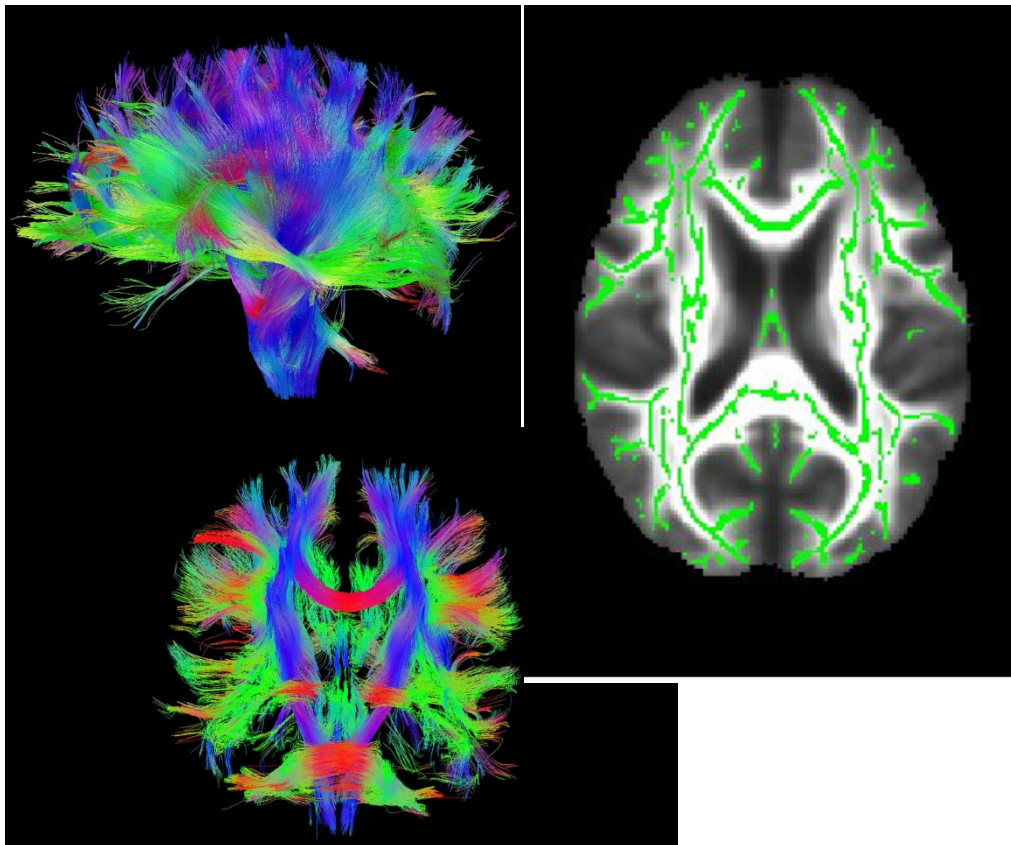
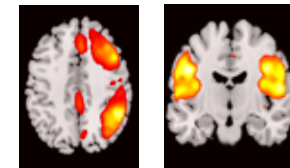
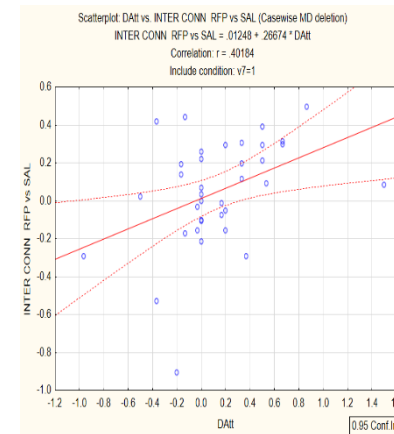
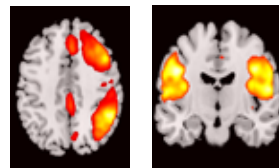
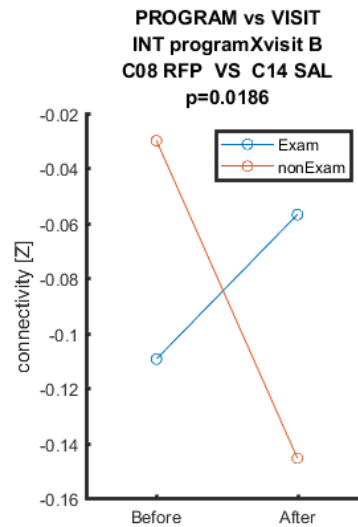
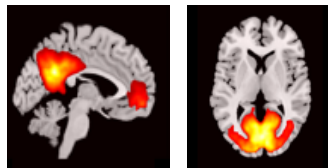
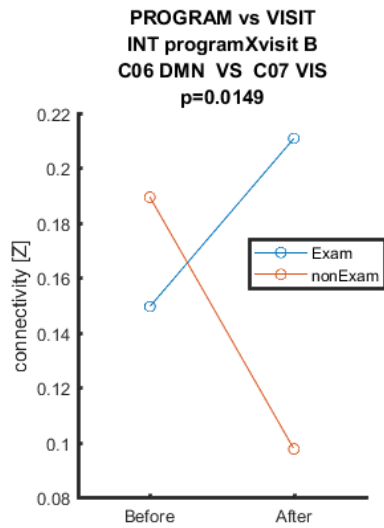


Figure 2 Relationship between change in FA and change in performance in 30-s Chair Stand Test

Šejnoha-Minsterová et al., J Alzheimer Dis 2020

# Zvýšení mezisíťové konektivity: DI vs. kontrolní skupina





# Dynamic Functional Connectivity Signifies the Joint Impact of Dance Intervention and Cognitive Reserve

Kristína Mitterrová<sup>1,2</sup>, Martin Lamoš<sup>3</sup>, Radek Mareček<sup>3</sup>, Monika Puplíková<sup>1,2</sup>, Patrik Šímko<sup>1,2</sup>, Roman Grmela<sup>4</sup>, Alena Skotáková<sup>5</sup>, Pavlína Vaculíková<sup>2</sup> and Irena Rektorová<sup>1,6\*</sup>

<sup>1</sup> Applied Neuroscience Research Group, Central European Institute of Technology, Masaryk University, Brno, Czechia, <sup>2</sup> Brain and Mind Research Program, Central European Institute of Technology, Masaryk University, Brno, Czechia, <sup>3</sup> Brain and Mind Research Program, Faculty of Sports Studies, Masaryk University, Brno, Czechia, <sup>4</sup> Department of Health Promotion, Faculty of Sports Studies, Masaryk University, Brno, Czechia, <sup>5</sup> Department of Gymnastics and Combatives, Faculty of Sports Studies, Masaryk University and St. Anne's University Hospital, Brno, Czechia, <sup>6</sup> First Department of Neurology, Faculty of Medicine, Masaryk University and St. Anne's University Hospital, Brno, Czechia

Research on dance interventions (DIs) in the elderly has shown promising benefit to physical and cognitive outcomes. The effect of DIs on resting-state functional connectivity (rs-FC) varies, which is possibly due to individual variability. In this study, we assessed the moderation effects of residual cognitive reserve (CR) on DI-induced changes in dynamic rs-FC and their association on cognitive outcomes. Dynamic rs-FC (rs-dFC) and cognitive functions were evaluated in non-demented elderly subject before and after a 6-month DI ( $n = 36$ ) and a control group, referred to as the life-as-usual (LAU) group ( $n = 32$ ). Using linear mixed models and moderation, we examine the interaction effect of DIs and CR on changes in the dwell time and coverage of rs-dFC. Cognitive reserve and the performance predicted by brain state. Partially observed memory performance for CR evaluated the unique association between changes in rs-dFC and cognition in the DI group. In subjects with lower residual CR, we observe correlations accounting for CR evaluated the unique association between changes in rs-dFC and cognition in the DI group. In subjects with lower residual CR, we observe DI-induced increases in dwell time [ $t(58) = -2.14, p = 0.036$ ] and coverage [ $t(58) = 2.22, p = 0.030$ ] of a rs-dFC state, which was implicated in bottom-up information processing. Increased dwell time was also correlated with a DI-induced improvement in Symbol Search ( $r = 0.42, p = 0.02$ ). In subjects with higher residual CR, we observe a DI-induced increase in coverage [ $t(58) = 2.11, p = 0.039$ ] of another rs-dFC state which was implicated in top-down information processing. The study showed that DI have a differential and behaviorally relevant effect on dynamic rs-dFC, but these benefit depend on the current CR level.

**Keywords:** cognitive reserve, dance intervention, dynamic resting-state functional connectivity, attention bottom-up processing, top-down processing, dwell time, coverage

## INTRODUCTION

Some lifestyle factors are known to ameliorate the risk of cognitive decline and dementia. A study by Fratiglioni et al. (2004) proposed three factors that play this role, namely, social network, cognitive leisure, and physical activity. Dance interventions (DIs) represent a unique synergy of these three factors, which can affect a variety of age-related outcomes, including reducing the

## OPEN ACCESS

### Edited by:

Lye Zou, Shenzhen University, China

### Reviewed by:

Aarti Mishra, AbjWU, United States  
Rajkumar S. Kalra, Okinawa Institute of Science and Technology Graduate University, Japan

### \*Correspondence:

Irena Rektorová  
irena.rektorova@fnusa.cz

Received: 11 June 2021

Accepted: 18 August 2021

Published: 10 September 2021

### Citation:

Mitterrová K, Lamoš M, Mareček R, Puplíková M, Šímko P, Grmela R, Skotáková A, Vaculíková P and Rektorová I (2021) Dynamic Functional Connectivity Signifies the Joint Impact of Dance Intervention and Cognitive Reserve. *Front. Aging Neurosci.* 13:724094. doi: 10.3389/fnagi.2021.724094

## scientific reports



# Impact of cognitive reserve on dance intervention-induced changes in brain plasticity

Kristína Mitterrová<sup>1,2</sup>, Patriciá Klobužíaková<sup>1,2,3</sup>, Alžběta Šejnoha Minsterová<sup>4,2</sup>, Sylvie Kropáčová<sup>2</sup>, Zuzana Balážová<sup>4,2</sup>, Jaroslav Točík<sup>1,2</sup>, Pavlína Vaculíková<sup>2</sup>, Alena Skotáková<sup>5</sup>, Roman Grmela<sup>5</sup> & Irena Rektorová<sup>1,4,6\*</sup>

Dance is a complex sensorimotor activity with positive effects on physical fitness, cognition, and brain plasticity in the aging population. We explored whether individual levels of cognitive reserve (CR) probed by education moderate dance intervention (DI)-induced plasticity assessed by resting-state functional connectivity (rs-FC) changes of the sensorimotor network (SMN), and between the dorsal attention network (DAN) and anterior default mode network (ADMN). Our cohort consisted of 99 subjects, randomly assigned to either a DI group who underwent a 6-month intervention ( $n = 49$ ) or a control group ( $n = 50$ ). Moderation analyses revealed that CR moderated DI-induced increase of the SMN rs-FC with significant changes observed in participants of the DAN-ADMN crosstalk change ( $b = 0.05, t(62) = 3.17, p = 0.002$ ). Only DI alone was a significant predictor of SMN rs-FC increase ( $b = 0.06, t(64) = 2.16, p = 0.035$ ). The rs-FC increase in the SMN was correlated with an improved physical fitness measure, and changes in the DAN-ADMN connectivity were linked to better performance on figural fluency. Consistent with the passive CR hypothesis, we observed that CR correlated only with baseline behavioral scores, not their change.

Dance is a complex sensorimotor activity that involves learning new motor skills, bestows attentional action effects even on an aging brain. Considerable experimental research on dance intervention (DI) in the elderly has shown compelling benefits in postural and gait parameters<sup>1</sup>, physical fitness<sup>2</sup>, and cognition in the memory<sup>3,4</sup>, attention<sup>5,6</sup>, and psychosocial domains<sup>7</sup>. A recent meta-analysis supported the rich benefits of DI on global cognition and memory, but not on the inhibition and task-switching aspects of executive functioning<sup>8</sup>. DI-induced behavioral benefits are key in preserving mobility and independence in older age<sup>9</sup> and the importance of studying them stems particularly from the low efficacy of current pharmacological treatment for dementia patients<sup>10</sup>.

Our previous research of an optimized, structured 6-month-long dance intervention (DI) on non-demented seniors demonstrated its positive effects in comparison with “life activities as usual” (LAU) on the performance of the 8-Foot Up-and-Go (RUG) and the 30-Second Chair Stand (30CS) tests<sup>11</sup> which target dynamic balance, agility, lower body strength, and physical endurance<sup>12</sup>; and of the Five Point Test (FPT)<sup>13,14</sup>, which assesses figural planning, and mental flexibility<sup>15</sup>. Interestingly, despite the fact that figural fluency is known to decline in the elderly and in patients with Alzheimer’s disease (AD)<sup>16</sup>, the observed improvements were independent of hippocampal volumes<sup>17</sup>. This finding indicates an individual capacity to recruit additional neural resources in order to meet the demands of the intervention. To test this hypothesis, the current work aims at studying neural changes associated with the described behavioral improvements in terms of neural compensation. This accords well with Lövdén and colleagues, who postulated that any acquisition of new skills (dancing, in our case) requires changes in neuronal connections provided by the brain’s capacity for plasticity termed as a cognitive

<sup>1</sup>Applied Neuroscience Research Group, Central European Institute of Technology, Masaryk University, Kamenice 5, 62500 Brno, Czech Republic. <sup>2</sup>Faculty of Medicine, Masaryk University, Kamenice 5, 62500 Brno, Czech Republic. <sup>3</sup>Surgeon General Office of the Slovak Armed Forces, Ul. generála Mlôha Vesela 21, 034-01 Ružomberok, Slovak Republic. <sup>4</sup>Department of Gymnastics and Combatives, Faculty of Sports Studies, Masaryk University, Kamenice 5, 62500 Brno, Czech Republic. <sup>5</sup>Department of Health Promotion, Faculty of Sports Studies, Masaryk University, Kamenice 5, 62500 Brno, Czech Republic. <sup>6</sup>First Department of Neurology, Faculty of Medicine, Masaryk University and St. Anne’s University Hospital, Pekářská 664/53, 65691 Brno, Czech Republic. <sup>\*</sup>email: irena.rektorova@fnusa.cz

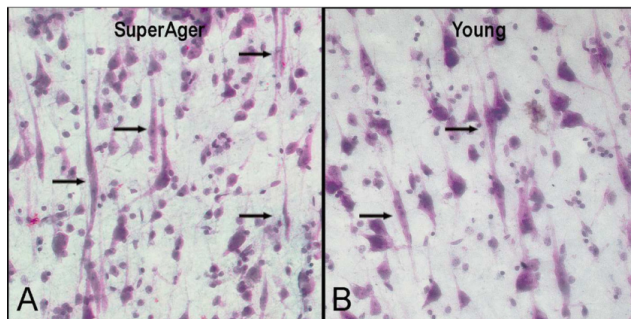
<https://doi.org/10.1038/s41598-021-97323-2>

# Cíl našich studií

- Moderuje KR efekt tanečně-pohybové intervence (DI) na rs-fMRI klidovou funkční konektivitu (FK) a na behaviorální změny?
- Efekt DI na paměť (Meng et al., 2020); exekutivní funkce/figurální fluenci (Kropáčová et al., 2019)
  - Nekonzistentní výsledky
- Efekt DI na FK doposud neznámý **vs.** vliv KR na FK bohatě studovaný (e.g. Conti et al., 2021; Lin et al., 2021)

# Kognitivní rezerva (CR)

- Variabilita v kognitivním výkonu mezi subjekty při normálním i patologickém stárnutí je obrovská
- **SuperAgers**: ↑ šířka kortexu v ACC,
- ↑ density ‘Von Economo neurons’  
 (Gefen et al., 2018)



Cabeza et al., 2018

# Centenarians - Rozdíly oproti běžné populaci

- Vyšší socio-ekonomický status
- Vyšší vzdělání
- Více dětí (možná spojené se soc. statusem)
- Méně kouří
- Spíše silnější jedinci
- optimističtější

The centenarians from the 100-plus Study: Lifestyle



lucid



High social economic status



Higher educated



Slightly more children



smoking



Alcohol consumption



stout persons

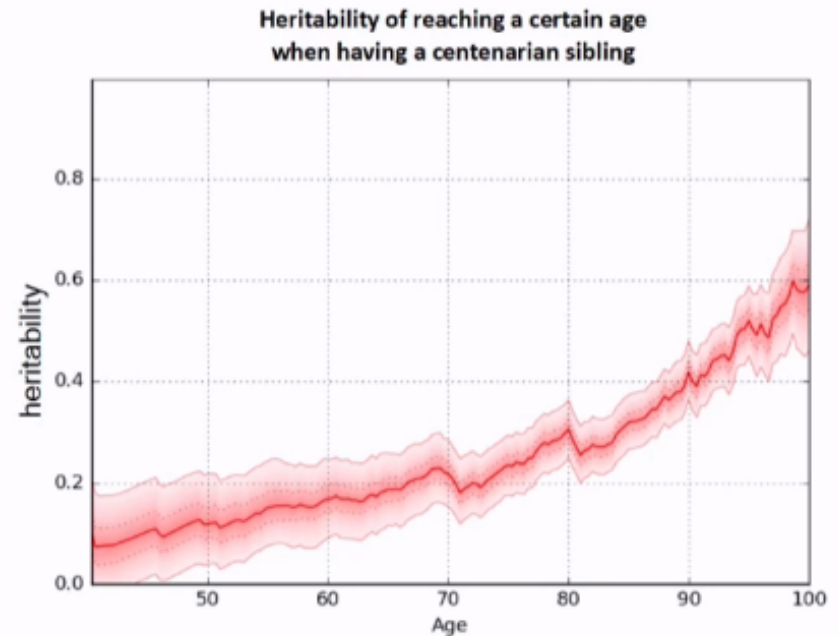


optimistic



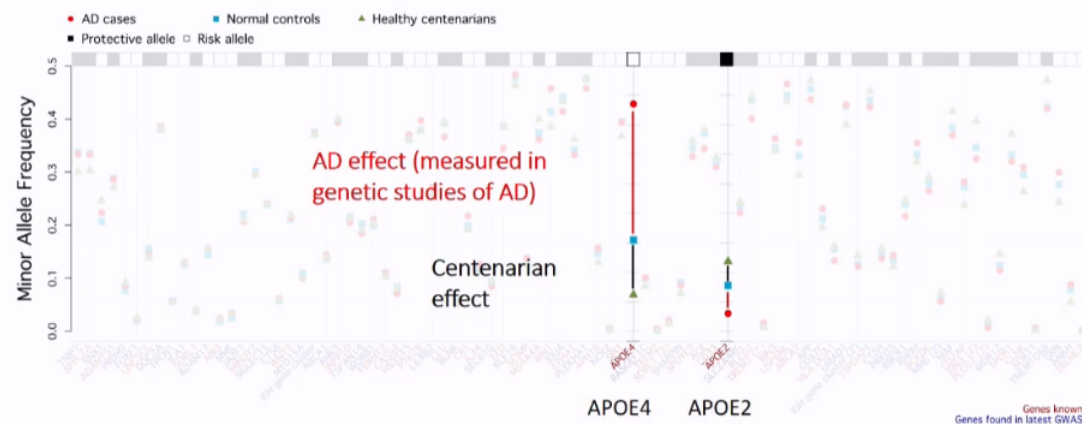
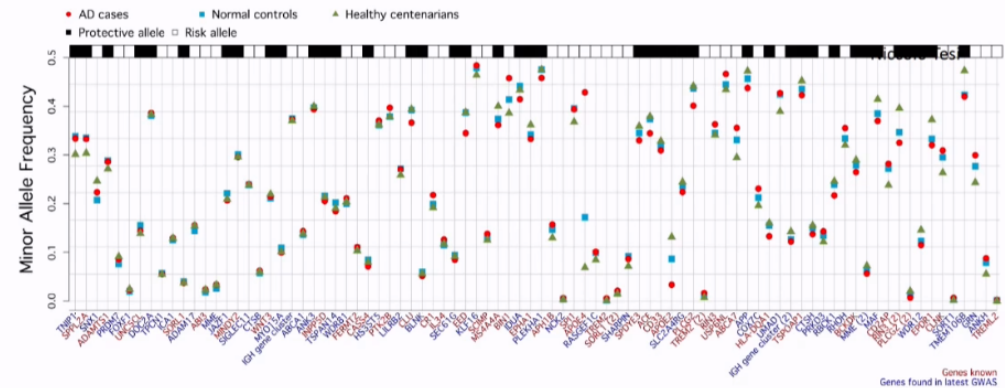
# Faktory ovlivňující zdravé stárnutí

- Genetika hraje velkou roli – dožít se 100 let záleží ze 60% na genetice



# Genetika

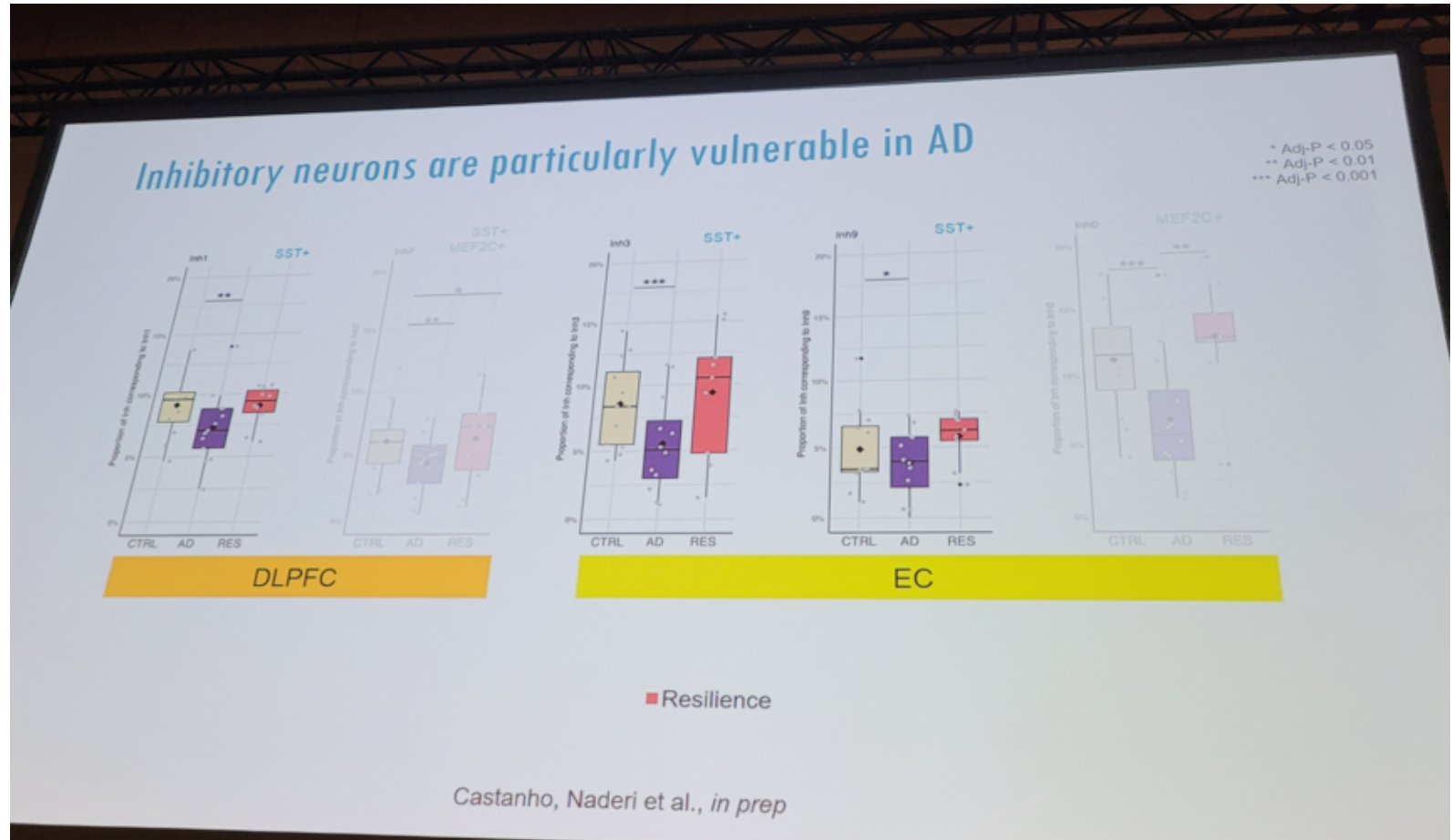
- Geny spojené s AD – pro 85% Centariáni měli nejnižší frekvence zatěžujících alel a nejvyšší frekvence protektivních alel
- Největší rozdíly v genech spojených s imunitním a endo-lysosomálním systémem → ten pravděpodobně u centariánů lépe funguje



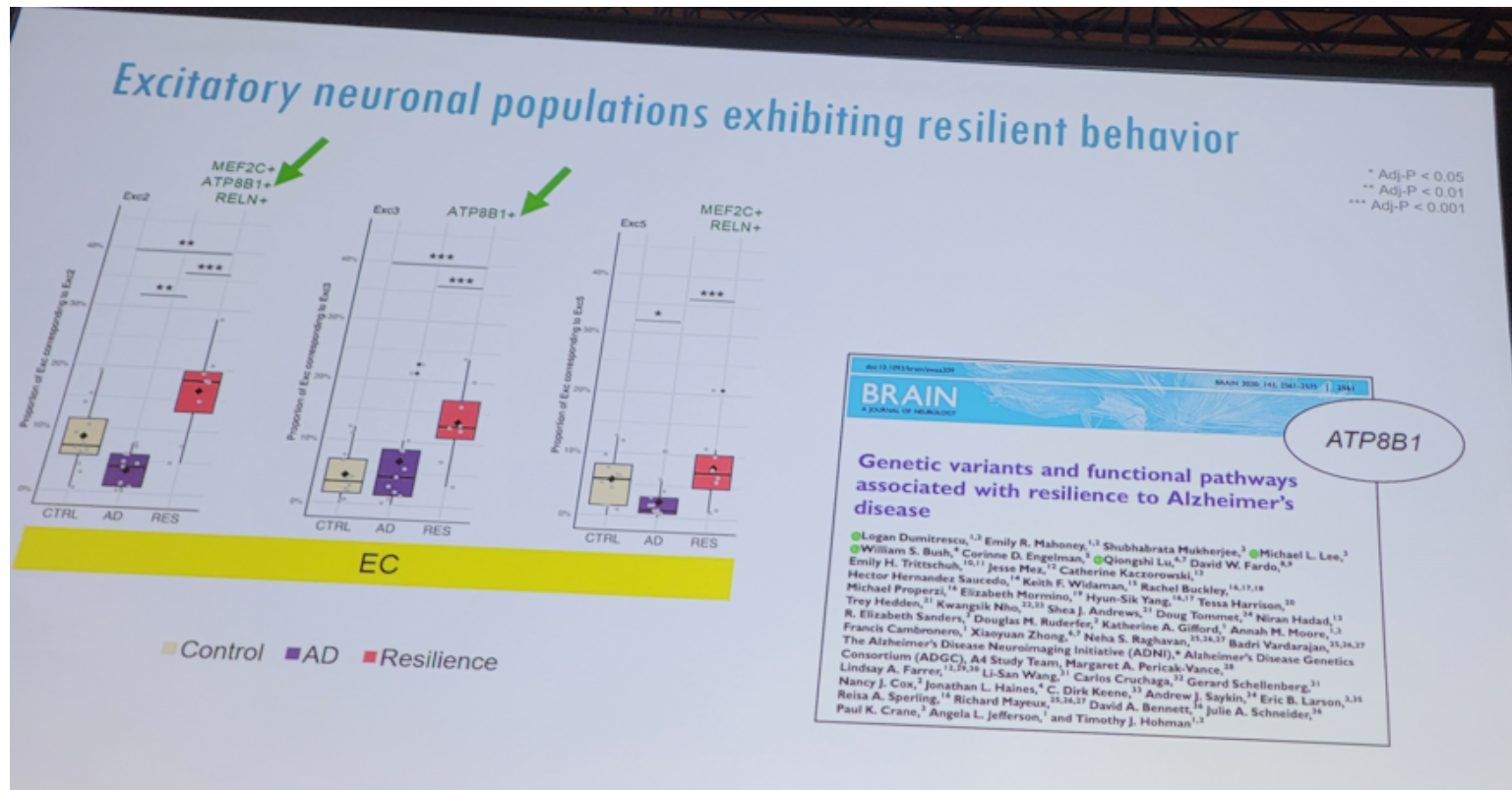
Cognitively Healthy Centenarians are genetically protected against Alzheimer's disease specifically in immune and endo-lysosomal systems

Niccolo Tei, Sven van der Lee, Marc Hulman, Natasja M. van Schoor, Martijn Huisman, Yolande Pijneburg, Wiesje M. van der Flier, Marcel Reinders, Henne Holstege  
doi: <https://doi.org/10.1101/2023.05.16.23290049>

# AN a odolnost



# AN a odolnost



# What do the centenarians say?

Eat an egg every day

Never be bored

Never complain!

No drugs, no smoking,  
no alcohol and  
not too many women

Eat lots of onions and fish

Celebrate Carnival until  
at least age 90



One dismisses the labor and solely regards the purpose

Eat a teaspoon of peanut butter every day

Drink nice (expensive) red wine, never drink white wine

# Kognitivní rezerva (KR) a mozková plasticita

– Neurální rezerva: premorbidní **vlastnosti** sítě, které zvyšují odolnost vůči patologickým změnám mozku

– zahrnuje:

- a) Kapacitu: max úroveň aktivity, kterou mohou síť generovat
- b) Efektivitu: jak efektivně se aktivita sítě promítá do kognitivních schopností

– Neurální kompenzace: **obranyschopnost** mozku vůči patologickým změnám

– Závisí na flexibilitě (adaptabilitě sítí a míře, v jaké se mohou síť navzájem nahrazovat, zvýšeně mezi sebou propojovat)

Stern (2012; in Lancet)

# Determinanty KR

## –Vzdělání

–Povolání

–Volnočasové aktivity

–Pravidelné (aerobní) cvičení

–IQ

–Premorbidní objem mozku

–Genetické faktory

# Odhad KR

– Hypotetický konstrukt → není měřitelný přímo

– Determinanty KR jako vhodné proxy

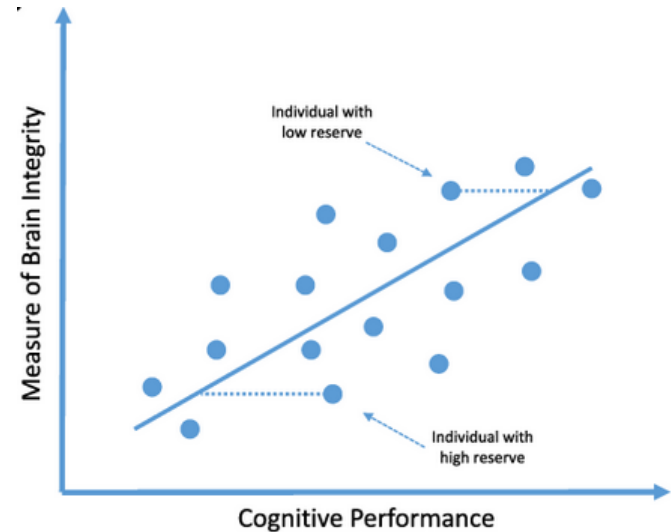
- ! Souvisí se vzděláním a životním stylem
- ! Vzájemně spolu korelují
- ! **Jsou statické** (od určitého věku neměnné)



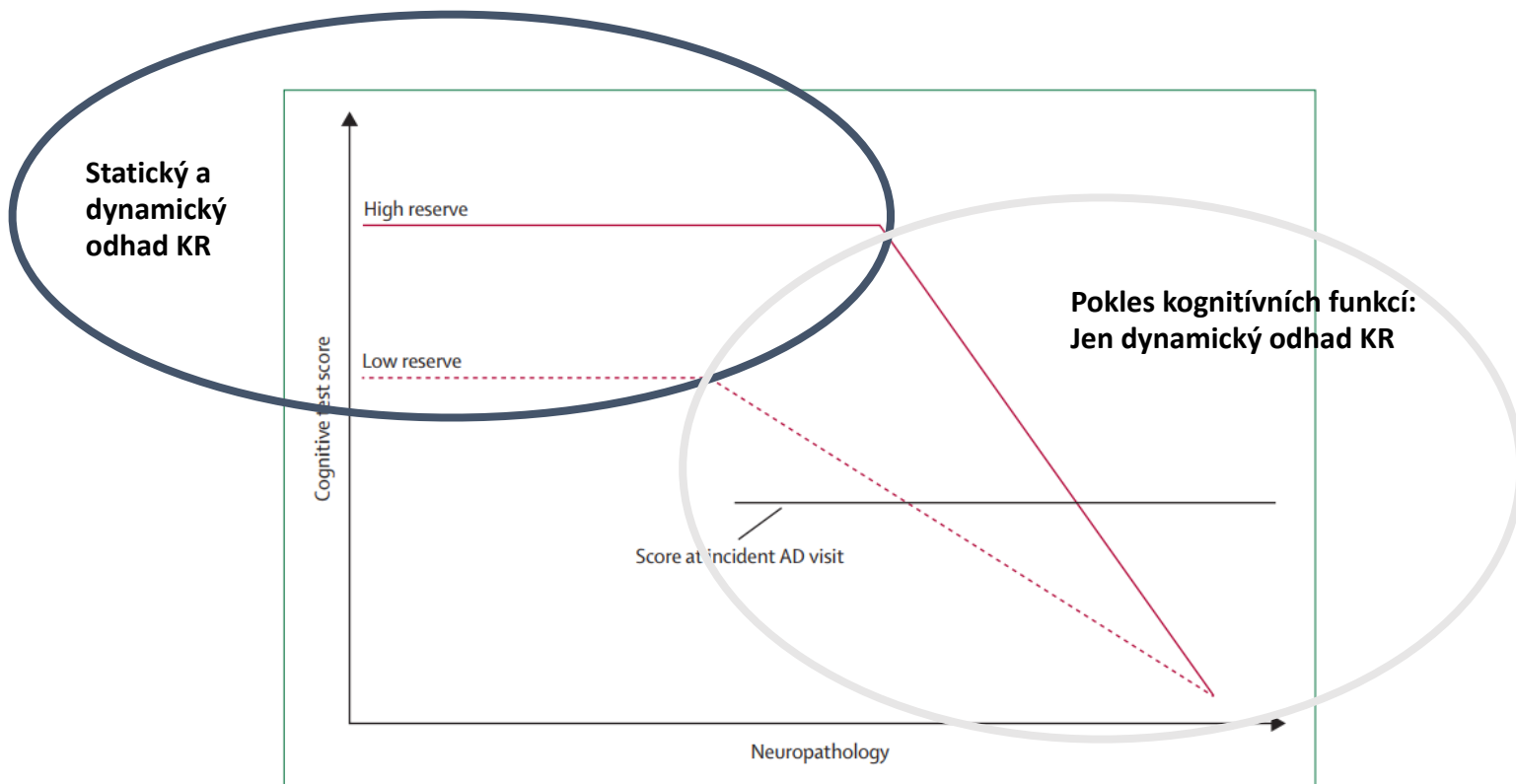
– vs. **dynamické odhady**

– Např. reziduální odhad

Jones et al. (2011)

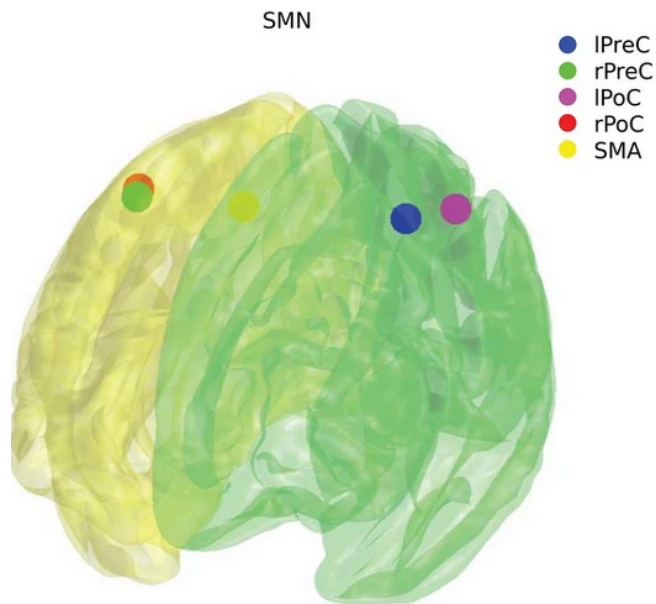




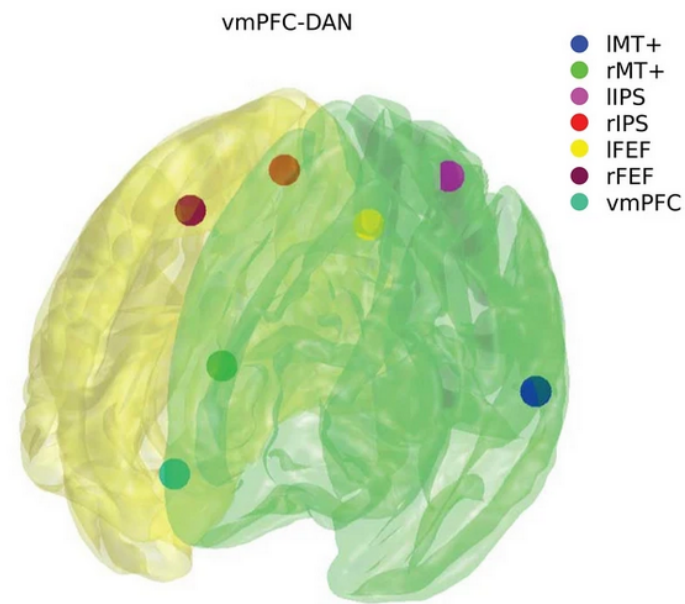


**Figure 1: Hypothesised change in memory function over time in individuals with high and low cognitive reserve**

Zdroj: Stern, Y (in Lancet, 2012)

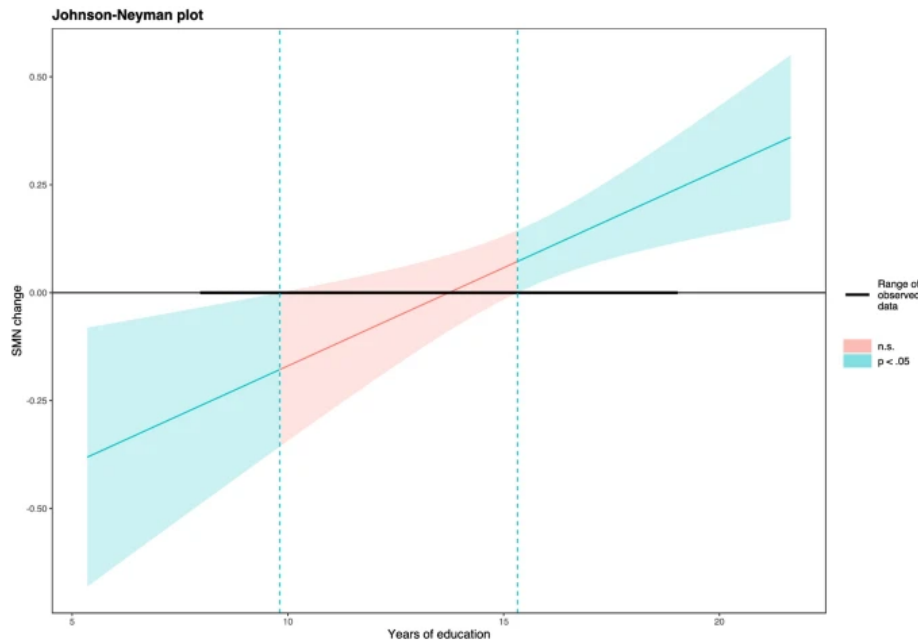


- SMN: senzomotorická síť: Posílení po motorických intervencích  
(i.e. McGregor et al., 2018; Voss et al., 2010)



- Mezisíťová konektivita aDMN-DAN (přední části DMN – dorsální pozornostní síť) má výraznou regulační funkci a souvisí s kognitivní efektivitou, pracovní a epizodickou pamětí  
(i.e. Spreng et al., 2017; Crosson et al., 1999, Novakova et al., 2020)

# Výsledky moderačních analýz



–Zvýšení funkční konektivity SMN po DI u jedinců s vyšší KR (15,34 let vzdělání;  $t(58) = 3.17, p = .002$ )

–Nezávislé na věku, pohlaví

–Změny funkční konektivity aDMN-DAN souvisely pozitivně s DI ( $t(58) = 2.16, p = .035$ )

–Nezávislé na KR ( $p = .49$ ), věku, pohlaví

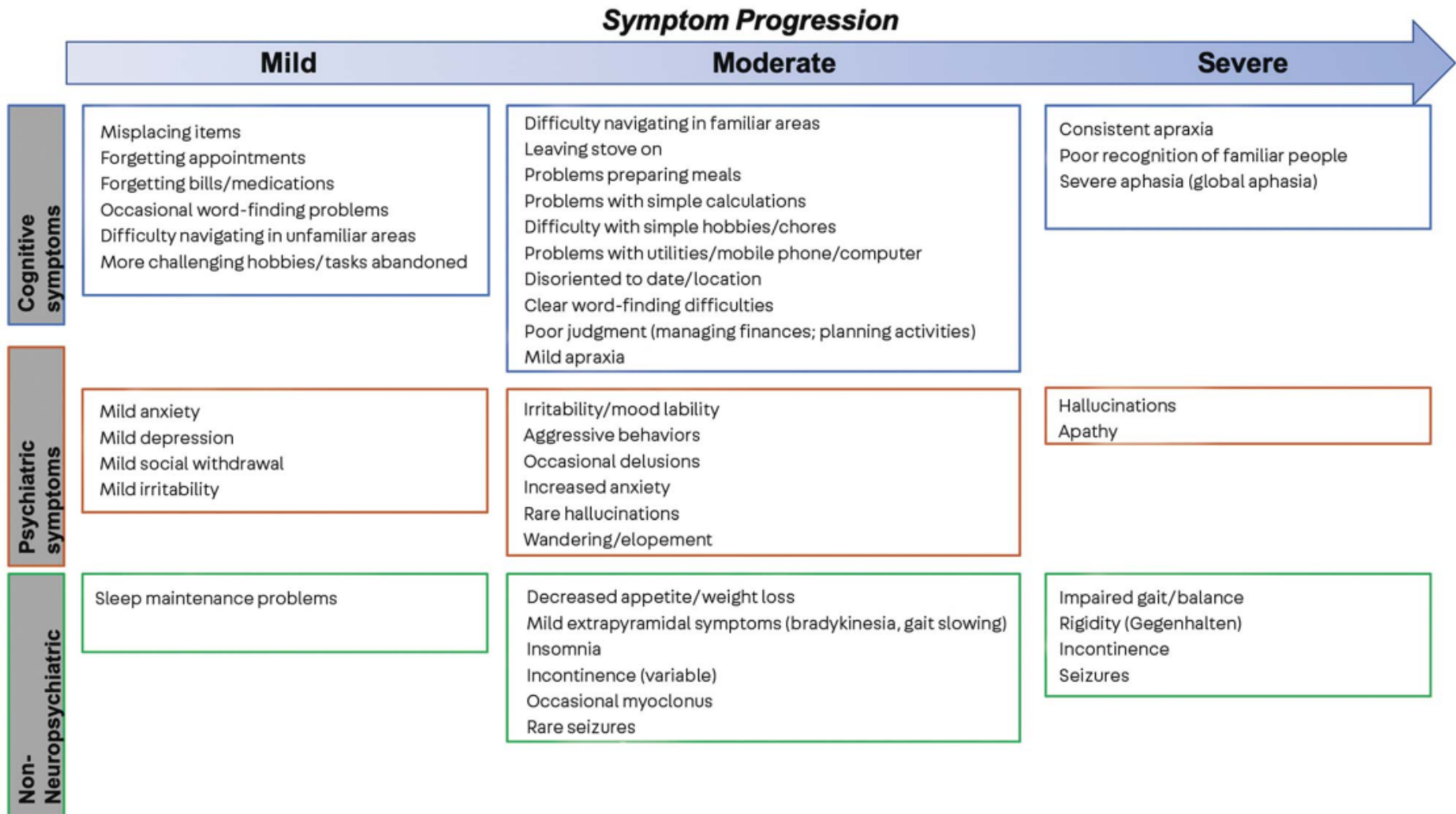
# Výsledky korelačních analýz

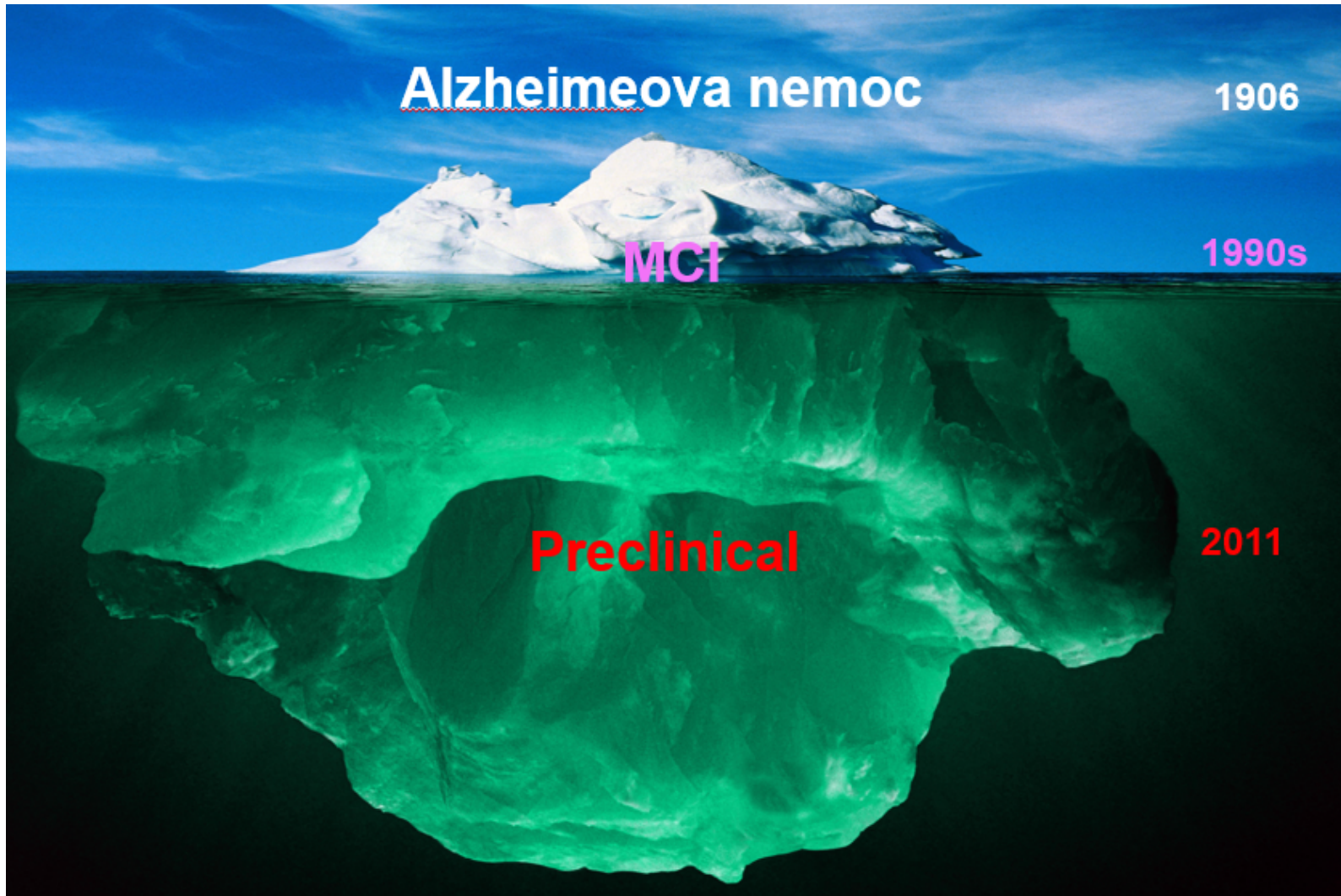
- Zvýšení FK SMN korelovalo se zlepšením v testu 8-Foot up and Go ( $r = -.21, p < .05$ ) – hodnotí funkční zdatnost
- Zvýšení FK DAN-aDMN korelovalo se zlepšením ve figurální fluenci (FPT) ( $r = .21, p < .05$ ) – hodnotí exekutivní funkce
  - Vstupní FK SMN a DAN-aDMN nekorelovala s testy

# Take home message

- Tanec – zábavnější trénink, sociální interakce, učení se novým pohybům, hudba, rytmus,...
- Neurogeneze, zvýšené prokrvení, angiogeneze, synaptogeneze → zlepšení kognitivních funkcí, nálady, fyzické zdatnosti, rovnováhy
- Změny plasticity mozku včetně zvětšení šířky kortexu
- Míra a kvalita plastických změn v závislosti na kognitivní rezervě

# Progrese symptomů AN





## NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease

Clifford R. Jack Jr.<sup>a,\*</sup>, David A. Bennett<sup>b</sup>, Kaj Blennow<sup>c</sup>, Maria C. Carrillo<sup>d</sup>, Billy Dunn<sup>e</sup>, Samantha Budd Haerberlein<sup>f</sup>, David M. Holtzman<sup>g</sup>, William Jagust<sup>h</sup>, Frank Jessen<sup>i</sup>, Jason Karlawish<sup>j</sup>, Enchi Liu<sup>k</sup>, Jose Luis Molinuevo<sup>l</sup>, Thomas Montine<sup>m</sup>, Creighton Phelps<sup>n</sup>, Katherine P. Rankin<sup>o</sup>, Christopher C. Rowe<sup>p</sup>, Philip Scheltens<sup>q</sup>, Eric Siemers<sup>r</sup>, Heather M. Snyder<sup>d</sup>, and Reisa Sperling<sup>s</sup>

		Cognitive stage		
		Cognitively Unimpaired	Mild Cognitive Impairment	Dementia
Biomarker Profile	A <sup>-</sup> T <sup>-</sup> (N) <sup>-</sup>	normal AD biomarkers. cognitively unimpaired	normal AD biomarkers with MCI	normal AD biomarkers with dementia
	A <sup>+</sup> T (N)	Preclinical Alzheimer's pathologic change	Alzheimer's pathologic change with MCI	Alzheimer's pathologic change with dementia
	A <sup>+</sup> T <sup>+</sup> (N) <sup>-</sup>	Preclinical Alzheimer's disease	Alzheimer's disease with MCI(Prodromal AD)	Alzheimer's disease with dementia
	A <sup>+</sup> T <sup>+</sup> (N) <sup>+</sup>			
	A <sup>+</sup> T (N) <sup>+</sup>	Alzheimer's and concomitant suspected non Alzheimer's pathologic change, cognitively unimpaired	Alzheimer's and concomitant suspected non Alzheimer's pathologic change with MCI	Alzheimer's and concomitant suspected non Alzheimer's pathologic change with dementia
	A <sup>-</sup> T <sup>+</sup> (N) <sup>-</sup>	non-Alzheimer's pathologic change, cognitively unimpaired	non-Alzheimer's pathologic change with MCI	non-Alzheimer's pathologic change with dementia
	A <sup>-</sup> T <sup>-</sup> (N) <sup>+</sup>			
A <sup>-</sup> T <sup>+</sup> (W) <sup>+</sup>				



# AD revidovaná kritéria pro výzkum (ATN 2018, Jack et al), revidovaná verze pro 2024


**2024 Revised Criteria: Core-2 Biomarkers**  
*Nonspecific Processes and Co-Pathology*

Role in monitoring and prognosis

Core-2	Plasma	CSF	Imaging
T <sub>2</sub> (AD tau proteinopathy)	▪ p-tau205	▪ p-tau205 ▪ MTBR-243 ▪ np-tau fragments	▪ Tau PET
N (injury/dysfunction of neuropil)	▪ NfL	▪ NfL	▪ Anatomic MR, FDG PET
I (inflammation)	▪ GFAP	▪ GFAP	
V (vascular)	▪ NfL	▪ NfL	▪ Infarction on MRI or CT, WMH
S (α synuclein)		▪ αSyn-SAA	

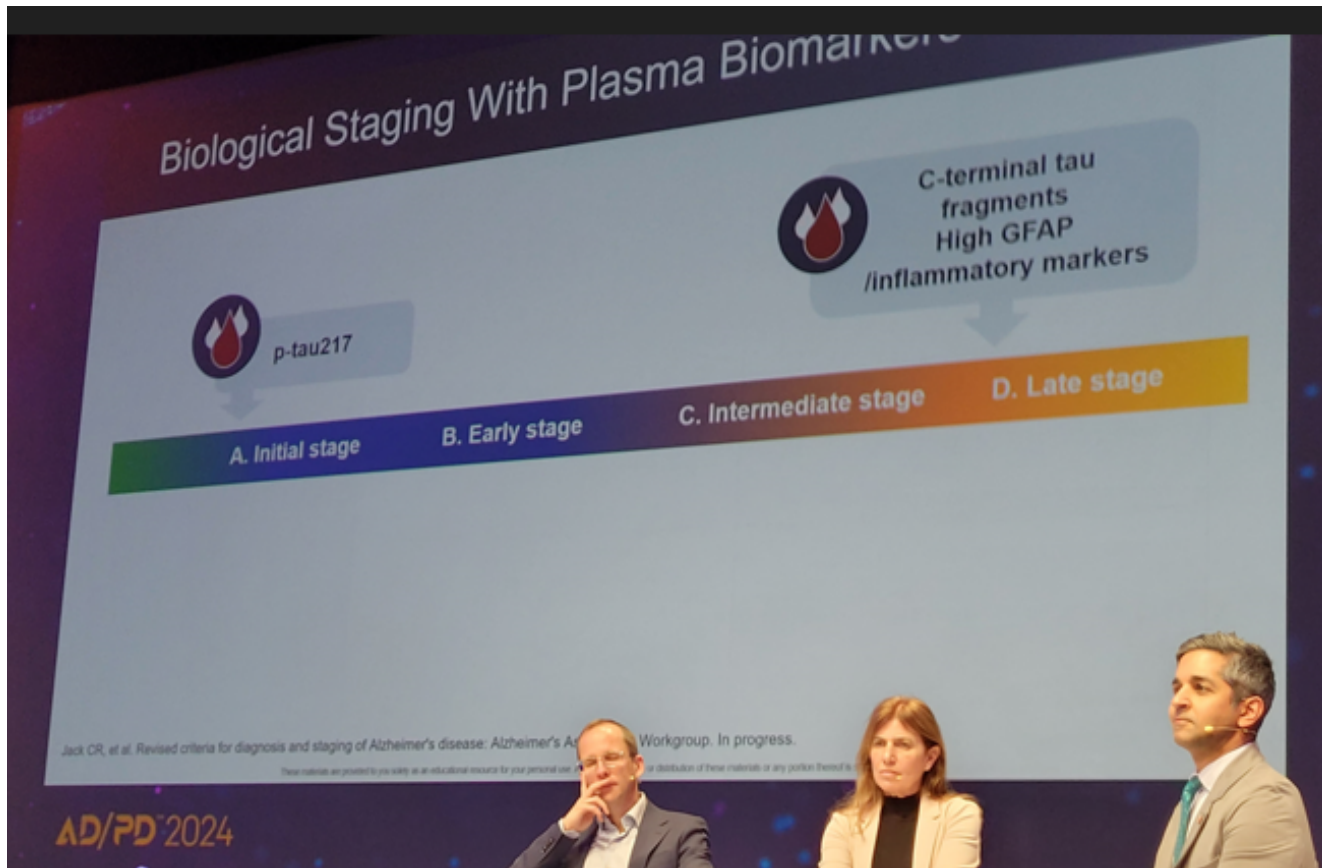
Jack CR, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. In progress.  
These materials are provided to you solely as an educational resource for your personal use. Any distribution of these materials or any portion thereof is prohibited.

**AD/PD 2024**



Z ADPD kongresu, Lisabon, 3/2024, publikace v přípravě

# Biological staging in AD



**Biological Staging With Plasma Biomarkers**

**A. Initial stage** (Green bar): p-tau217

**B. Early stage** (Blue bar)

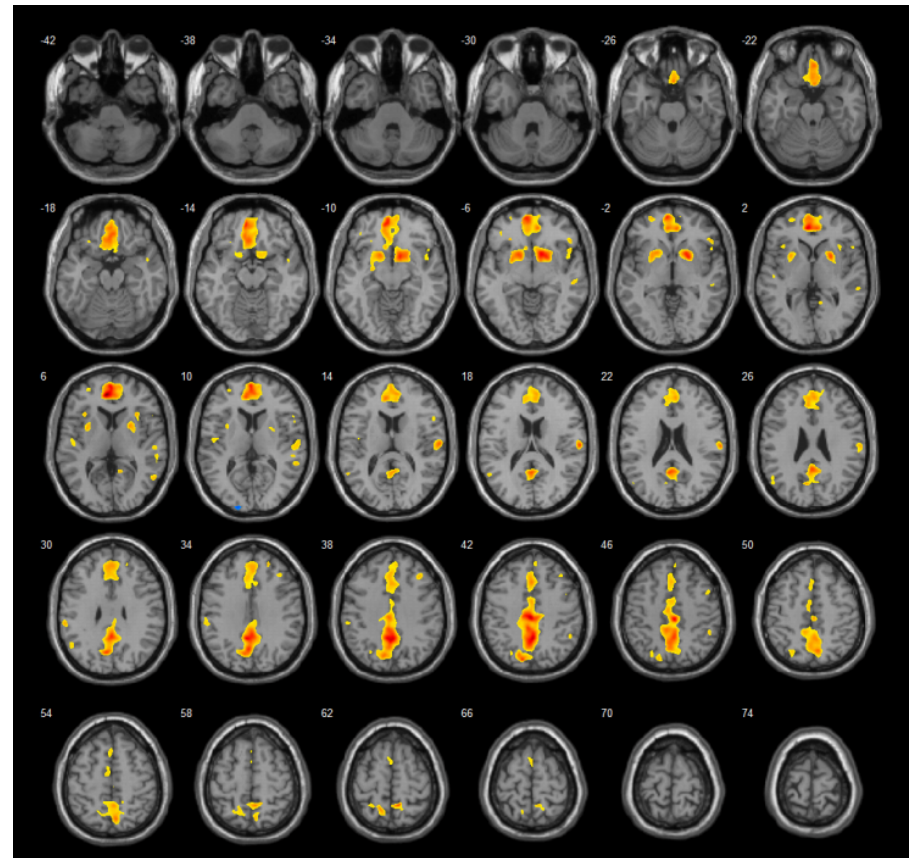
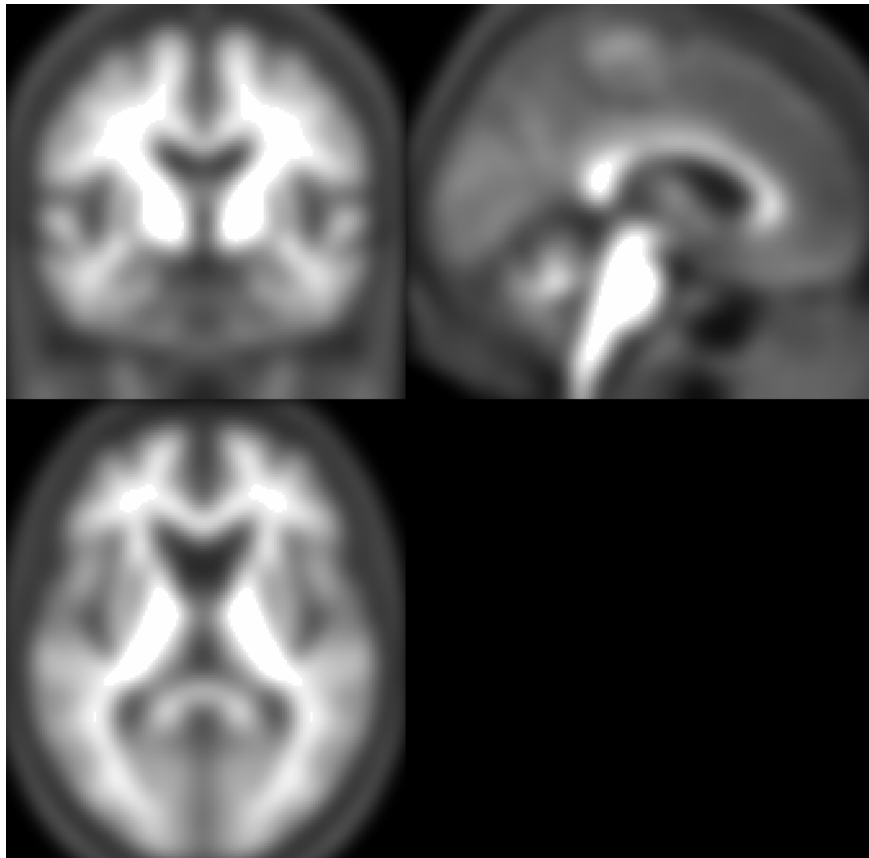
**C. Intermediate stage** (Orange bar)

**D. Late stage** (Yellow bar): C-terminal tau fragments, High GFAP, /inflammatory markers

Jack CR, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. In progress.  
These materials are provided to you solely as an educational resource for your personal use. No distribution of these materials or any portion thereof is permitted.

**AD/PD 2024**

# Amyloidový PET s flutemetamolem



# CSF tau/Ab42 poměr

- tau/Ab42 poměr  $> 0.52$  robustní CSF-AD profil pro odlišení AD od jiných typů demence (senzitivita 91%–93%; specificita 81%–84%)
- predikuje konverzi MCI do AD demence

# Moving fluid biomarkers for Alzheimer's disease from research tools to routine clinical diagnostics

2021

Henrik Zetterberg<sup>1,2,3,4\*</sup> and Kaj Blennow<sup>1,2\*</sup>



## Blood-based biomarkers for Alzheimer's disease: towards clinical implementation

Lancet Neurol 2022

*Charlotte E Teunissen, Inge M W Verberk, Elisabeth H Thijssen, Lisa Vermunt, Oskar Hansson, Henrik Zetterberg, Wiesje M van der Flier, Michelle M Mielke, Marta del Campo*

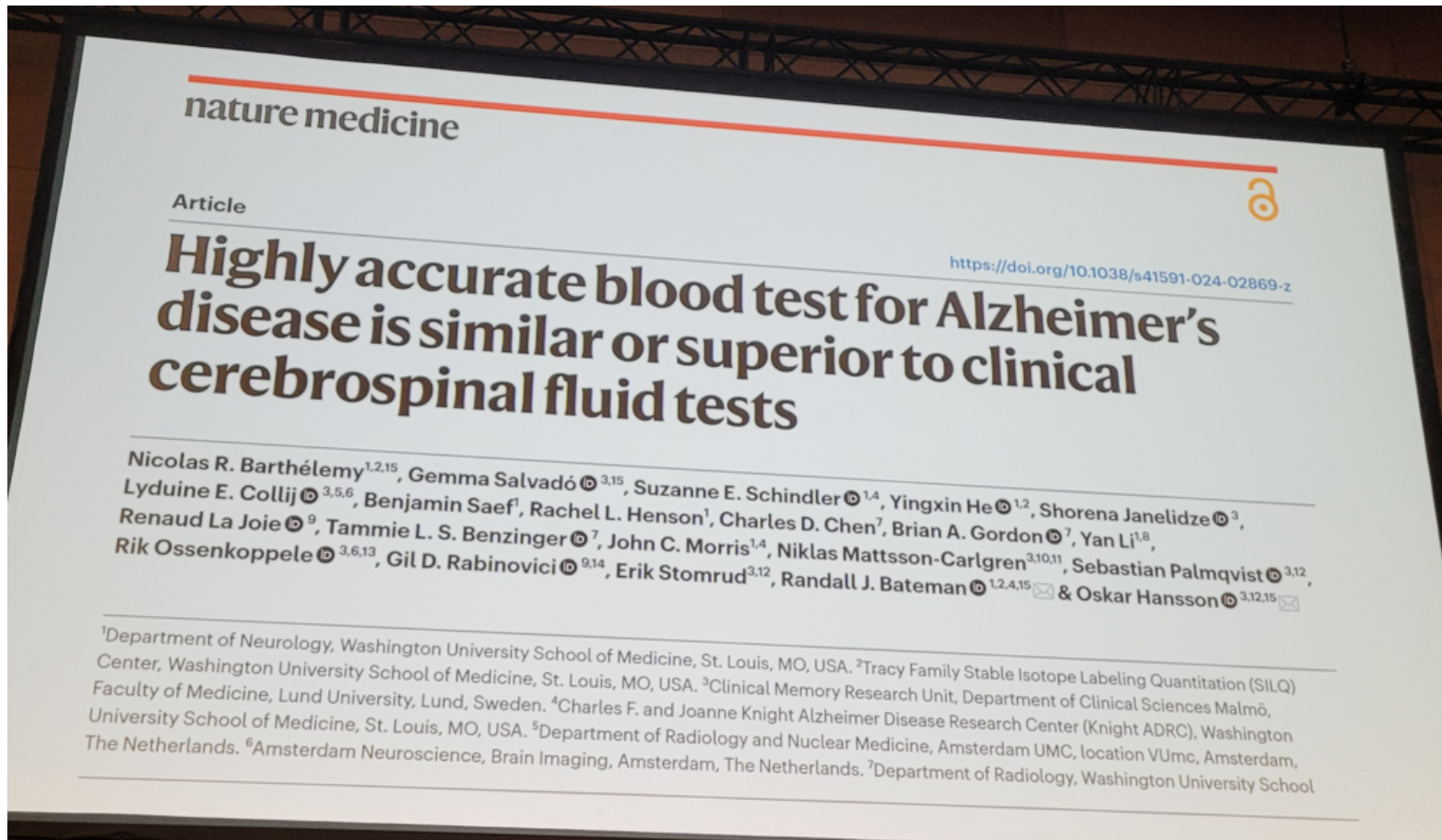
JAMA Neurology | **Original Investigation**

## Mitigating the Associations of Kidney Dysfunction With Blood Biomarkers of Alzheimer Disease by Using Phosphorylated Tau to Total Tau Ratios

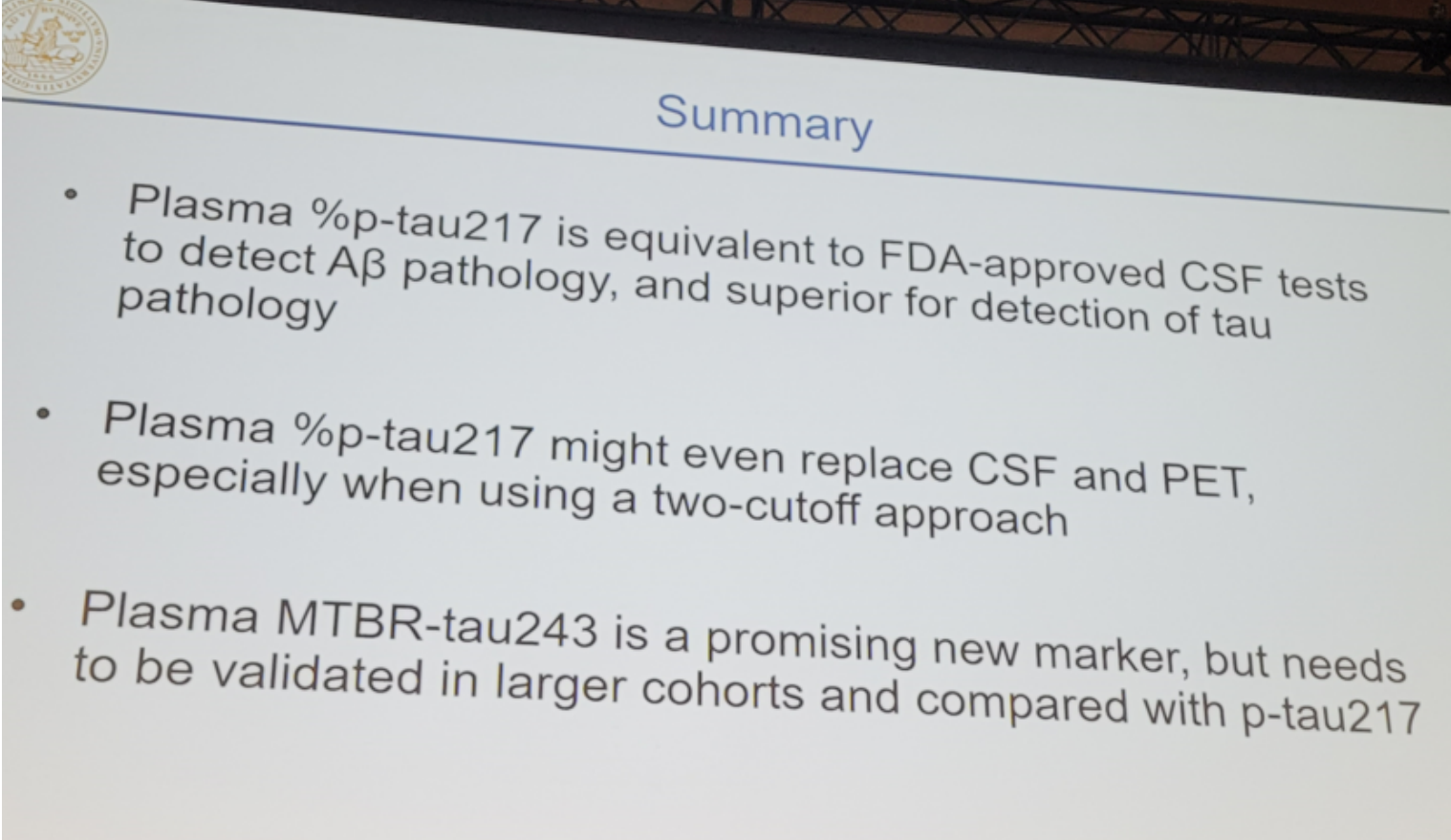
Shorena Janelidze, PhD; Nicolas R. Barthélemy, PhD; Yingxin He, PhD; Randall J. Bateman, MD; Oskar Hansson, MD, PhD

2023

# Tekutinové BM: plazma



# Tekutinové BM: plazma



Summary

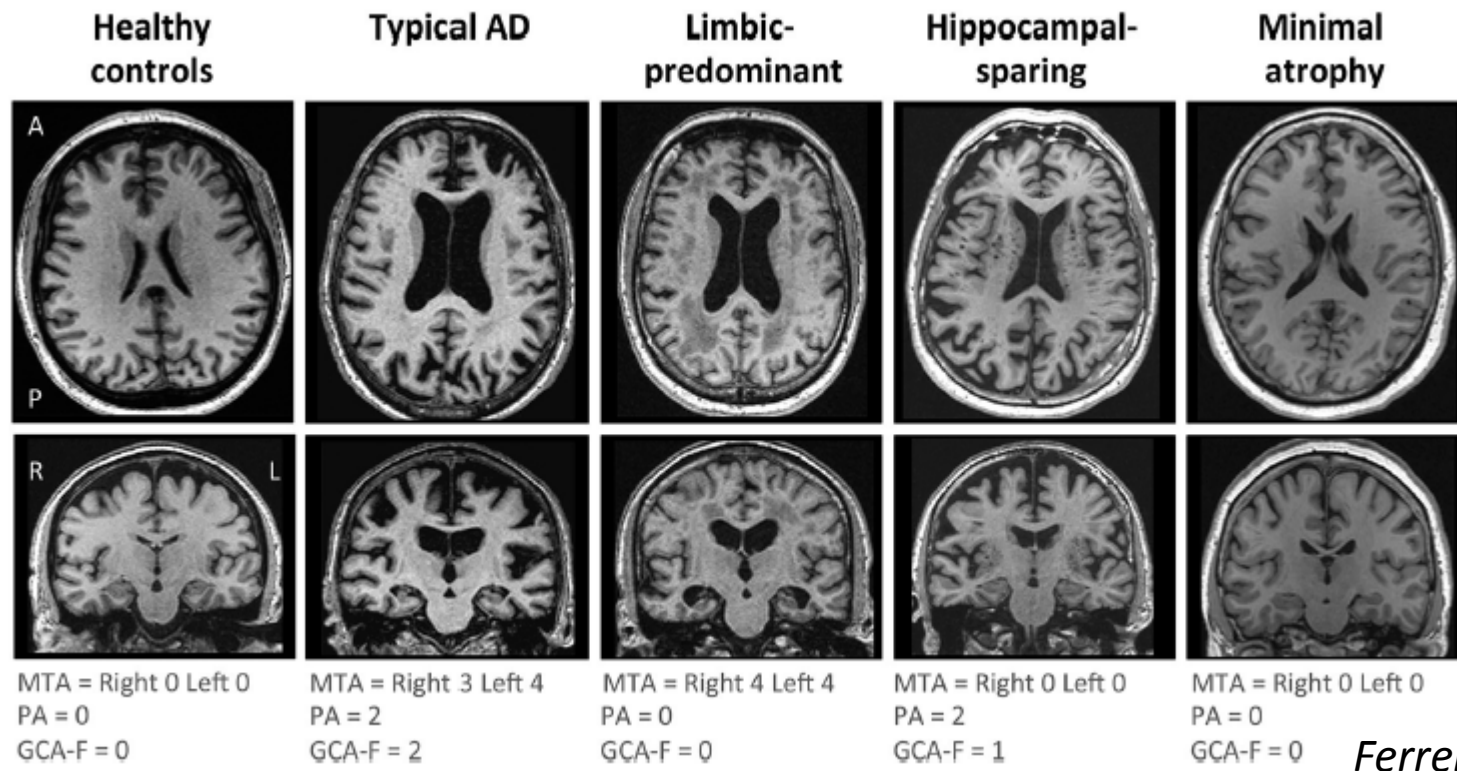
- Plasma %p-tau217 is equivalent to FDA-approved CSF tests to detect A $\beta$  pathology, and superior for detection of tau pathology
- Plasma %p-tau217 might even replace CSF and PET, especially when using a two-cutoff approach
- Plasma MTBR-tau243 is a promising new marker, but needs to be validated in larger cohorts and compared with p-tau217

# Neuropatologicky definované varianty AN

“limbická”, “šetřící hippocampus”

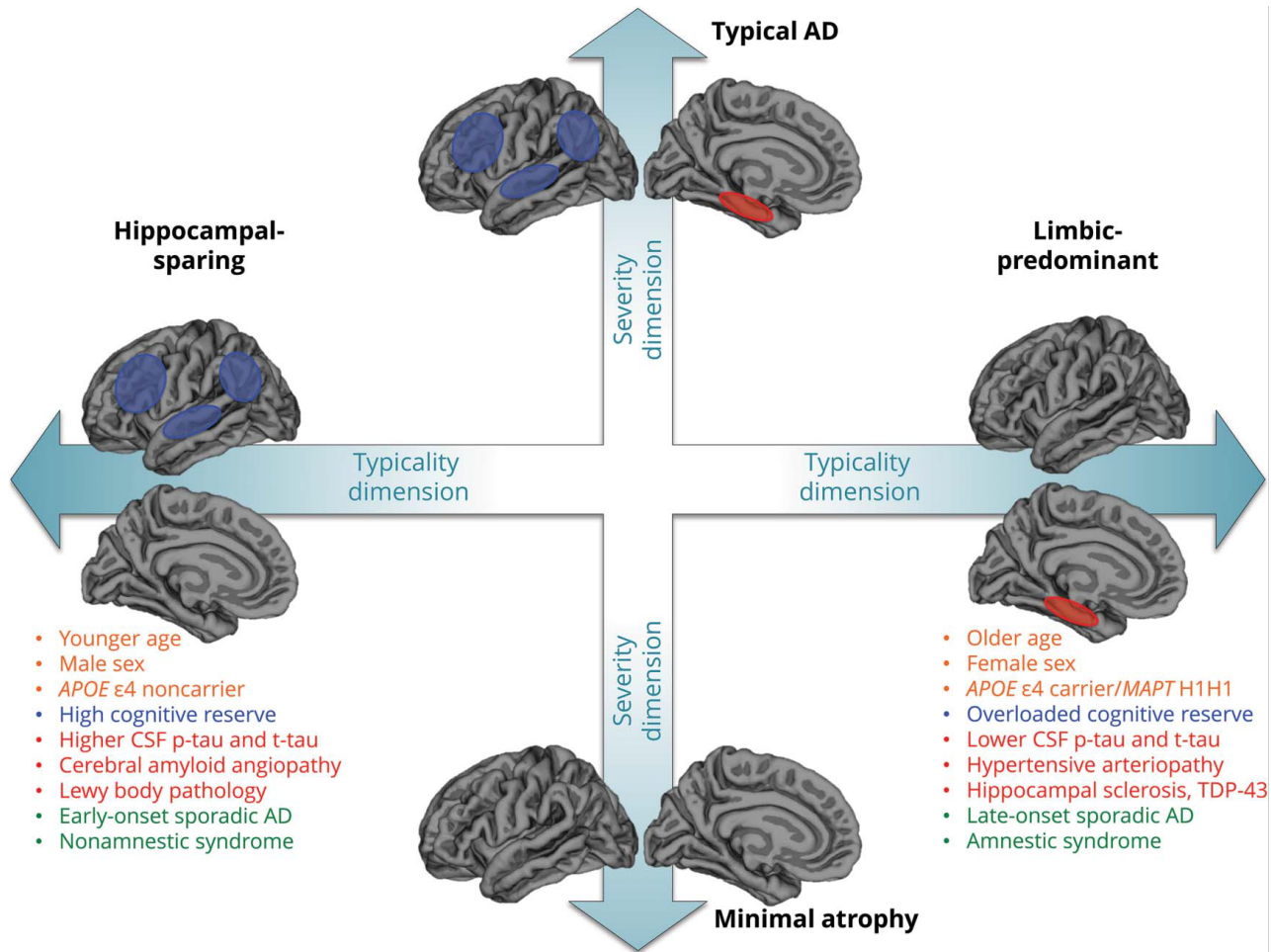
“typická” (kombinovaná limbická + šetřící hipp)

(Murray et al. 2011, Whitwell et al. 2012, Risacher et al. 2017, Ossenkoppele et al. 2020)



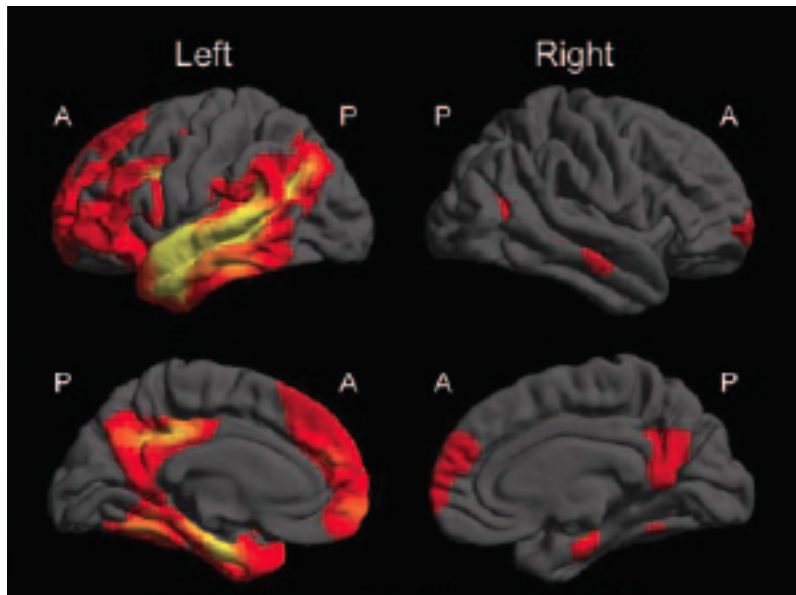


# Biologické subtypy AD

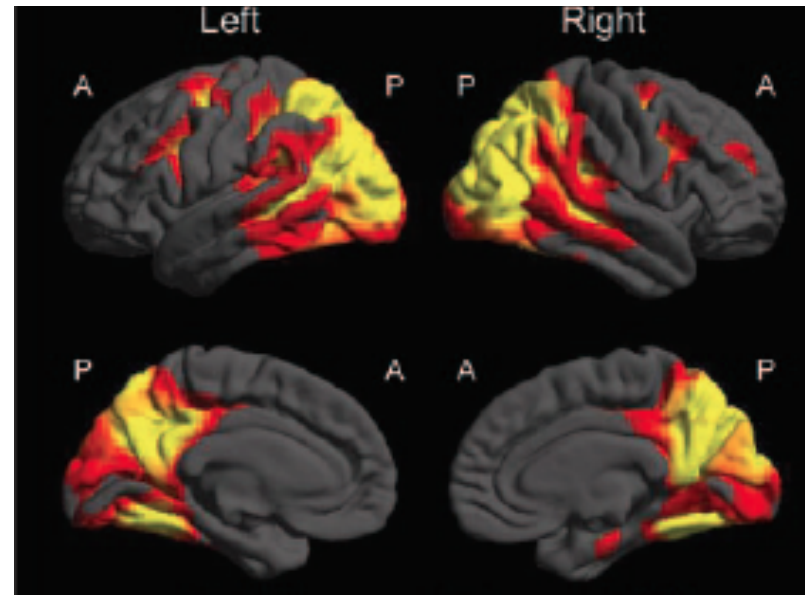


# Atypické varianty AN

## Logopenická varianta PPA



## Zadní kortikální atrofie



Frontální varianta (těžko odlišitelný od behaviorální varianty FTD, přínos biomarkerů CBS (syndrom kortikobazální degenerace), z cca 50% se jedná o AD patologii (obě varianty viz další přednáška Tauopatie, TDP-43 a FTD spektrum)



ELSEVIER



CrossMark

Alzheimer's & Dementia 13 (2017) 870-884

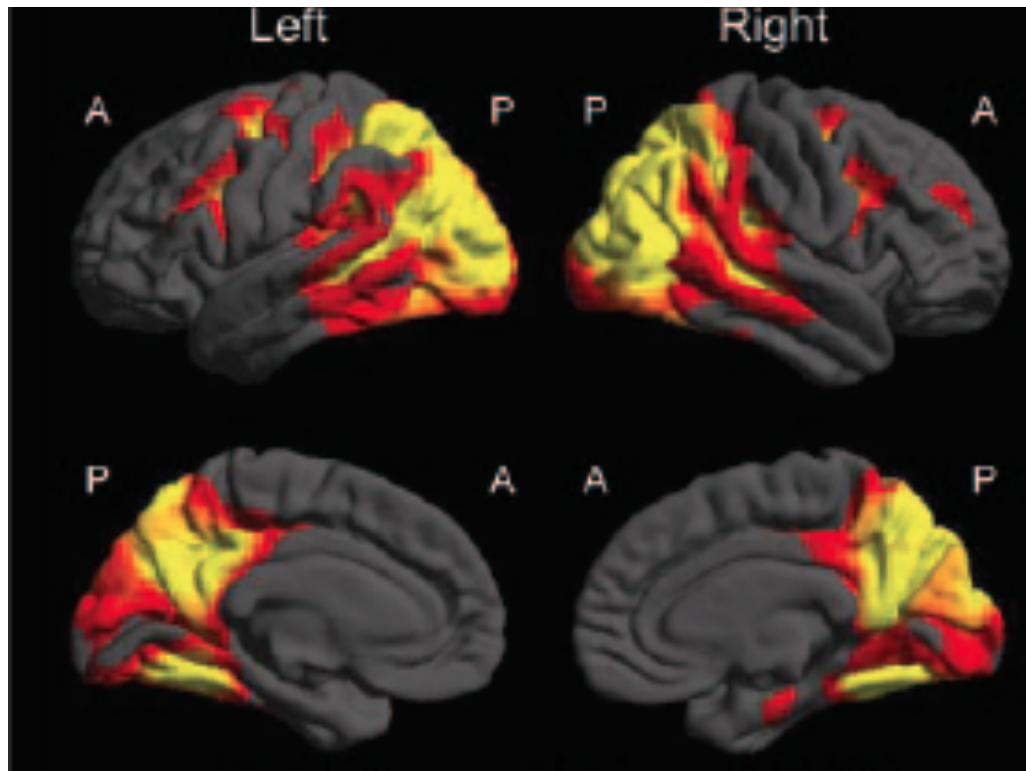
Alzheimer's  
&  
Dementia

Featured Article

## Consensus classification of posterior cortical atrophy

Sebastian J. Crutch<sup>a,\*</sup>, Jonathan M. Schott<sup>a</sup>, Gil D. Rabinovici<sup>b</sup>, Melissa Murray<sup>c</sup>,  
Julie S. Snowden<sup>d,e</sup>, Wiesje M. van der Flier<sup>f,g</sup>, Bradford C. Dickerson<sup>h</sup>, Rik Vandenberghe<sup>i</sup>,  
Samrah Ahmed<sup>j</sup>, Thomas H. Bak<sup>k</sup>, Bradley F. Boeve<sup>l</sup>, Christopher Butler<sup>i</sup>, Stefano F. Cappa<sup>m</sup>,  
Mathieu Ceccaldi<sup>n</sup>, Leonardo Cruz de Souza<sup>o</sup>, Bruno Dubois<sup>p</sup>, Olivier Felician<sup>q,r</sup>,  
Douglas Galasko<sup>s</sup>, Jonathan Graff-Radford<sup>l</sup>, Neill R. Graff-Radford<sup>t</sup>, Patrick R. Hof<sup>u,v</sup>,  
Pierre Krolak-Salmon<sup>w</sup>, Manja Lehmann<sup>a,b</sup>, Eloi Magnin<sup>x</sup>, Mario F. Mendez<sup>y</sup>, Peter J. Nestor<sup>z</sup>,  
Chiadi U. Onyike<sup>aa</sup>, Victoria S. Pelak<sup>bb,cc</sup>, Yolande Pijnenburg<sup>f,g</sup>, Silvia Primativo<sup>a</sup>,  
Martin N. Rossor<sup>a</sup>, Natalie S. Ryan<sup>a</sup>, Philip Scheltens<sup>f,g</sup>, Timothy J. Shakespeare<sup>a</sup>,  
Aida Suárez González<sup>a,dd</sup>, David F. Tang-Wai<sup>ee</sup>, Keir X. X. Yong<sup>a</sup>, Maria Carrillo<sup>ff</sup>, Nick C. Fox<sup>a</sup>,  
on behalf of the Alzheimer's Association ISTAART Atypical Alzheimer's Disease and Associated  
Syndromes Professional Interest Area

# Zadní kortikální atrofie (PCA)



Ridgway et al., 2012

# Typické symptomy PCA

Porucha vnímání  
prostoru

Simultanagnózie

Zraková  
agnózie.prozopagnózie

Konstrukční apraxie

Okulomotorická  
apraxie

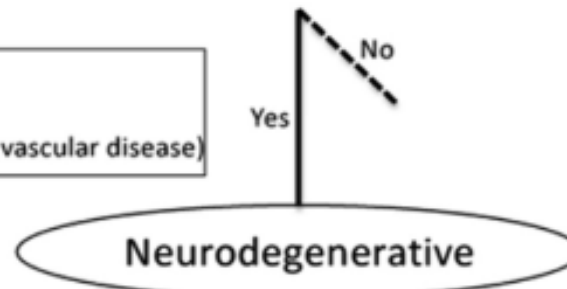
Optická ataxie

Alexie, agrafie

Gerstmannův syndrom

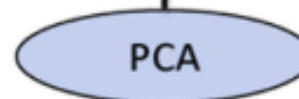
**Is it neurodegenerative?**

1. Insidious onset
2. Gradual progression
3. No other cause (e.g. tumor, vascular disease)



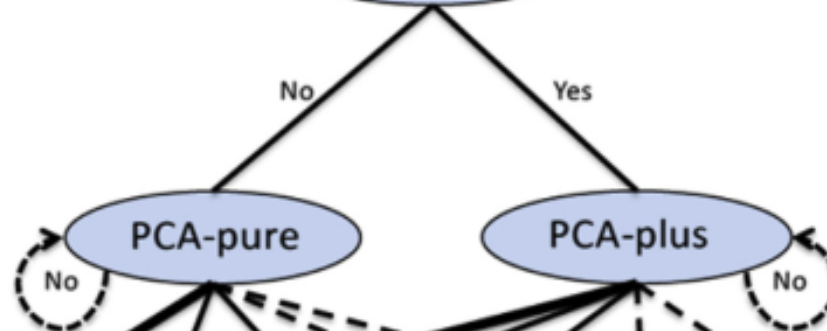
**Is it preferentially posterior?** Fulfills PCA core clinical/cognitive features +/- supportive evidence of predominant occipital, parietal and/or occipitotemporal atrophy/dysfunction on brain imaging

*Classification Level 1:*



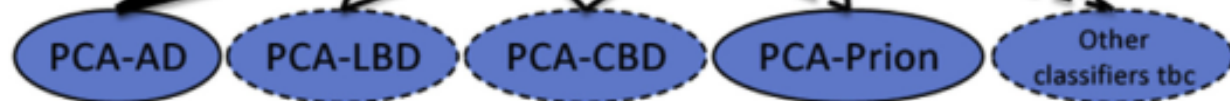
**Does the patient also meet core criteria for another neurodegenerative syndrome?**

*Classification Level 2:*

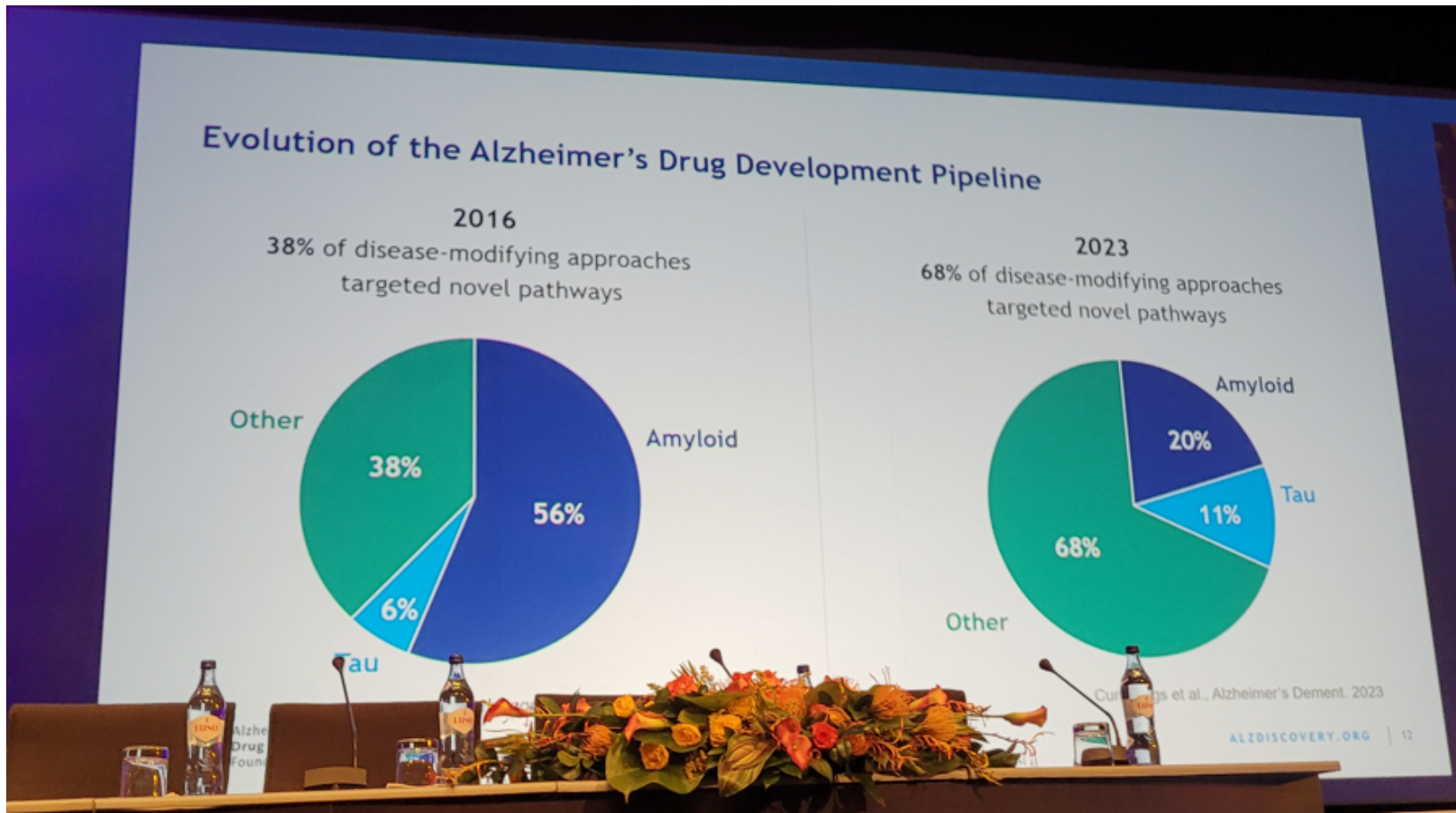


**Are biomarkers available and conclusive?**  
 [solid ovals: existing biomarkers; dashed ovals: biomarkers pending]

*Classification Level 3:*



# AN a léčba (lecanemab: Lequembli Lilly)



# ARIA (amyloid-related imaging abnormalities)

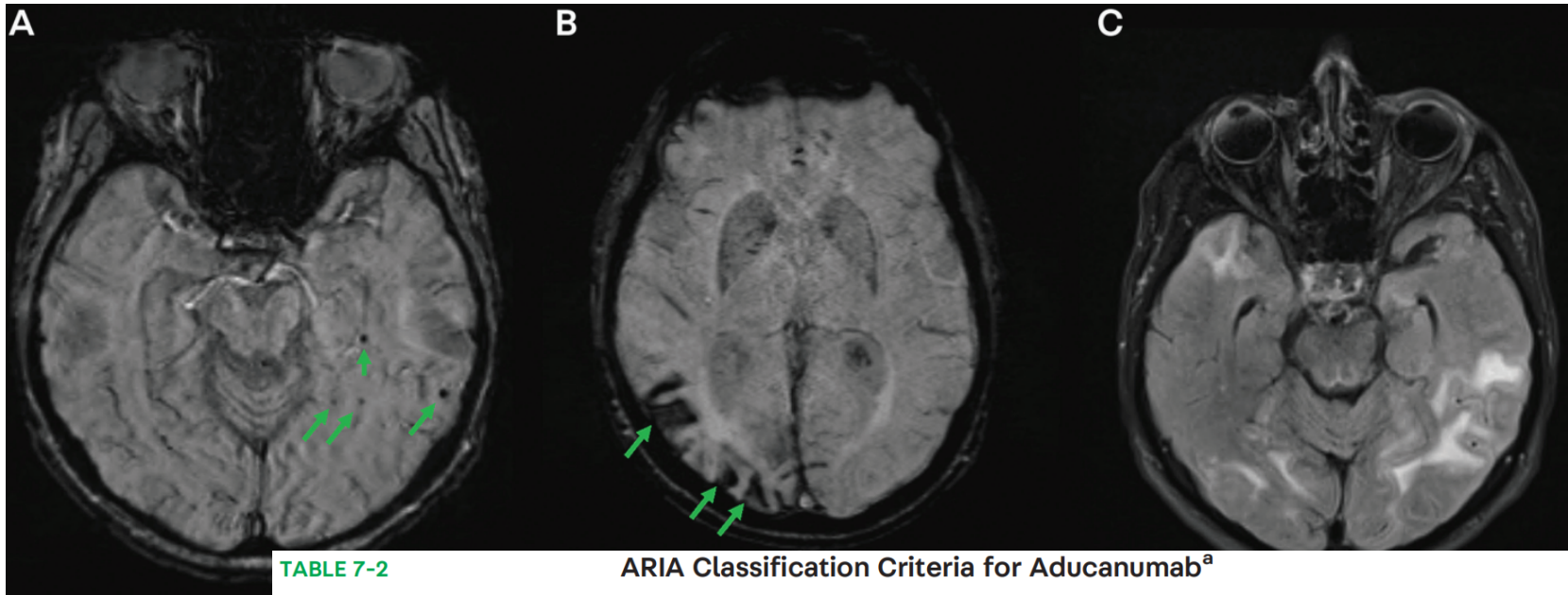
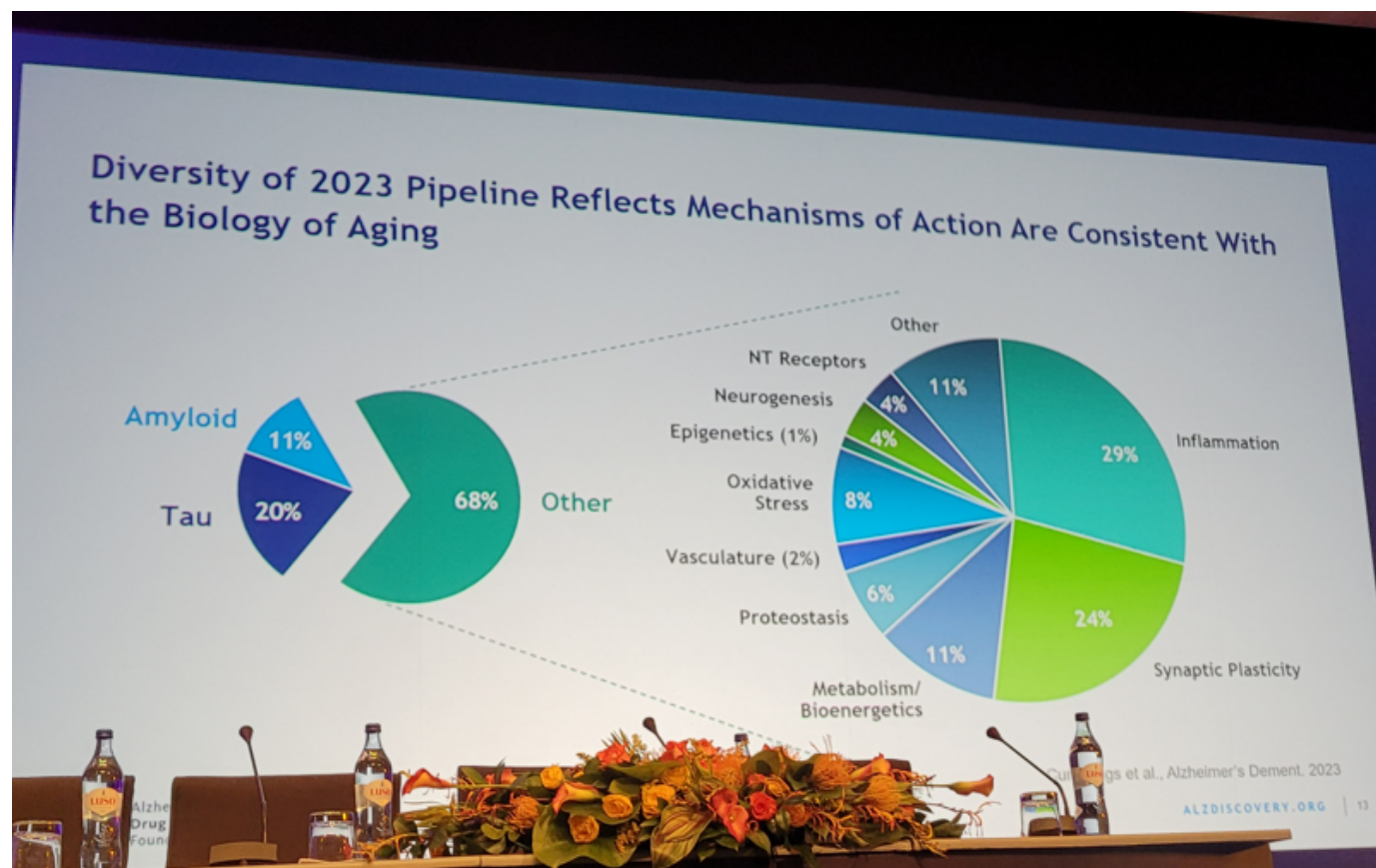


TABLE 7-2 ARIA Classification Criteria for Aducanumab<sup>a</sup>

ARIA type	Radiographic severity		
	Mild	Moderate	Severe
<b>ARIA-E</b>	Fluid-attenuated inversion recovery (FLAIR) hyperintensity confined to sulcus and/or cortex/subcortical white matter in one location <5 cm	FLAIR hyperintensity 5 to 10 cm or more than one site of involvement, each measuring <10 cm	FLAIR hyperintensity measuring >10 cm, often with significant subcortical white matter and/or sulcal involvement; one or more separate sites of involvement may be noted
<b>ARIA-H microhemorrhage</b>	≤4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more new incident microhemorrhages
<b>ARIA-H superficial siderosis</b>	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	>2 focal areas of superficial siderosis

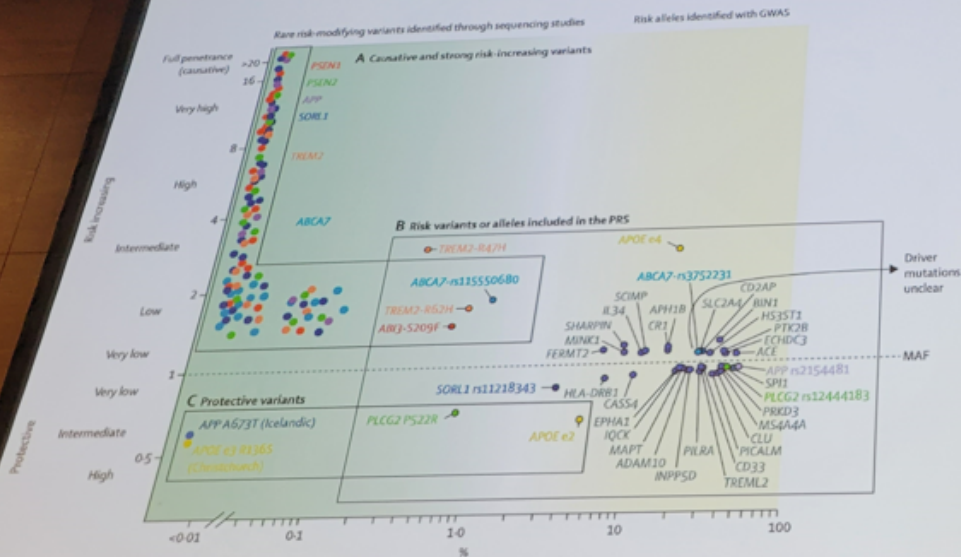


# AN a léčba

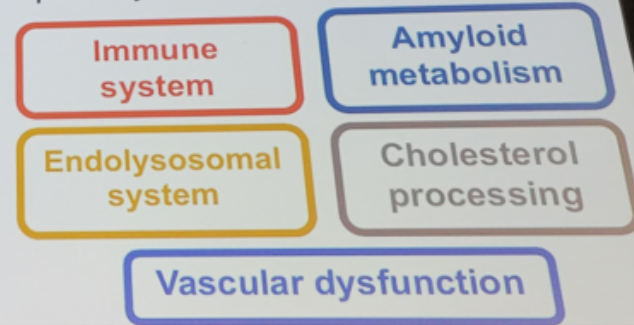


# Genetika AN a léčba

## Genetics of Alzheimer's disease



- GWAS of AD with increasing sample size have shaped our knowledge of the genetics of AD
- Now we know that at least 86 common genetic variants modify the risk of AD
- Variants affect genes, which affect the function of proteins in specific pathways



Cheltnens et al., Lancet, 2021

# Synukleinopatie: druhá nejčastější příčina degenerativní demence

Demence s  
Lewyho tělísky  
(DLB)

Parkinsonova  
nemoc  
(± MCI,  
demence)

*MSA  
(multisystémová  
atrofie)*



# A biological classification of Parkinson's disease: the SynNeurGe research diagnostic criteria

*Günter U Höglinger, Charles H Adler, Daniela Berg, Christine Klein, Tiago F Outeiro, Werner Poewe, Ronald Postuma, A Jon Stoessl, Anthony E Lang*

Lancet Neurol 2024

## **$\alpha$ -Synuclein – Neurodegeneration - Gene**

### **Imaging for neurodegeneration**

- Nigrostriatal denervation: highest sensitivity but not specific
- Cardiac denervation: moderate to high sensitivity and specificity
- PD-related metabolic pattern: but not widely available to be used in individual subjects
- Other investigational biomarkers – **MRI?**

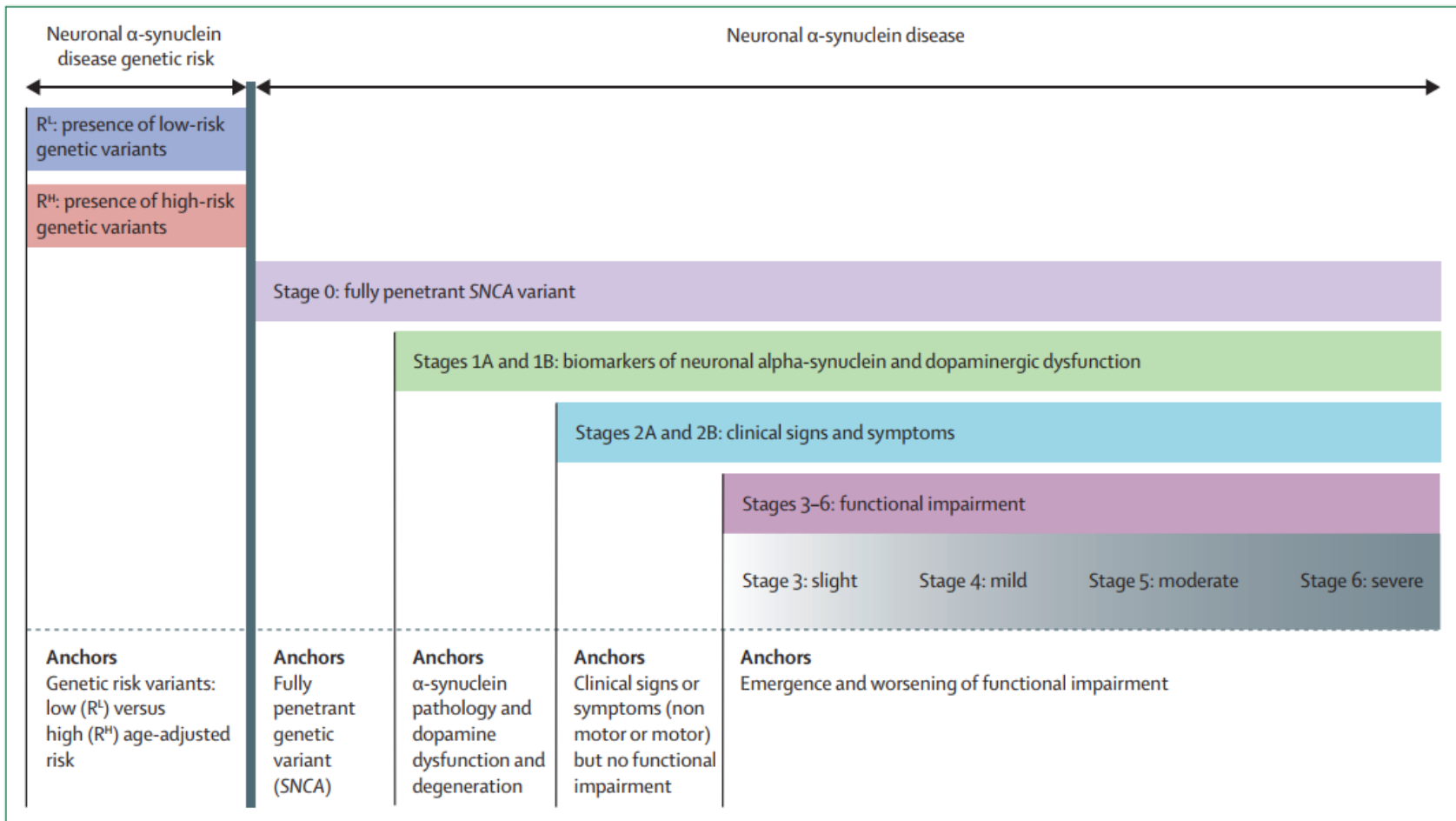


# A biological definition of neuronal $\alpha$ -synuclein disease: towards an integrated staging system for research

Tanya Simuni\*, Lana M Chahine\*, Kathleen Poston, Michael Brumm, Teresa Buracchio, Michelle Campbell, Sohini Chowdhury, Christopher Coffey, Luis Concha-Marambio, Tien Dam, Peter DiBiaso, Tatiana Foroud, Mark Frasier, Caroline Gochanour, Danna Jennings, Karl Kiebertz, Catherine M Kopil, Kalpana Merchant, Brit Mollenhauer, Thomas Montine, Kelly Nudelman, Gennaro Pagano, John Seibyl, Todd Sherer, Andrew Singleton, Diane Stephenson, Matthew Stern, Claudio Soto, Caroline M Tanner, Eduardo Tolosa, Daniel Weintraub, Yuge Xiao, Andrew Siderowf, Billy Dunn, Kenneth Marek

Lancet Neurol 2024; 23: 178–90

Parkinson's disease and dementia with Lewy bodies are currently defined by their clinical features, with  $\alpha$ -synuclein





# CSF: průkaz hyperfosforylovaného $\alpha$ -synukleinu

## Detection of $\alpha$ -synuclein in CSF by RT-QuIC in patients with isolated rapid-eye-movement sleep behaviour disorder: a longitudinal observational study

*Alex Iranzo, Graham Fairfoul, Anutra Chumbala Na Ayudhaya, Monica Serradell, Ellen Gelpi, Isabel Vilaseca, Raquel Sanchez-Valle, Carles Gaig, Joan Santamaria, Eduard Tolosa, Renata L Riha, Alison J E Green*

Lancet Neurol 2021

## RT-QuIC Detection of Pathological $\alpha$ -Synuclein in Skin Punches of Patients with Lewy Body Disease

Angela Mammana, MSc,<sup>1</sup> Simone Baiardi, MD, PhD,<sup>1,2</sup>  
Corinne Quadalti, PhD,<sup>1</sup> Marcello Rossi, MSc,<sup>1</sup>  
Vincenzo Donadio, MD,<sup>1</sup>  Sabina Capellari, MD,<sup>1,3</sup>  
Rocco Liguori, MD,<sup>1,3</sup> and Piero Parchi, MD, PhD<sup>1,2\*</sup> 

Mov Disord, 2021

# RT-QuIC z mozkomíšního moku

- Vysoce specifické a ultrasenzitivní vyšetření v likvoru:  
**RealTime Quaking Induced Conversion RT-QuIC (Seeding Amplification Assay; SAA)** (Fairfoul et al, *Ann Clin Transl Neurol.* 2016; Shahnawaz et al., *JAMA Neurol.* 2017)
- Reakce je iniciována biologickým vzorkem (zrno), kdy hyperfosforylovaný  $\alpha$ Syn vyvolá agregaci rekombinantního  $\alpha$ Syn v substrátu
- Kinetika vyvolané agregace rekombinantního  $\alpha$ Syn je měřena v reálném čase
- Výsledkem vyšetření je odpověď synukleinopatie ANO/ NE

# SAA v krevní plazmě

nature medicine



Article


<https://doi.org/10.1038/s41591-023-02358-9>












## Propagative $\alpha$ -synuclein seeds as serum biomarkers for synucleinopathies

Received: 1 July 2022

Accepted: 21 April 2023

Published online: 29 May 2023

 Check for updates

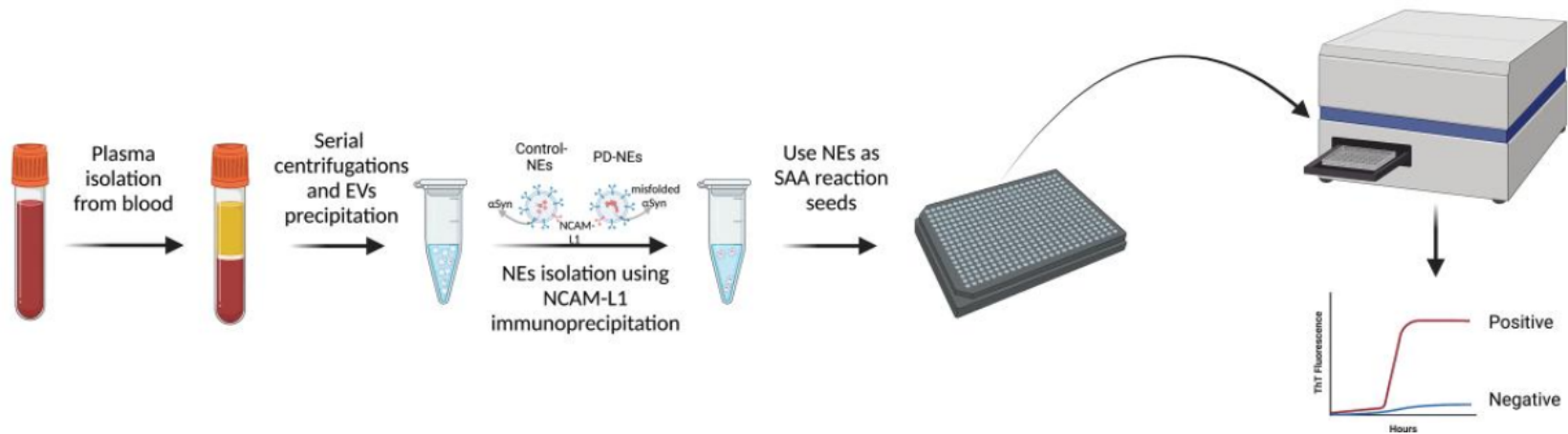
Ayami Okuzumi <sup>1</sup>, Taku Hatano <sup>1</sup>, Gen Matsumoto<sup>2</sup>, Shuko Nojiri<sup>3</sup>,  
Shin-ichi Ueno <sup>1</sup>, Yoko Imamichi-Tatano <sup>1</sup>, Haruka Kimura <sup>1</sup>,  
Soichiro Kakuta <sup>4</sup>, Akihide Kondo <sup>5</sup>, Takeshi Fukuhara<sup>6</sup>, Yuanzhe Li<sup>1</sup>,  
Manabu Funayama <sup>1</sup>, Shinji Saiki <sup>1,7</sup>, Daisuke Taniguchi<sup>1</sup>, Taiji Tsunemi<sup>1</sup>,  
Deborah McIntyre<sup>8</sup>, Jean-Jacques Gérardy<sup>9</sup>, Michel Mittelbronn<sup>9</sup>,  
Rejko Kruger<sup>8,10</sup>, Yasuo Uchiyama<sup>11</sup>, Nobuyuki Nukina<sup>12</sup> & Nobutaka Hattori <sup>1,6</sup> 



# Extracellular vesicles and seeding amplification: a step closer to a Parkinson's disease blood test

## 1) Isolate neuron-derived $\alpha$ Syn from plasma samples

## 2) Perform $\alpha$ Syn SAA



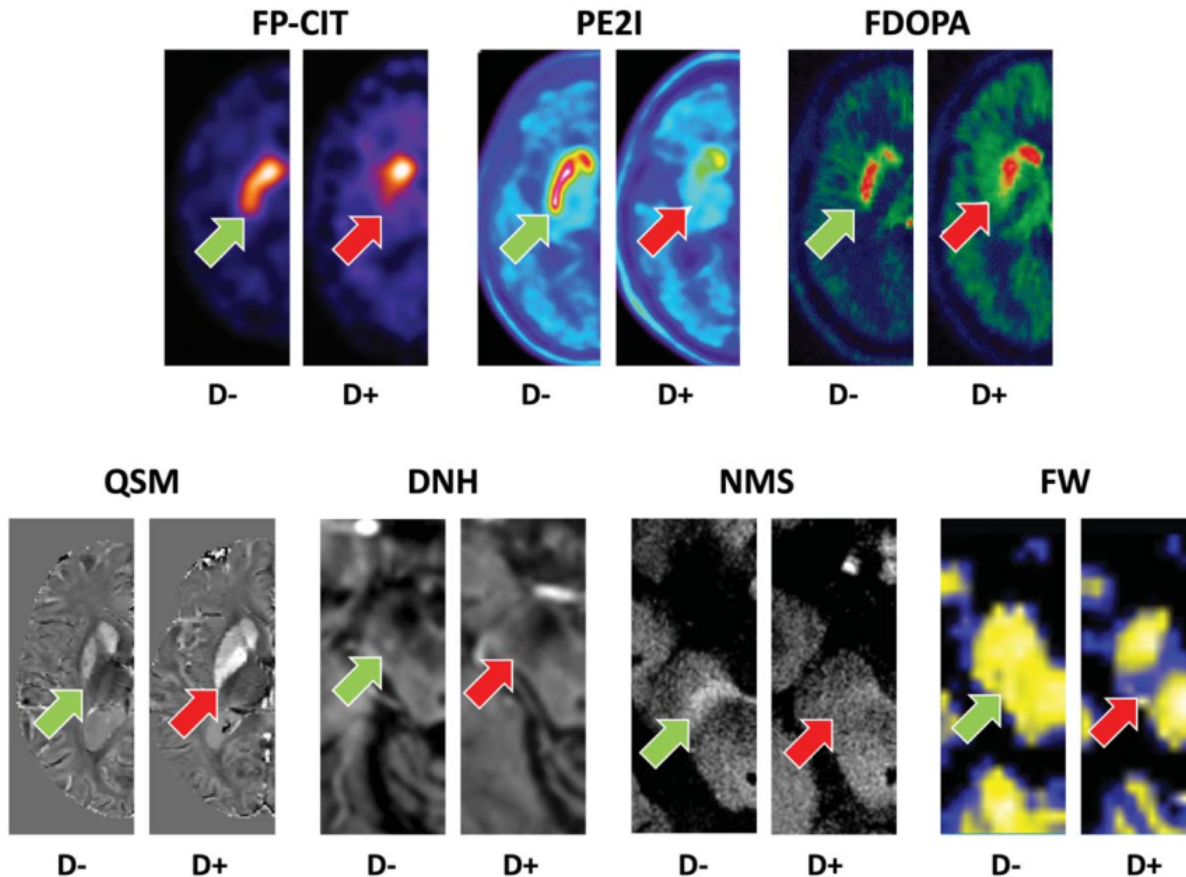
- EVs are lipid-bound vesicles secreted by cells into the extracellular space

Kluge et al., Brain 2022; Commentary by Martinez-Valbuena, Kovacs and Lang

## Review

# Imaging Biomarkers in Prodromal and Earliest Phases of Parkinson's Disease

Hendrik Theis<sup>a,b</sup>, Nicola Pavese<sup>c,d</sup>, Irena Rektorová<sup>e,f,g</sup> and Thilo van Eimeren<sup>a,b,\*</sup>



# PD diagnostická kritéria a zobrazovací BM

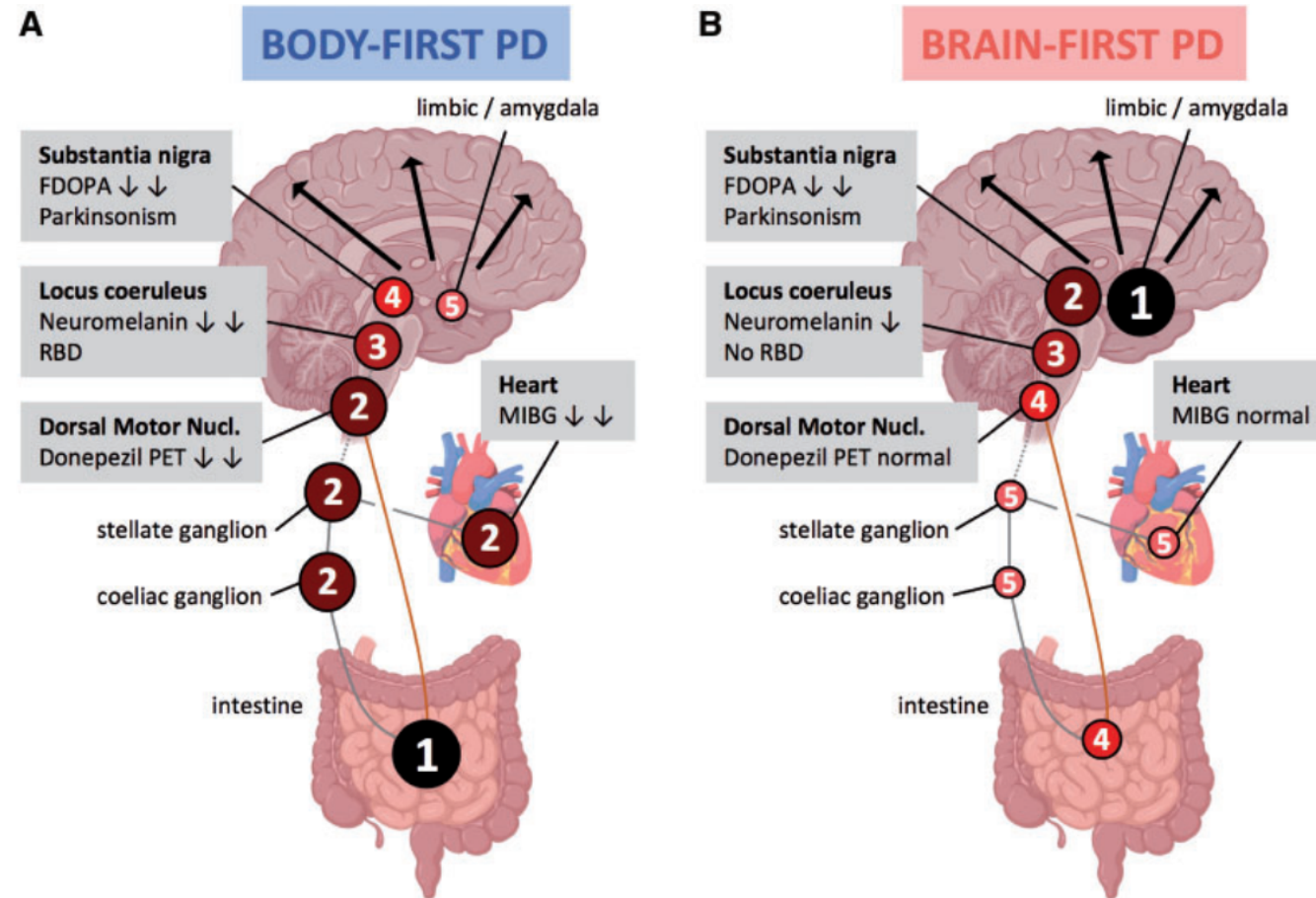
- Podporující dg:

**<sup>23</sup>iodine-MIBG** scintigrafie jasně dokumentující kardiální postganglionální denervaci sympatiku

- Absolutní vylučující kritériem pro dg

Normální DaT SPECT (DaT SCAN)

# Hypotéza šíření $\alpha$ -synukleinu (prion-like)





# Diagnosis and management of dementia with Lewy bodies

Fourth consensus report of the DLB Consortium

## Hlavní symptomy

- Fluktuace kognitivních funkcí a pozornosti
- Porucha chování v REM spánku
- Opakované zrakové halucinace
- Spontánní symptomy parkinsonismu

## Indikativní biomarkery

- Úbytek **dopaminergních transportérů v BGG dle SPECT/PET**
- Snížené vychytávání  **$^{123}$ iodine-MIBG dle kardiální scintigrafie**
- **Polysomnografie** s potvrzením poruchy chování v REM spánku se svalovou atonií

# Další podporující příznaky

Senzitivita na  
antipsychotika

Posturální instabilita,  
opakované pády

Synkopy nebo jiné  
přechodné poruchy  
vědomí

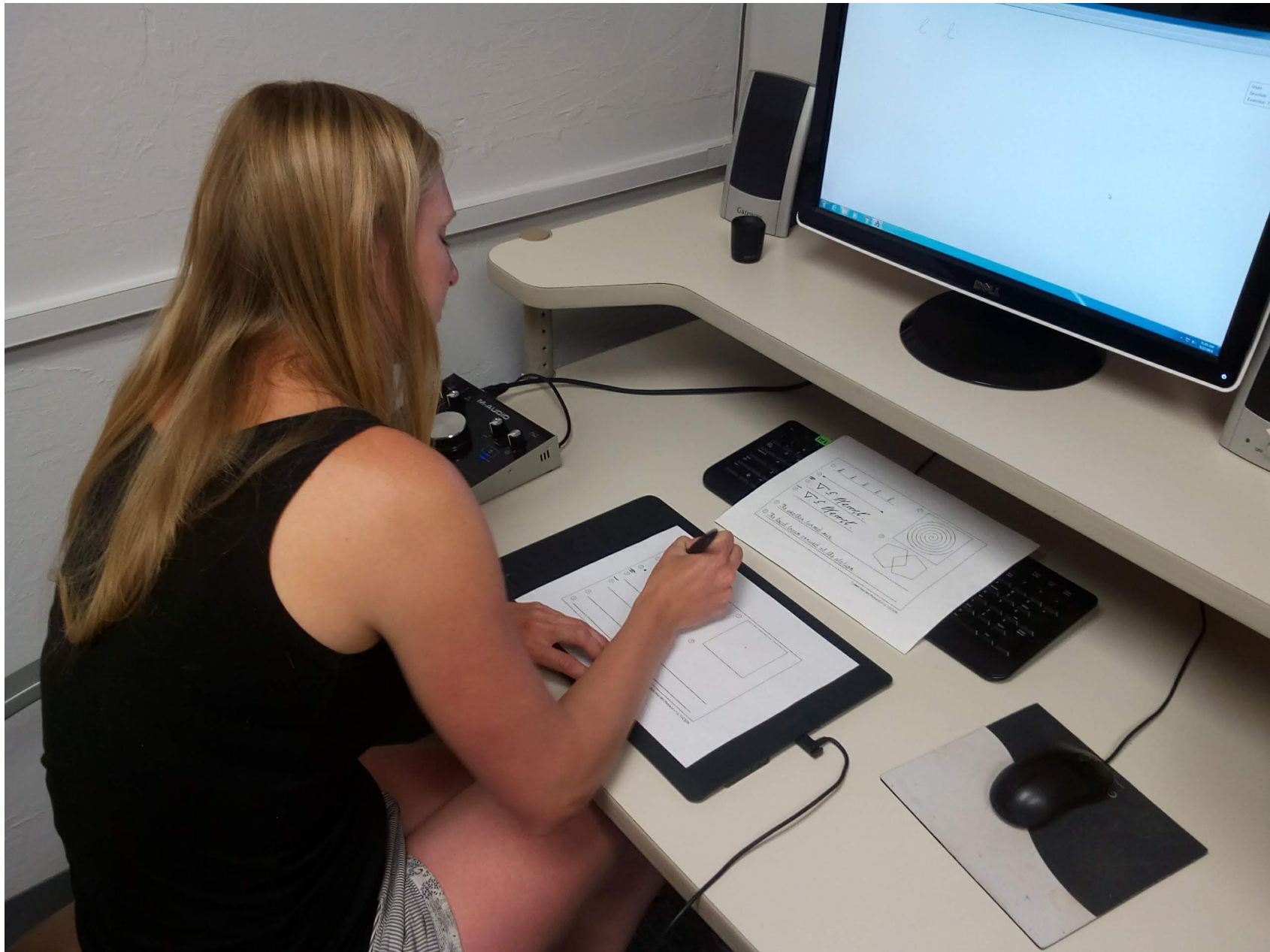
Těžká autonomní  
dysfunkce, např. zácpa,  
ortostatická hypotenze,  
močová inkontinence

Hypersomnie, poruchy  
spánku

Halucinace v jiných  
modalitách

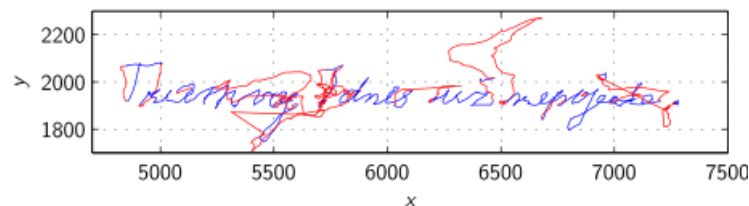
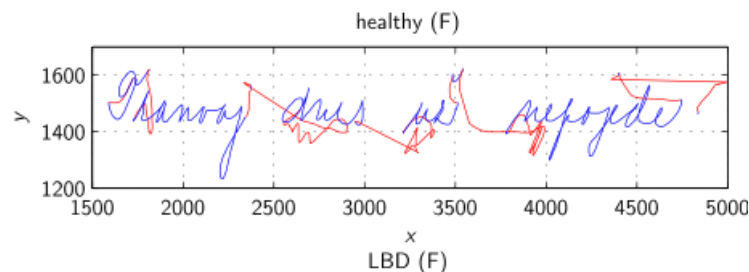
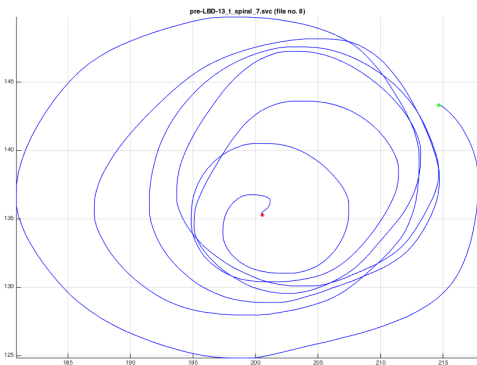
Bludy

Apatie, úzkost,  
deprese



# Kohorta

- **42** subjektů s pravděpodobnou MCI-LB (20 žen, 22 mužů, věk =  $69,9 \pm 6,5$  let)
- **103** subjektů bez MCI-LB (67 žen, 35 mužů, věk =  $66,3 \pm 6,3$  let)



Luboš Brabeneč



Paťa Klobušiaková



Jiří Mekyska

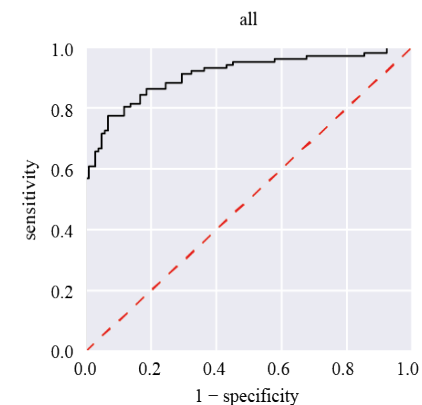
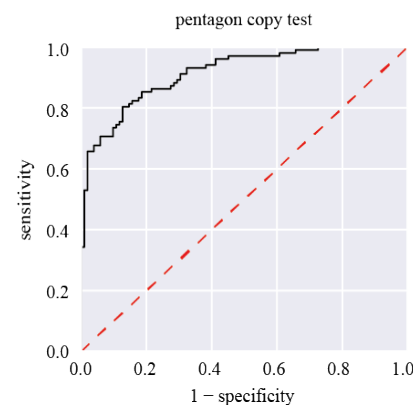
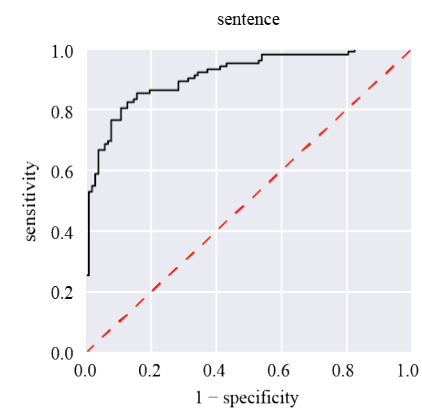
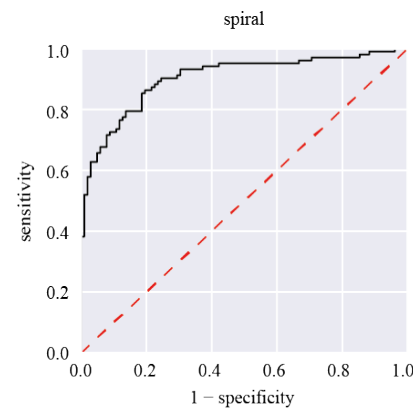


# Demografické a klinické údaje

	nonDLB group	DLB group	T-test p
<b>Age</b>	M = 66,3 ; SD = 6,26	M = 69,90; SD = 6,46	<b>p = 0,007</b>
<b>Gender</b>	67 F / 35 M	20 F / 22 M	p = 0,053
<b>UPDRS</b>	M = 2,63 ; SD = 3,68	M = 7,24 ; SD = 4,75	<b>p &lt; 0,001</b>
<b>MOCA</b>	M = 27,52 ; SD = 1,45	M = 23,62 ; SD = 3,09	<b>p &lt; 0,001</b>
<b>ESS</b>	M = 7,67 ; SD = 4,45	M = 7,19 ; SD = 4,24	p = 0,40
<b>RBDSQ</b>	M = 2,93 ; SD = 2,17	M = 4,32 ; SD = 2,68	<b>p = 0,012</b>
<b>GDS</b>	M = 6,93 ; SD = 5,06	M = 8,88 ; SD = 6,33	p = 0,074
<b>UPSIT</b>	M = 44,20 ; SD = 27,95	M = 30,09 ; SD = 26,97	<b>p = 0,031</b>

# Výsledky (ROC)

Task	Accuracy	Sensiivity	Specificity
spiral	83.3%	86.3%	80.4%
sentence	84.8%	80.4%	89.2%
PCT	83.8%	80.4%	87.3%
All tasks	85.3%	77.5%	93.1%



## Důležité parametry:

### Spirála

Kinetické (akcelerace a rychlost), tlak pera

### Psaní vět

Prostorové a kinetické

### Obkreslování pentagonů

Entropie, trvání, kinetické

# Take home message

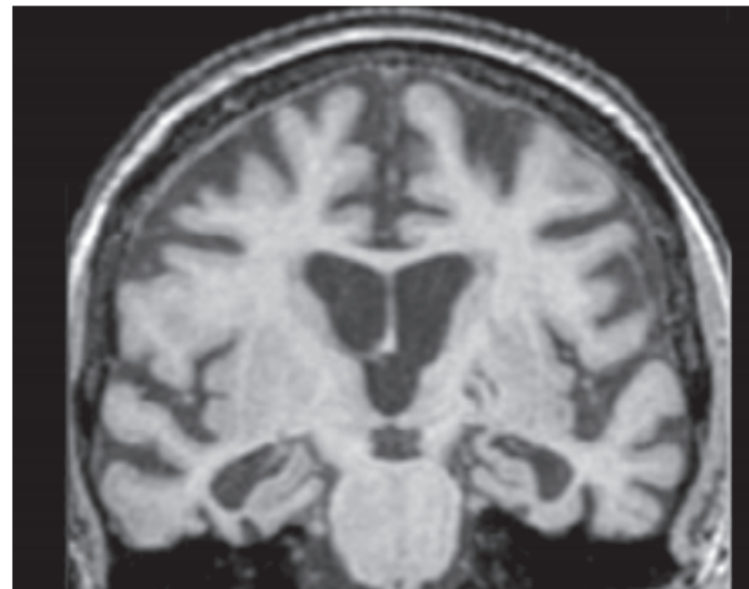
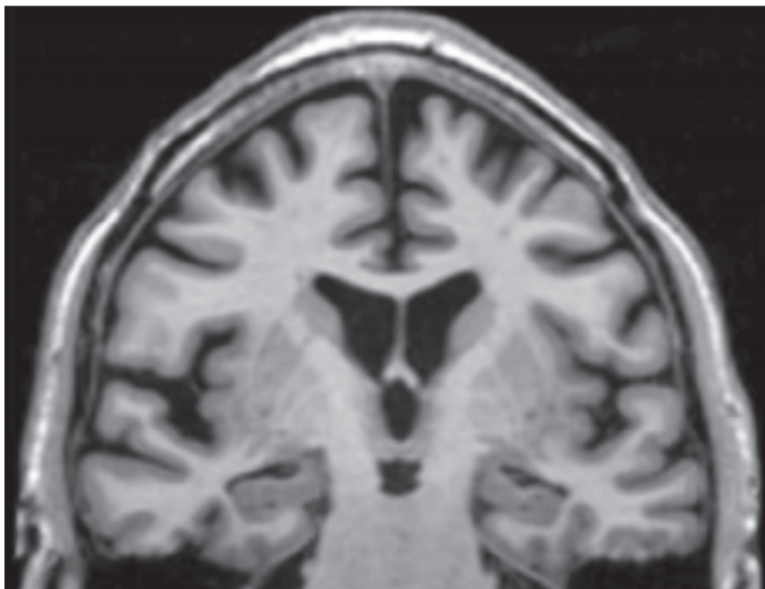
- Kresba spirály, pentagonů a písma na tabletu je krátké, levné a neinvazivní vyšetření, které hodnotí motorické, prostorové a kognitivní funkce
- Vyšetření samostatně a zejm. v kombinaci dokáže s přesností nad 85% odlišit MCI-LB (prodromální stádium PD/ DLB) od zdravého stárnutí

# sMRI u DLB: hipokampální atrofie?

Dementia with Lewy bodies

Alzheimer's disease dementia

Coronal  
T<sub>1</sub>-weighted  
MRI



**Hippocampal preservation** in patients with MCI supports progression to DLB instead of AD dementia with a **sensitivity of 85%** and a **specificity of 61%**

Kantarci et al, 2016

# FP-CIT SPECT: DLB vs. AN

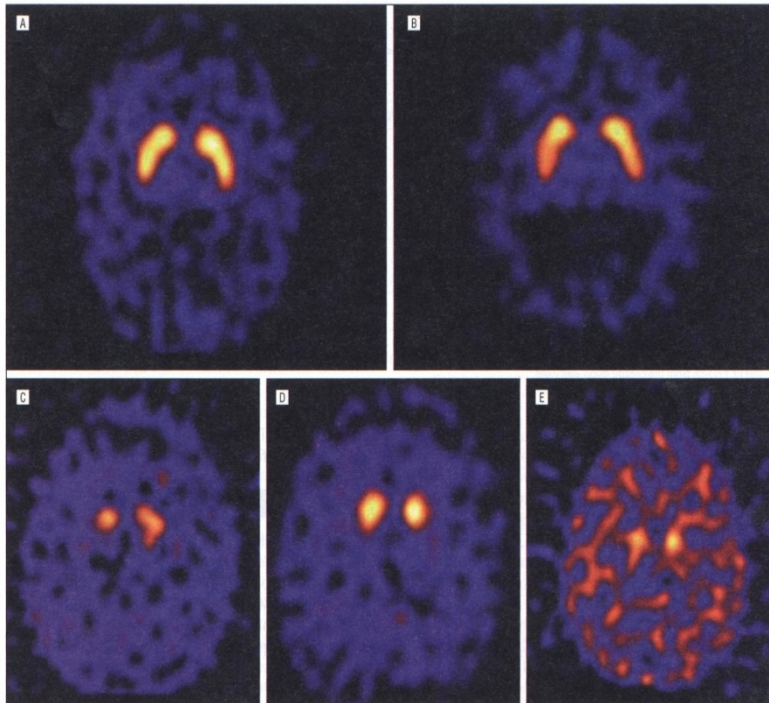



Figure 2. Iodine 123-radiolabeled 2 $\beta$ -carbomethoxy-3 $\beta$ -(4-iodophenyl)-N-(3-fluoropropyl) nortropane with single-photon emission computed tomographic images. A, A healthy older control subject. B, Subjects with Alzheimer disease. C, Subjects with dementia with Lewy bodies. D, Subjects with Parkinson disease. E, Subjects with Parkinson disease with dementia.

McKeith, 2007  
Sensitivita 77.7%  
Specificita 90.4%

O'Brien et al., 2004

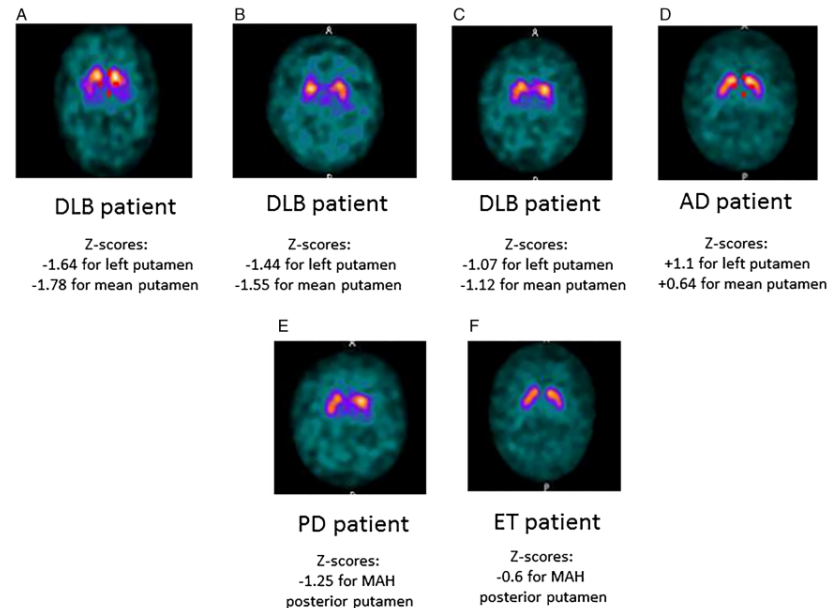


# Different z-score cut-offs for striatal binding ratio (SBR) of DaT SPECT are needed to support the diagnosis of Parkinson’s Disease (PD) and dementia with Lewy bodies (DLB)

Francesco Lanfranchi<sup>1</sup> · Dario Arnaldi<sup>2,3</sup> · Alberto Miceli<sup>1</sup> · Pietro Mattioli<sup>3</sup> · Francesca D’Amico<sup>1</sup> · Stefano Raffa<sup>1,2</sup> · Maria Isabella Donegani<sup>1</sup> · Silvia Chiola<sup>1,2</sup> · Federico Massa<sup>3</sup> · Matteo Pardini<sup>2,3</sup> · Tania Di Raimondo<sup>1</sup> · Gianmario Sambuceti<sup>1,2</sup> · Matteo Bauckneht<sup>1,2</sup> · Flavio Nobili<sup>2,3</sup> · Silvia Morbelli<sup>1,2</sup> 

225 patients included  
 De novo PD, DLB, AD, ET

Less stringent cut-offs for specific striatal regions?

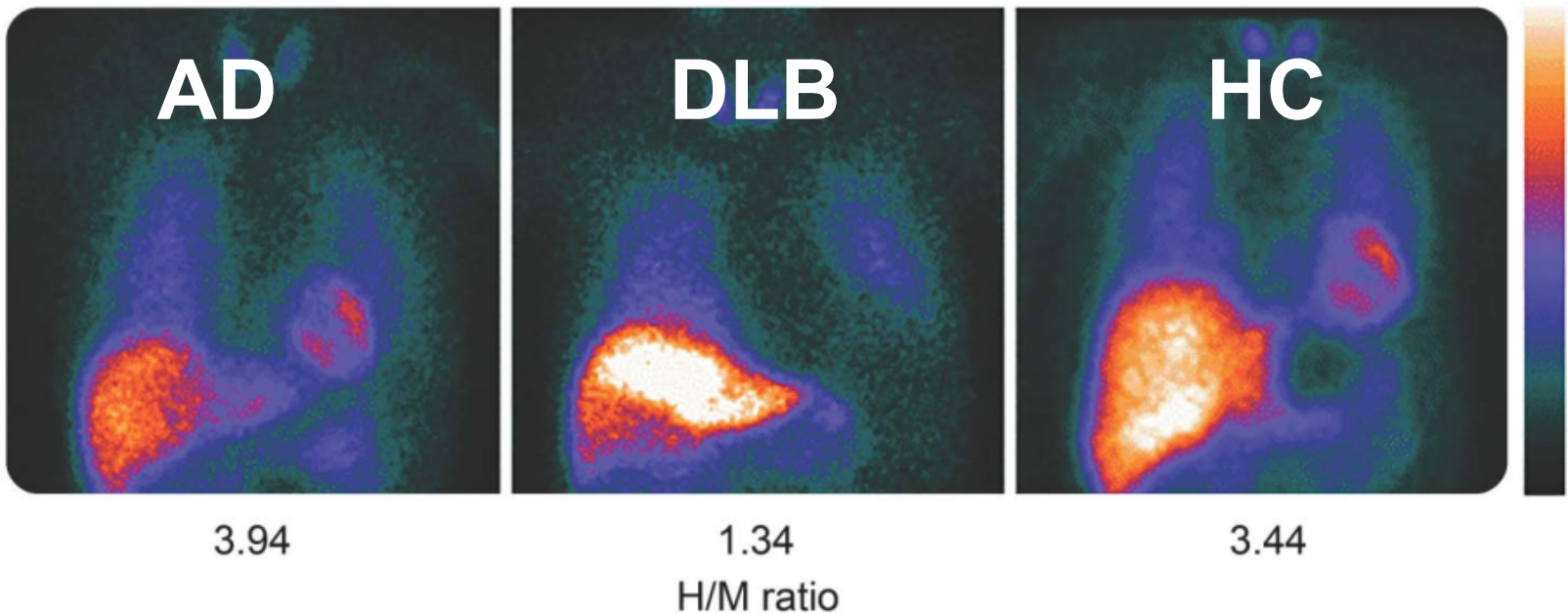


# $^{123}\text{I}$ -meta-iodobenzylguanidine: MIBG

analog norepinefrinu; změny postgangliových sympatických vláken

- Sensitivita 77% a specificita 94% pro odlišení pravděpodobné DLB od pravděpodobné AD

*Yoshita et al., 2015*



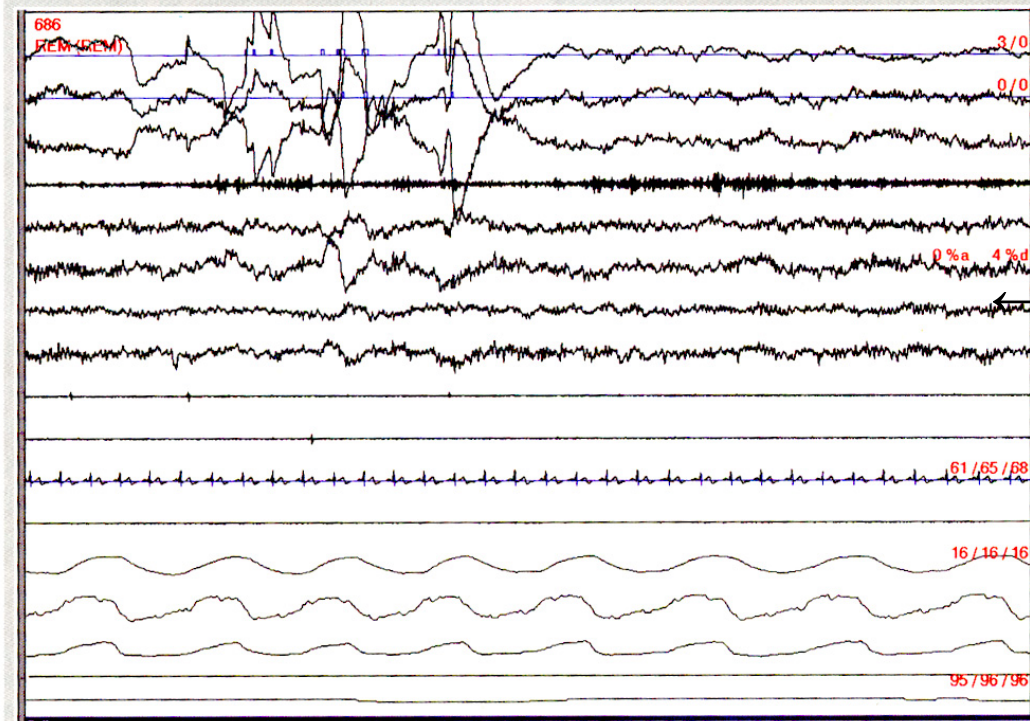
# Porucha chování v REM spánku

Obrázek 1. Polysomnografický záznam poruchy svalové atonie v REM spánku při RBD. Svody 1–3: pohyby očí, 4: povrchový EMG mm. mentales, 5: C3–A2, 6: C4–A1, 7: O1–A2, 8: O2–A1, 9 a 10: povrchové EMG tibiales anteriores, 11: EKG, 12: dýchací zvuky – grafický záznam, 13: proud vzduchu před nosem a ústy, 14 a 15: pohyby hrudníku a břicha, 16: pulzní oxymetrie z prstu (nad touto poslední křivkou je pomocná přímková symbolizující saturaci 100%). Trvání zaznamenaného záznamu – 30 s. Na obrázku jsou patrné intenzivní rychlé pohyby očí, kolísavá, ale rozhodně zvýšená aktivita bradových svalů, desynchronizovaná EEG aktivita, svalová atonie mm. tibiales bilaterales a normální kardioventilační křivky

**1/3 pacientů s PN**  
**Většina s DLB**  
**90% během 15 let**

*Postuma et al., 2015*

aktivita ve svalu m. mentalis



*Šonka 2008*



# REM sleep behavioural disorder

ICD-9-CM code: 327.42

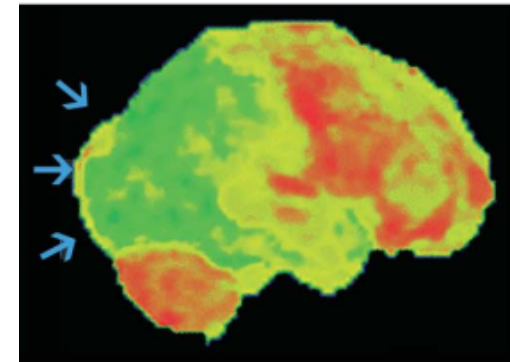
ICD-10-CM code: G47.52

- **Criteria A-D must be met**
- A. Repeated episodes of sleep related vocalization and/or complex motor behaviors
- B. These behaviors are documented by polysomnography to occur during REM sleep or, based on clinical history of dream enactment, are presumed to occur during REM sleep
- C. Polysomnographic recording demonstrates REM sleep without atonia (RWA)
- D. The disturbance is not better explained by another sleep disorder, mental disorder, medication, or substance use

*American Academy of Sleep Medicine. International classification of sleep disorders, 3rd ed. Darien, IL: American Academy of Sleep Medicine, 2014.*

# Symptomy podporující dg DLB FDG PET, MRI?

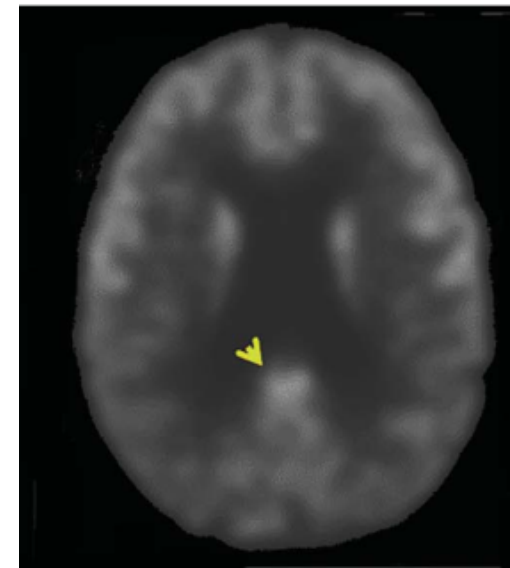
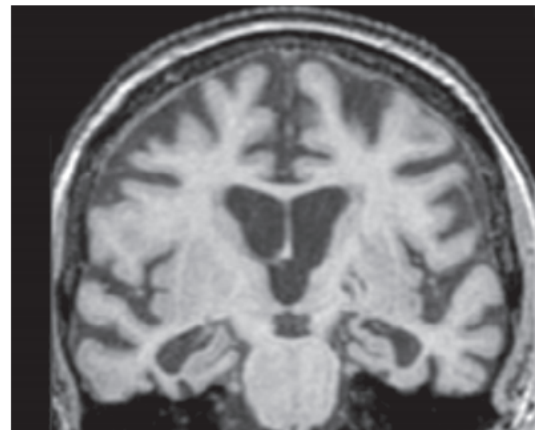
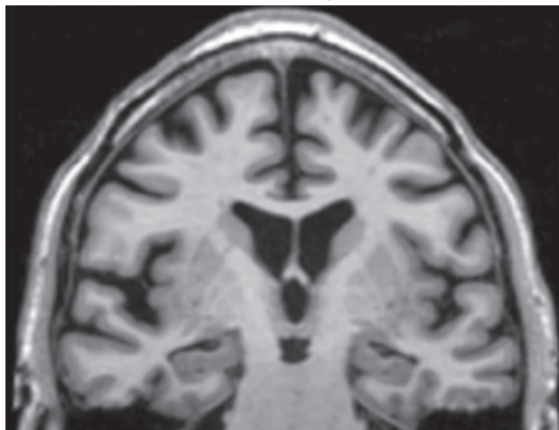
DLB



Dementia with Lewy bodies

Alzheimer's disease dementia

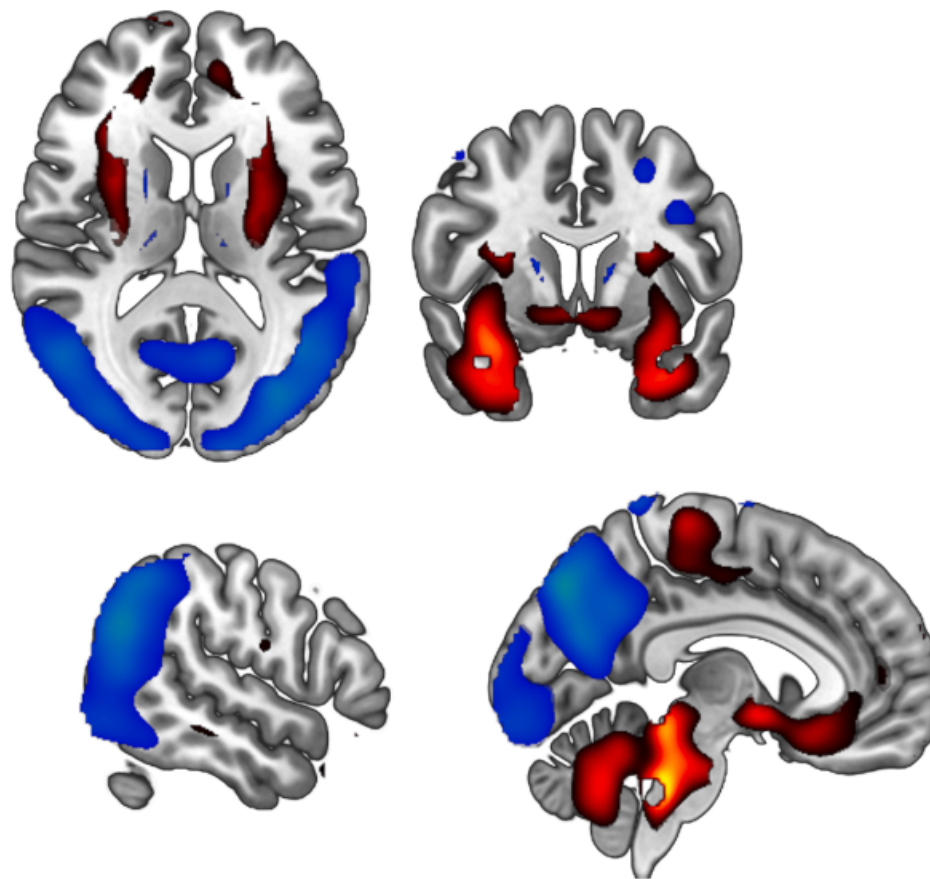
Coronal T<sub>1</sub>-weighted MRI



„Cingulate island“

*Walker et al., Lancet Neurol 2015*  
*KcKeith et al., 2017*

# FDG PET metabolický obraz u DLB



# EEG jako podpůrný biomarker

Kvantitativní EEG:

- Dominantní  $\alpha < 8$  Hz
- Variabilita  $\alpha$  frekvence  $>1.5$  Hz

83% MCI pacientů s  
pozitivitou EEG BM  
při vstupním vyšetření  
konvertovalo do DLB  
během dalších 3 let

Bonanni et al., 2015

# Studovat iRBD jako prodromální DLB?

- **Ano, ale ne pouze!**
- RBD není přítomno u VŠECH pacientů s PN/DLB!! → **iRBD nemůže identifikovat všechny prodromální PN/ DLB!!**
- **Latence rozvoje PN/DLB (MSA) může být velmi dlouhá!** Riziko fenokonverze je 35–45% v průběhu 5 let

# Revisiting DLB Diagnosis: A Consideration of Prodromal DLB and of the Diagnostic Overlap With Alzheimer Disease

Journal of Geriatric Psychiatry  
and Neurology  
2016, Vol. 29(5) 249-253  
© The Author(s) 2016  
Reprints and permission:  
sagepub.com/journalsPermissions.nav  
DOI: 10.1177/0891988716656083  
jgpn.sagepub.com



Ian McKeith, F Med Sci<sup>1</sup>, John-Paul Taylor, PhD<sup>1</sup>, Alan Thomas, PhD<sup>1</sup>,  
Paul Donaghy, PhD<sup>1</sup>, and Joseph Kane, MRC Psych<sup>1</sup>

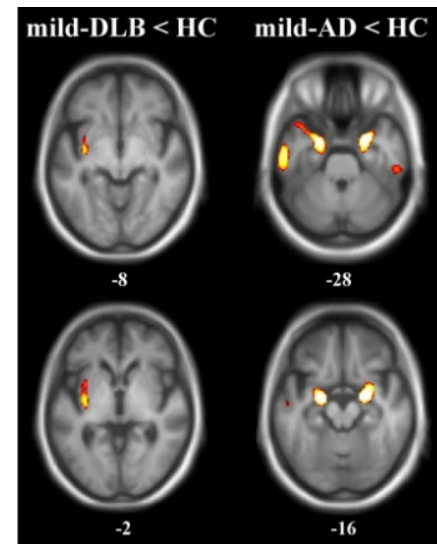
- **MCI** s časnými **deficity ve zrakově-prostorových a exekutivních funkcích**
- **Delirium** (vyvolané nebo spontánní)
- **Psychiatrický počátek**: afektivní porucha nebo psychóza

# Prodromální MCI-LB

- MCI + 1 nebo 2 hlavních symptomů nebo indikativních biomarkerů dle klinických DLB kritérií z roku 2017
- FP-CIT SPECT: 75 subjektů, 54% mělo pozitivní DAT SCAN, 1/2 z nich neměla symptomy parkinsonismu; specificita 89%, **senzitivita pouze 54%! (Thomas, 2018)**
- *Postmortem studie – až 50% případů se synukleinopatií neměla LB v mesencephalu (Zaccai, 2008)*

# MRI zobrazování u prodromální DLB:

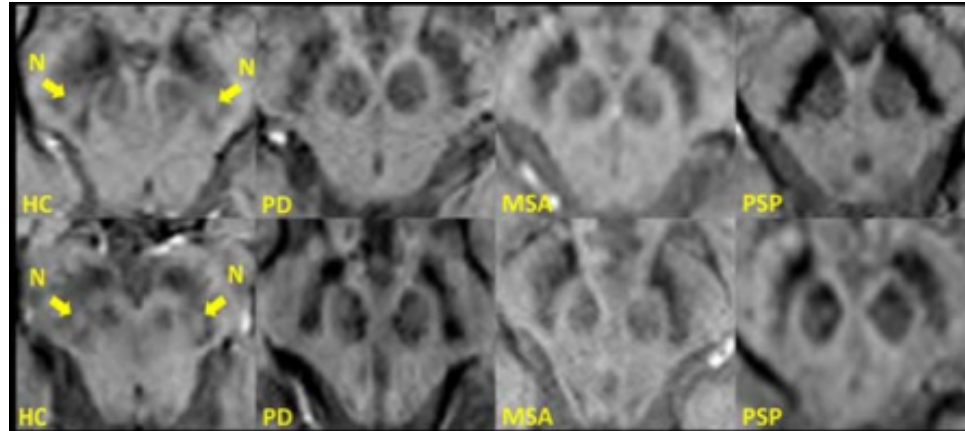
- Zachování objemů hippokampů (Kantarsi 2016)?
- **Ztenčení šířky kortexu v obl. pravé insuly**  
*(Blanc 2015, Roquet 2017)?*



Durcan et al, 2019



# Susceptibilitou vážené zobrazování (SWI)



*Reiter et al., 2015*

- Hodnotí nigrosome-1, **kvalitativní zobrazení!!**
- **Hyperintenzní ovoidní oblast** – dorsolaterální část SNc u zdravých kontrol: “swallow-tail-sign”
- Nepřítomnost příznaku - přítomna u 2/3 pacientů s iRBD

*Mahlknecht et al., 2016*

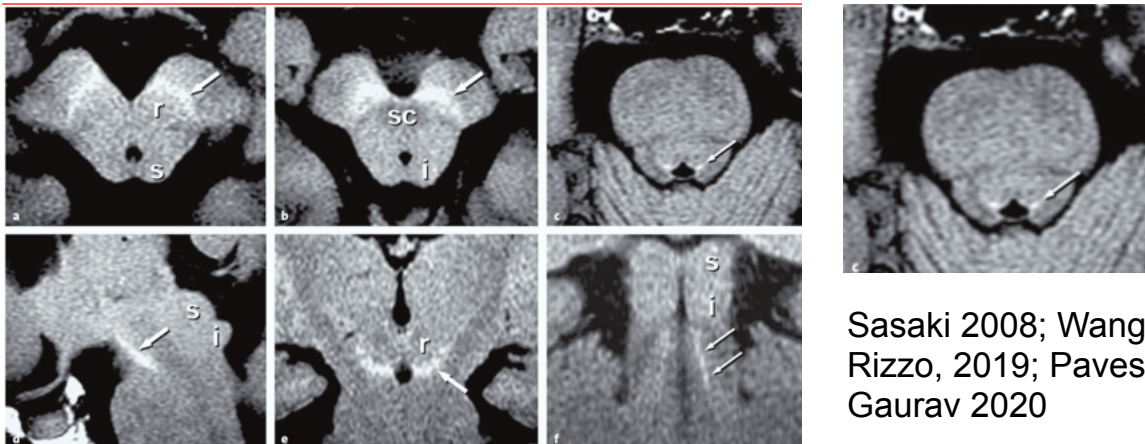
*De Marzi et al, 2016*

# MRI sekvence senzitivní na NEUROMELANIN (T1 fast spin echo sekvence)

Dopaminergní neurony v SNc a noradrenergní neurony v LC obsahují pigment neuromelanin

Neuromelanin je svázaný s metabolismem dopaminu (Sulzer, NPJ PD 2018)

Zdrojem NM kontrastu: NM vázaný na železo je paramagnetický

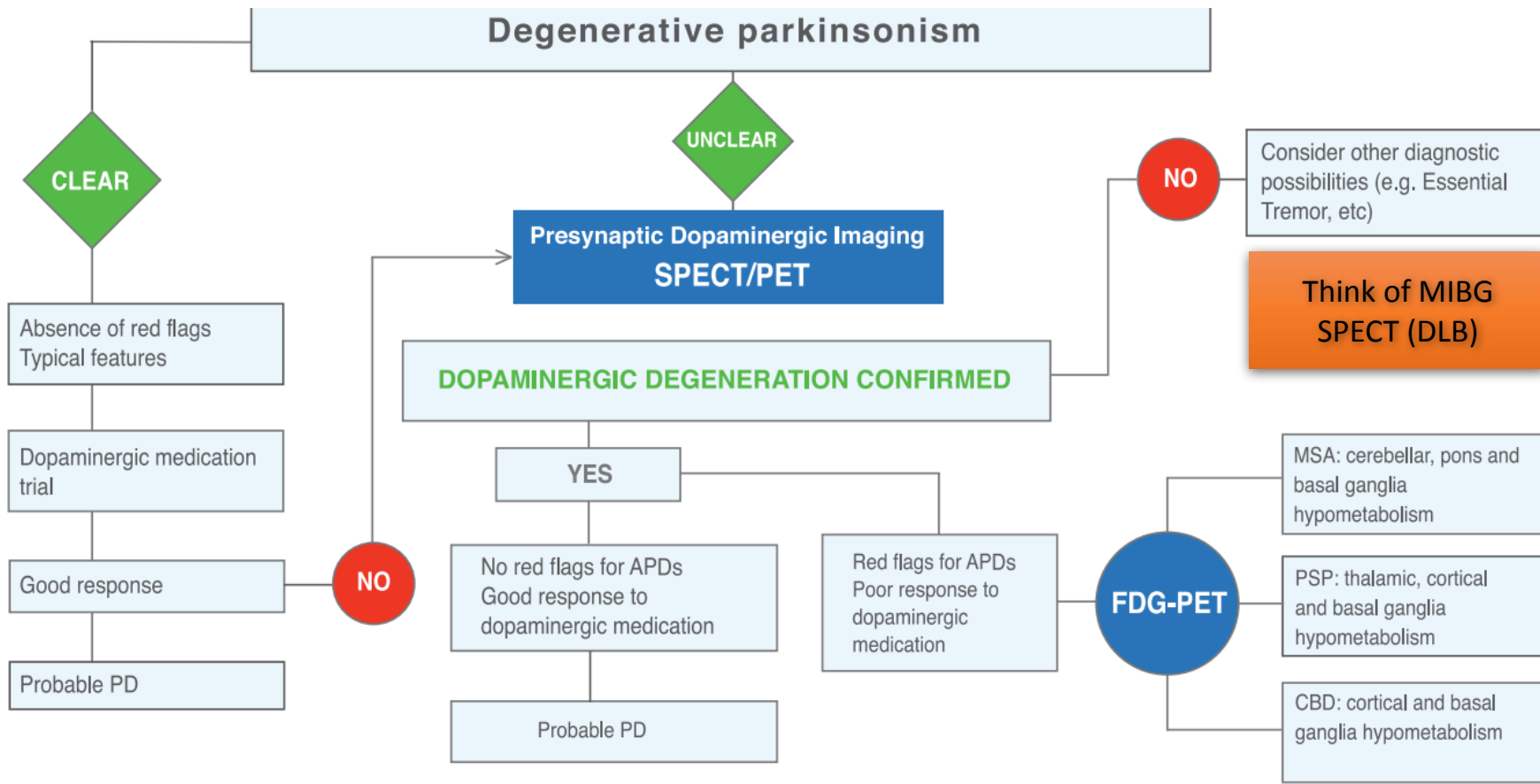


Sasaki 2008; Wang 2018;  
Rizzo, 2019; Pavese and Tai 2018;  
Gaurav 2020

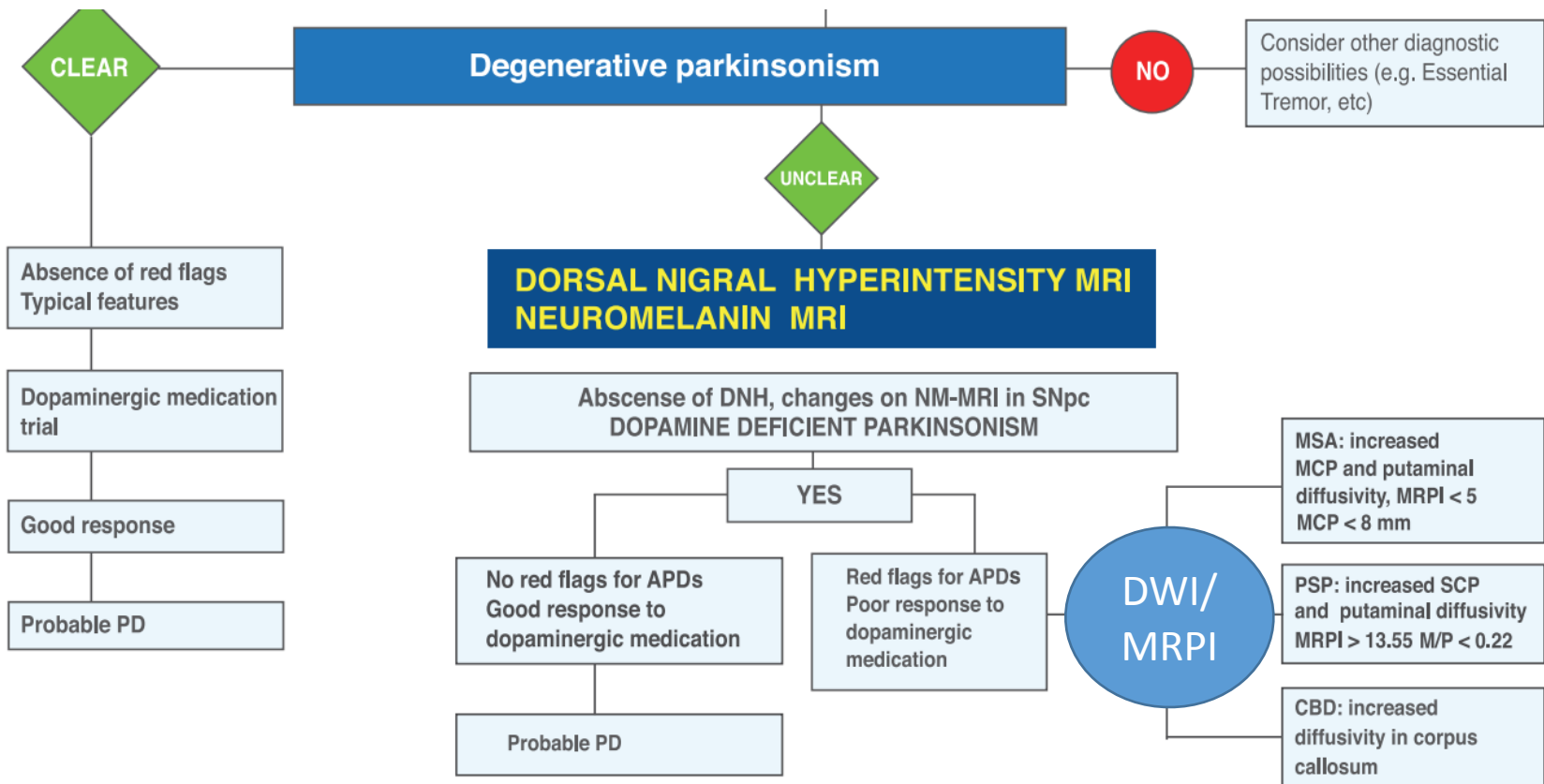
# NMS-MRI

- Marker degenerace dopaminergních neuronů v SNc
- Časný BM (5-6 let před začátkem, iRBD) (*Biondetti et al., Brain 2021*)
- Longitudinální BM, korelace s DAT, tíží motorických symptomů a s délkou nemoci (*Gaurav et al., Mov Disord 2021, Biondetti et al., Brain 2020 and 2021*)
- **Odliší degenerativní od nedegenerativního parkinsonismu**
- **Odliší PN/ DLB od atypického parkinsonismu (PSP, MSA, CBD)**

# Jak používat zobrazování v klinické praxi?



# Jak používat zobrazování v klinické praxi?



# Závěry: biomarkery pro časnou diagnostiku AN a DLB

- Amyloidový PET, triplet v MMM, plasma BM?
- Kardiální scintigrafie + DaT SCAN pro dg LBDs?
- MRI zachování MTL, ale cave možná komorbidita AD
- Specifické MRI sekvence (NMS, QSM)
- EEG jako podpůrný dg i prediktivní biomarker
- RT-QuIC z mozkomíšního moku (extracelulární váčky v plazmě..?) + marker časné fenokonverze?
- Strojové učení a kombinované techniky...

# Pozvání 1

## Pokročilý kurz Alzheimerova nemoc, Parkinsonova nemoc a jiné mozkové neurodegenerace

17. - 18. října 2024 Hotel Continental, Kounicova 6, Brno

### Základní informace

Kurz se bude konat pod odbornou garancí  
prof. MUDr. Ireny Rektorové, Ph.D. v Hotelu Continental,  
Kounicova 6, Brno.

Pro zájemce je dostupná také virtuální forma účasti.

Bližší informace o kurzu včetně registračního formuláře naleznete  
zde na webových stránkách.




## Pozvání 2

 **29th June - 2nd July, 2024**

# **EAN 2024**

**10th Congress of the European Academy of  
Neurology**

 Helsinki, Finland



# Pozvání 3




The 19<sup>th</sup> World Congress on  
**CONTROVERSIES IN NEUROLOGY**

**20-22.3.2025 • Prague, Czech Republic**

- CONy is a unique congress, consisting of debates on central contested topics in neurology.
- Our faculty includes Key Opinion Leaders (KOLs) from leading medical centers worldwide.
- The format of our meeting encourages discussion among speakers and attendees.



**Prof. Amos D. Korczyn**  
Israel  
President



**Prof. Irena Rektorová**  
Czech Republic  
Co-chair



**Prof. Natan Bornstein**  
Israel  
Co-chair

[cony@comtecint.com](mailto:cony@comtecint.com)  
[cony2025@comtecmed.com](mailto:cony2025@comtecmed.com)



Děkuji za  
pozornost 😊

Kontakt:  
[irena.rektorova@fnusa.cz](mailto:irena.rektorova@fnusa.cz)

