

# Dynamická a statická kognitivní rezerva a její vliv na efekt terapie

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# Kognitívna rezerva

- Neurálna rezerva: premorbídne **vlastnosti** siete, ktoré poskytujú odolnosť voči patologickým zmenám mozgu
  - Zhádza:
    - a) kapacitu (max úroveň aktivity, kt. môžu siete generovať)
    - b) efektívnosť: ako efektívne sa aktivita siete premieta do kognitívnych schopností
- Neurálna kompenzácia: **obranischopnosť** mozgu voči patologickým zmenám
  - Závisí od flexibility (adaptability sietí a miery, do akej sa môžu navzájom nahrádzať)

Stern (2012; in Lancet)

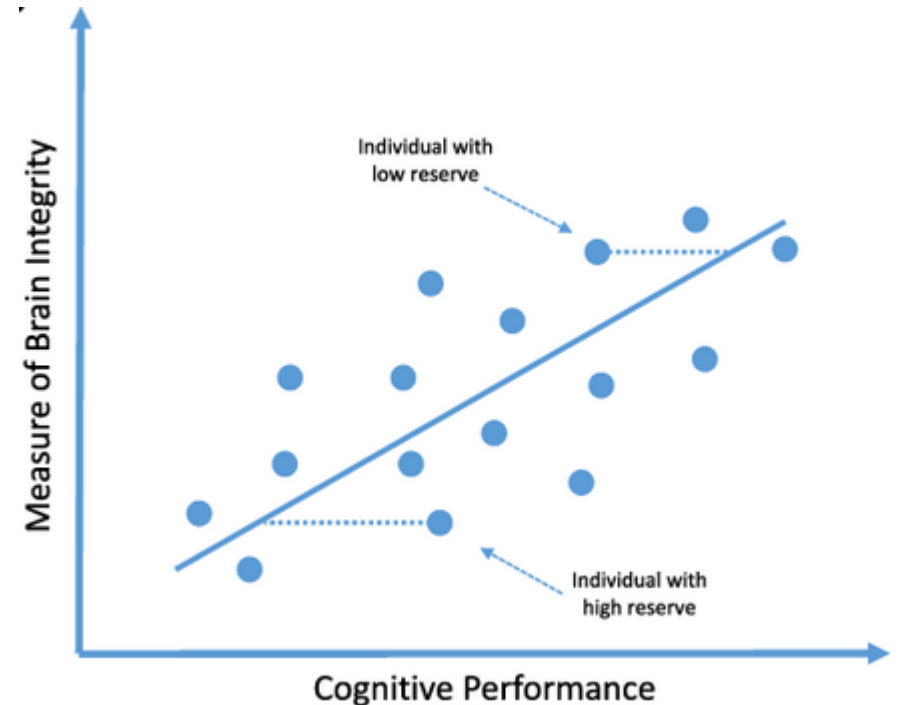
# Determinanty KR

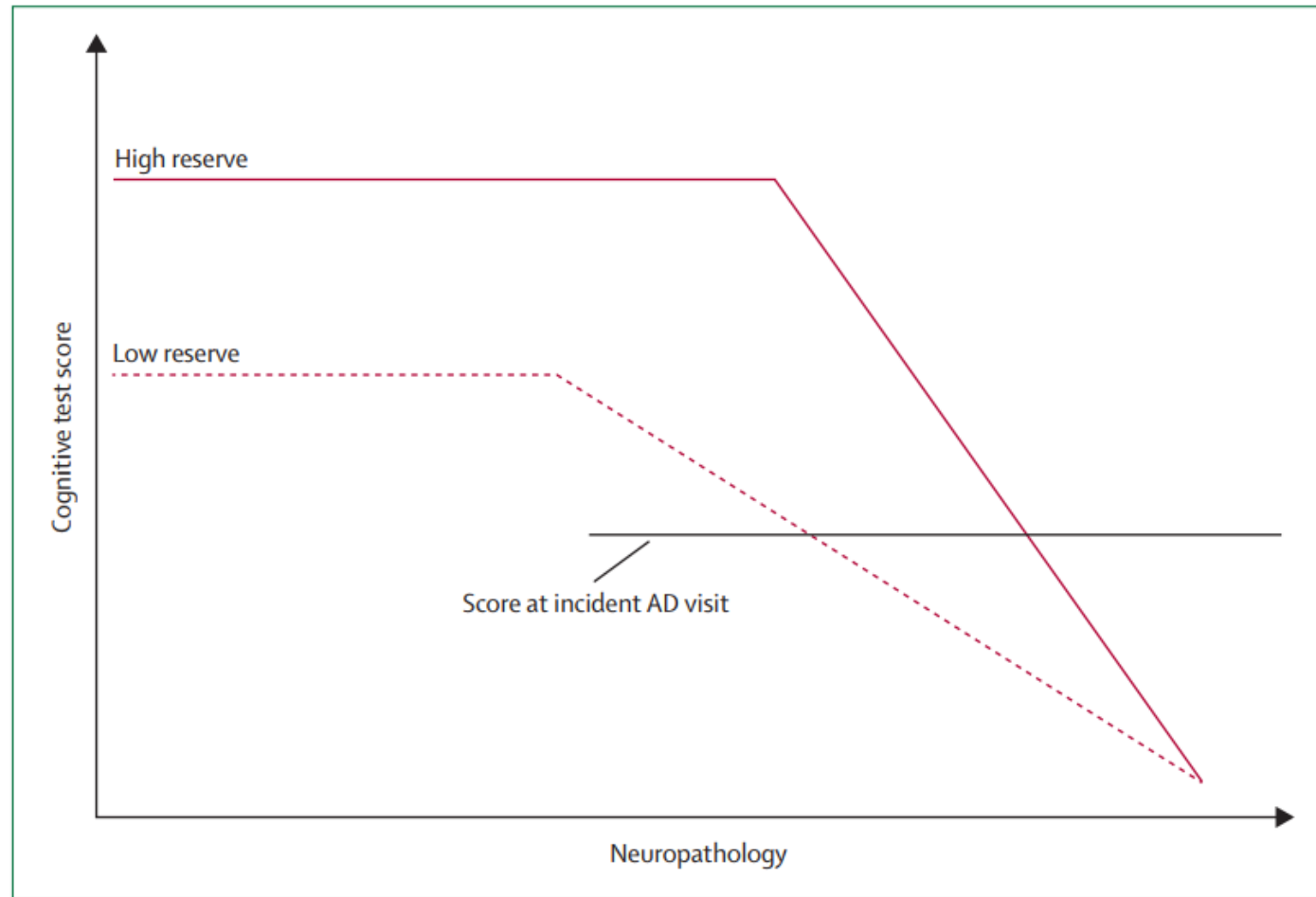
## — Vzdelanie

- Povolanie
- Voľnočasové aktivity
- Pravidelné (aerobné) cvičenie
- IQ
- Premorbidný objem mozgu

# Odhad KR

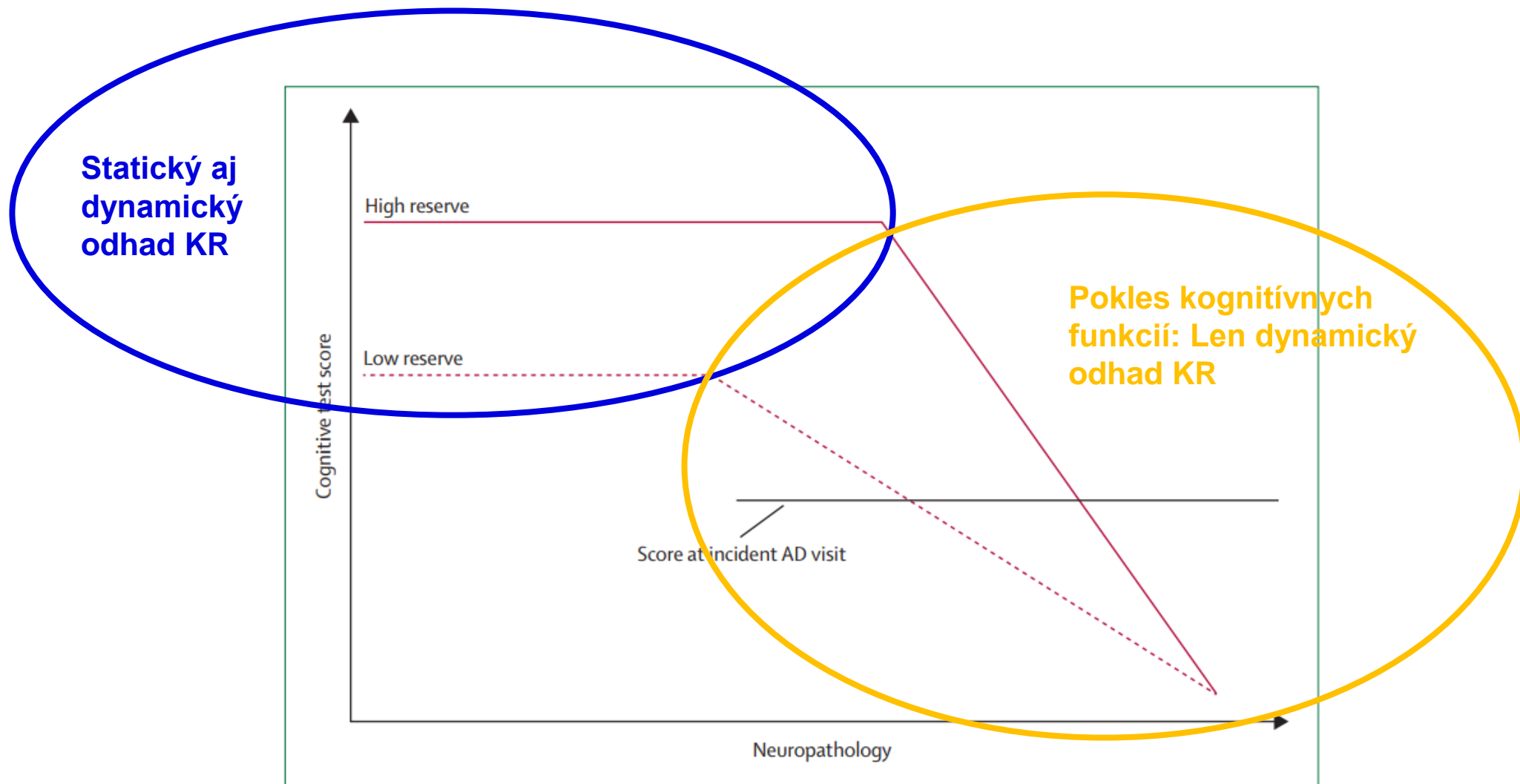
- Hypotetický konštrukt → nemerateľný priamo
- Determinanty KR ako „*convenient*“ proxi
  - ! Súvisia so životným štýlom
  - ! Vzájomne korelujú
  - ! Sú **statické** (od určitého veku nemenné)
- vs. **dynamické odhady**
  - Napr. reziduálny odhad
    - ✓ odrážajú zmeny





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

Zdroj: Stern, Y (in Lancet, 2012)



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

Zdroj: Stern, Y (in Lancet, 2012)





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

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Research on dance interventions (DIs) in the elderly has shown promising benefits 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 subjects 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 examined the interaction effect of DIs and CR on changes in the dwell time and coverage of rs-dFC. Cognitive reserve was calculated as the residual difference between the observed memory performance and the performance predicted by brain state. Partial 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 observed 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 observed 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 DIs have a differential and behaviorally relevant effect on dynamic rs-dFC, but these benefits depend on the current CR level.

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

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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) proxied 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 ( $n = 49$ ,  $M_{age} = 69.02 \pm 5.40$ ) or a control group ( $n = 50$ ,  $M_{age} = 69.37 \pm 6.10$ ). Moderation analyses revealed that CR moderated DI-induced increase of the SMN rs-FC with significant changes observed in participants with  $\geq 15$  years of education ( $b = 0.05, t(62) = 3.17, p = 0.002$ ). Only DI alone was a significant predictor of the DAN-aDMN crosstalk change ( $b = 0.06, t(64) = 2.16, p = 0.035$ ). 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, utilizes attentional action observation and imitation, and integrates sensory, motor, and cognitive demands<sup>1</sup> that bestow rehabilitative 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>2</sup>, physical fitness<sup>3</sup>, and cognition in the memory<sup>4,5</sup>, attention<sup>6,7</sup>, and psychosocial domains<sup>8</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>9</sup>. Overall, 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 (8UG) and the 30-Second Chair Stand (30CS) tests<sup>11</sup> which target dynamic balance, agility, lower body strength, and physical endurance<sup>3</sup>; and of the Five Point Test (FPT)<sup>12,13</sup>, which assesses figural fluency, i.e. the ability of executive functions to provide information about divergent reasoning, divided attention, planning, and mental flexibility<sup>14</sup>. Interestingly, despite the fact that figural fluency is known to decline in the healthy elderly and in patients with Alzheimer's disease (AD)<sup>15</sup>, the observed improvements were independent of hippocampal volumes<sup>12</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

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# Cieľ našich štúdií

- Moderuje KR efekt tanečnej intervencie (TI) na kľudovú funkčnú konektivitu (FK) a behaviorálne zmeny?
  - KR = schopnosť kompenzácie (Stern, 2012 in Lancet, Lövdén)
- Efekt TI na pamäť (Meng et al., 2020); exekutívne funkcie/figurálnu fluenciu (Kropáčová et al., 2019)
  - Avšak nekonzistentné výsledky
- Efekt TI na FK doposiaľ neznámy **vs.** vplyv KR na FK bohato študovaný (e.g. Conti et al., 2021; Lin et al., 2021)



# Metódy štúdie 1<sup>(1)</sup> a 2<sup>(2)</sup>

- Behaviorálne zmeny:

- Exekutívne <sup>1,2</sup> (*Tower of Hanoi, Five-point test*) a pozornosť <sup>2</sup> (*Symbol Search, Digit Span*) funkcie, globálny skrínink (*MoCA*)<sup>1,2</sup>, a telesná zdatnosť<sup>1</sup>

- Zmeny vo FK:

1. v senzomotorickej sieti (SMN) a medzi anteriórnou default mode sieťou-dorzálnou pozornosťou sieťou (aDMN-DAN)
2. v parametroch 5 dynamických funkčných stavov (metóda ICA)
  - Parametre: doba trvania (dwell time) a coverage (pokrytie) stavu

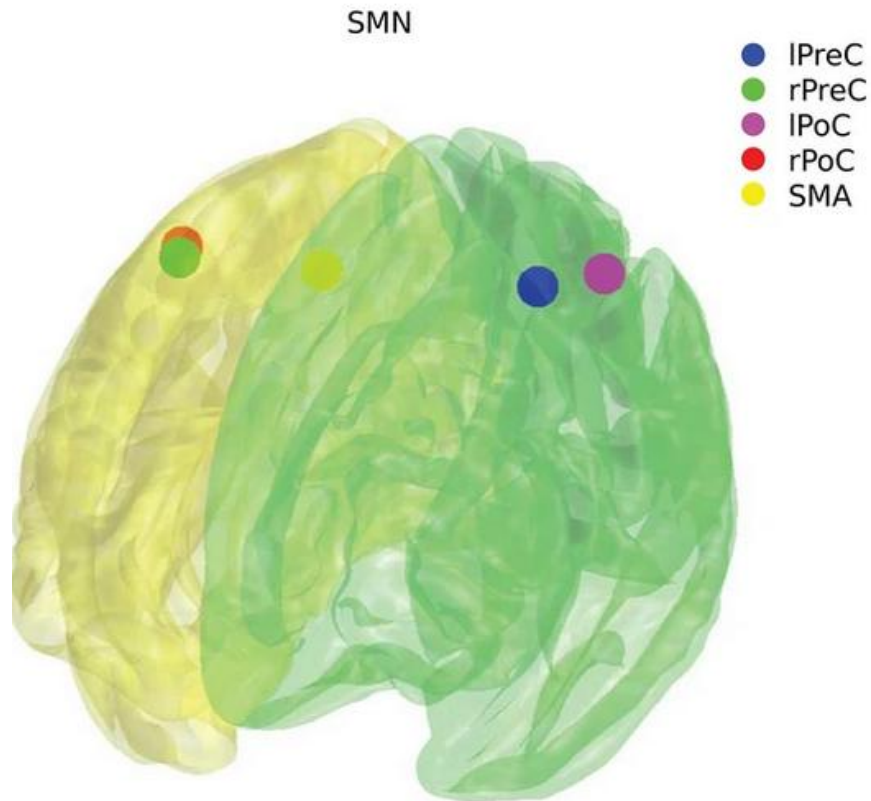
- Moderátor KR odhadovaná:

1. Staticky: pomocou vzdelania
2. Dynamicky: reziduálneho indexu

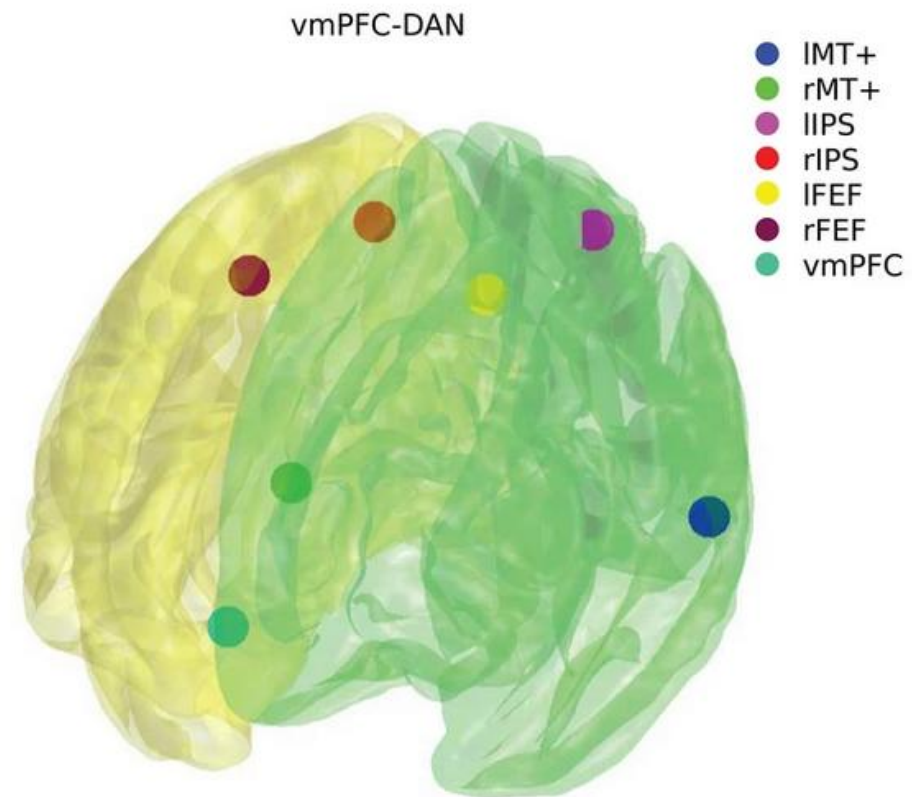
# Protokol štúdií

- 99 nedementných seniorov (~60 s úplnými dátami) randomizovaní do tanečnej a kontrolnej skupiny (Kropáčová et al., 2019)
- Neuropsychologická eval. pred a po 6-mesačnej intervencii
- Intervencia: 3x1h stredne intenzívnej tanečnej aktivity týždenne

# Výsledky štúdie 1

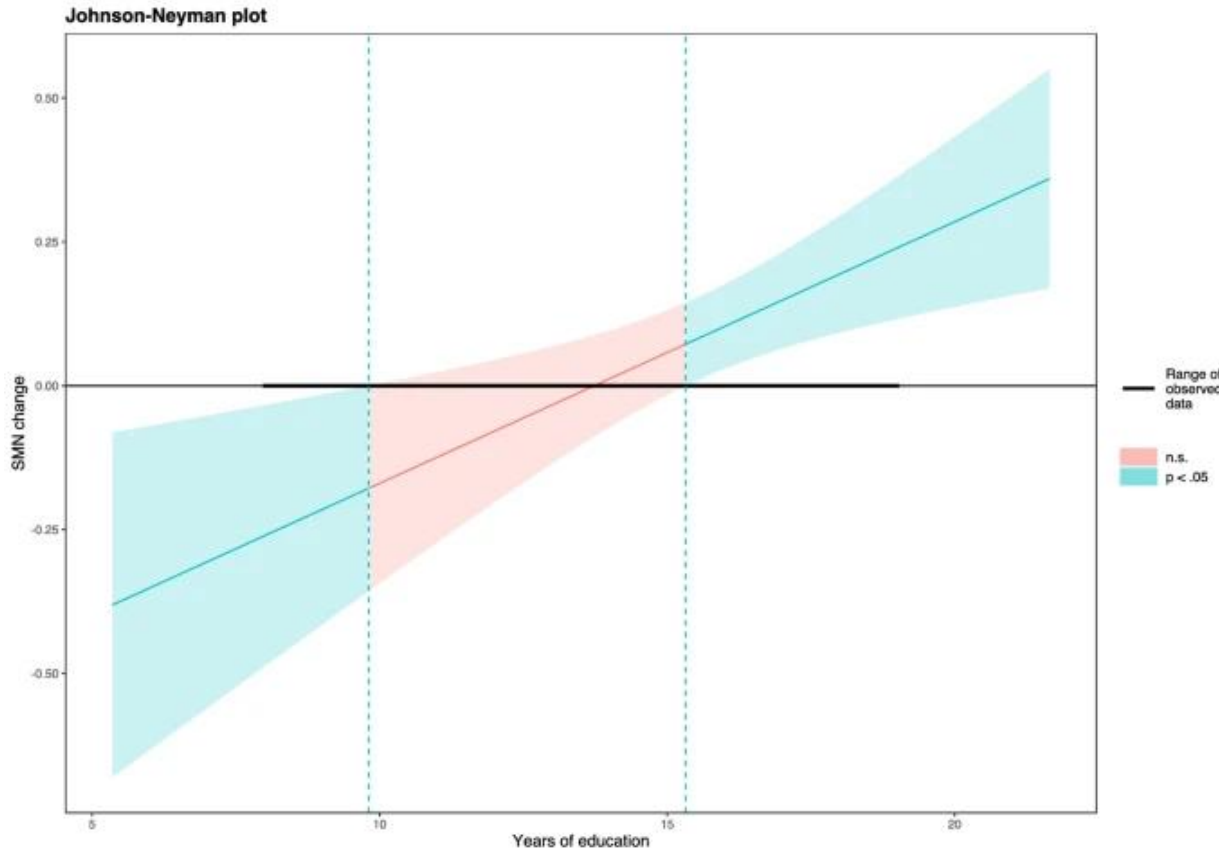


- posilnenie po motorických intervenciách
  - (i.e. McGregor et al., 2018; Voss et al., 2010)
- prekladá vonkajšie a vnútorné vstupy do motorických reakcií



- ↑ antikorelácia dôležitú regulačnú funkciu a súvisí s kognitívnou efektíviou, pracovnou a epizodickou pamäťou
- vmPFC modulácia reakčných časov a rezolúciu konfliktu, pozornosť
  - (i.e. Spreng et al., 2017; Crosson et al., 1999, Novakova et al., 2020)

# Výsledky moderačných analýz



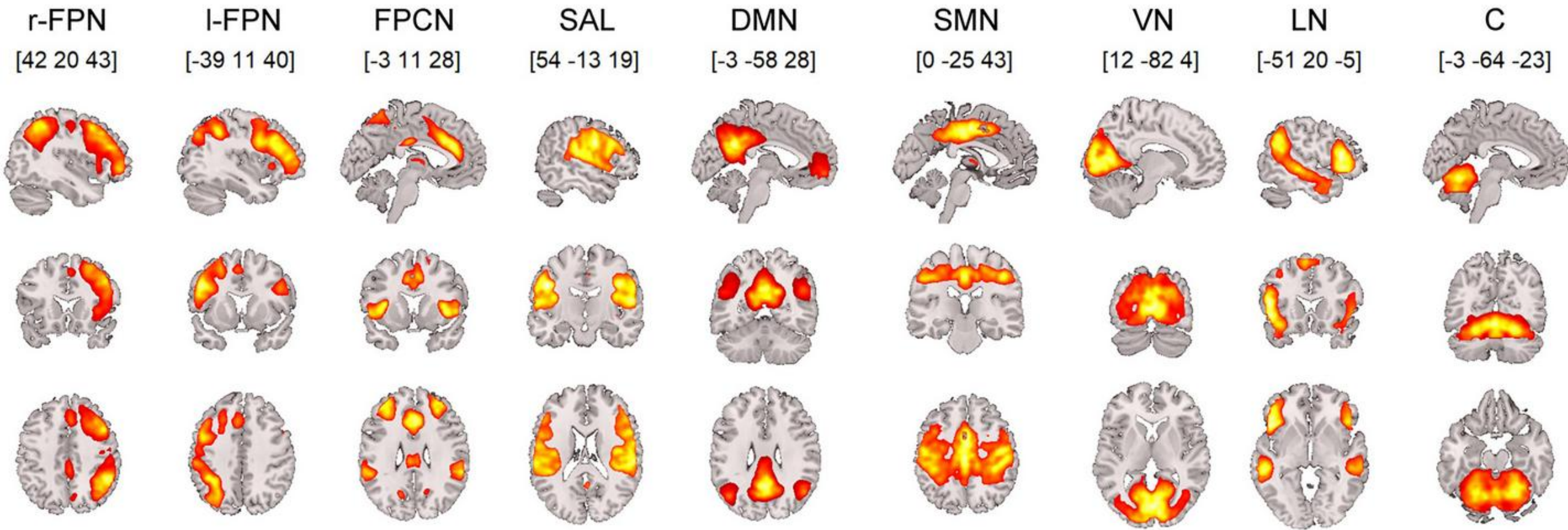
- Zvýšenie FK SMN po TI u participantov s vyššou KR (15.34 rokov vzdelania;  $t(58) = 3.17$ ,  $p = .002$ )
- Nezávislé na veku, pohlaví
- Zmeny FK aDMN-DAN súviseli pozitívne s TI ( $t(58) = 2.16$ ,  $p = .035$ )
- Nezávislé na KR ( $p = .49$ ), veku, pohlaví

# Výsledky korelačných analýz

- Zvýšenie FK SMN korelovalo so zlepšením v 8-Foot up and Go teste ( $r = -.21, p < .05$ )
- Zvýšenie FK DAN-aDMN korelovalo so zlepšením vo figurálnej fluencii (FPT) ( $r = .21, p < .05$ )
  - Vstupná miera FK SMN a DAN-aDMN nekorelovaná s testami

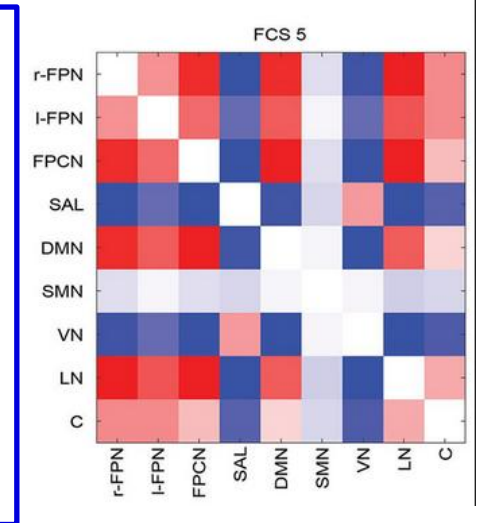
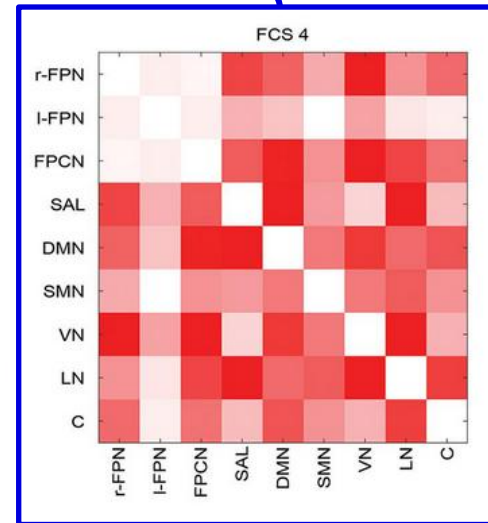
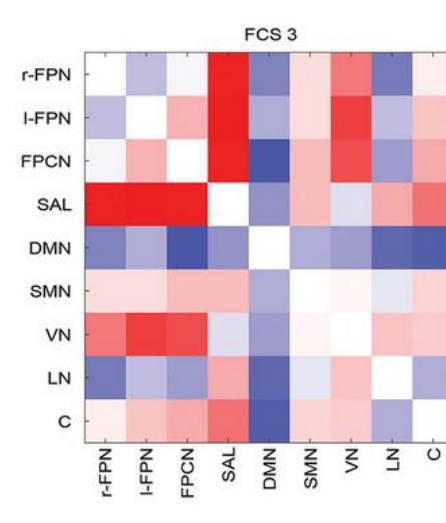
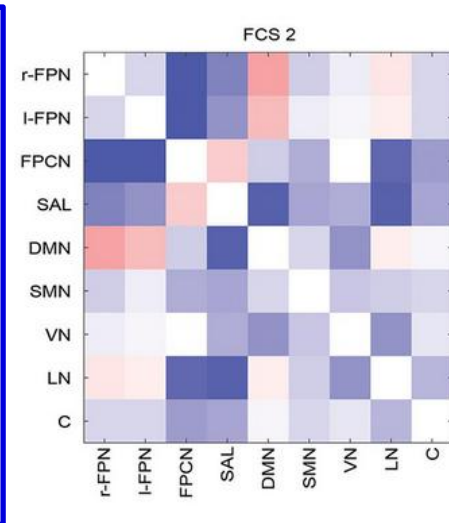
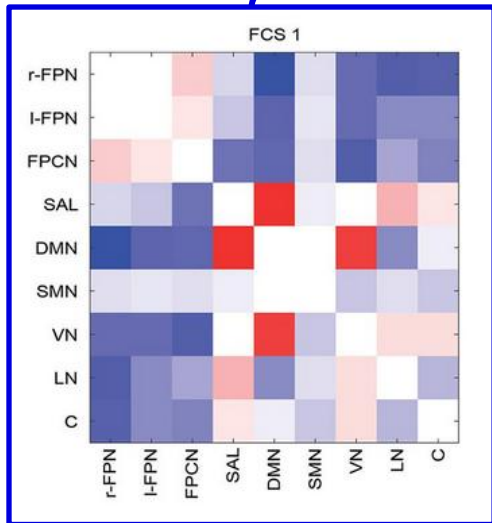
# Výsledky štúdie 2





# Výsledky ICA a LMM

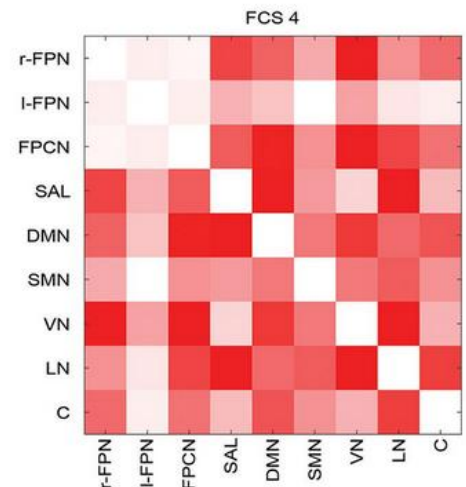
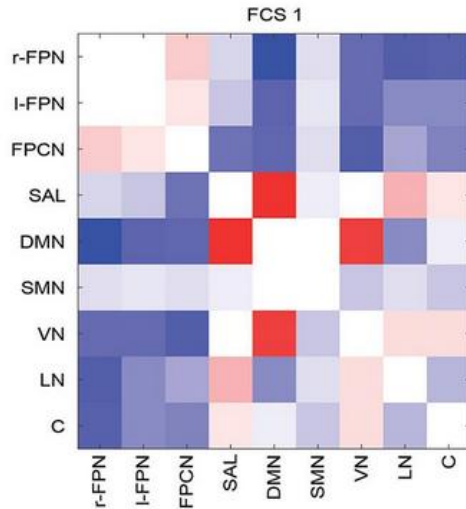
Zmeny závislé na TI\*KR interakcii



- **Doba zotrvania** ( $F(3,73) = 4.17, p = .009$ )
- **Pokrytie** ( $F(3,70) = 3.13, p = .031$ )

- **Pokrytie** ( $F(3,72) = 2.61, p = 0.058$ )

# Výsledky moderačných analýz



- Riedko prepojený stav charakteristický pre “bottom-up” spracovanie
- **Doba zotrvania** (od  $-0.5$  SD;  $t(58) = -2.14$ ,  $p = 0.036$ ) a **pokrytie** (od  $-1$  SD;  $t(58) = -2.22$ ,  $p = 0.030$ ) sa po TI zvýšili u participatov s nižšou reziduálnou KR;
  - Nezávislé od veku a pohlavia
- Zvýšenie doby trvania korelované so zlepšením skóre v **Symbol Search**
  - ( $r = 0.41$ ,  $p = .023$ )
- Husto prepojený stav charakteristický pre “top-down” spracovanie
- **Pokrytie** ( $t(58) = 2.11$ ,  $p = 0.039$ ) bolo zvýšené po TI u subjektov s priemernou až vyššou reziduálnou KR (od  $\sim +0.5$  SD)
  - Nezávislé od veku a pohlavia

# Záver: pre koho je TI vhodná?

- Z prvej štúdie vyplýva, že osoby s vyššou statickou KR sú pripravenejší k zmenám plasticity mozgu v oblastiach SMN  
**avšak**
- Z druhej štúdie: TI benefity sú individuálne a závisia od KR a toho aké siete sú využívané
- TI vhodná nie len pre participantov s normálnymi kompenzačnými mechanizmami, ale aj pre tých, ktorých mozog aktuálne čelí patológii → nutné KR operacionalizovať pomocou dynamického indexu

# Ďakujem za pozornosť