Recognition of dementia by hand movement and speech analysis

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HUNGARIAN ACADEMY OF SCIENCES · 1825 ·

Lendület program

Nemzeti Agykutatási Program 3.0

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EU-FINGERS
EUROPEAN MULTIDOMAIN INTERVENTIONS FOR DEMENTIA PREVENTION

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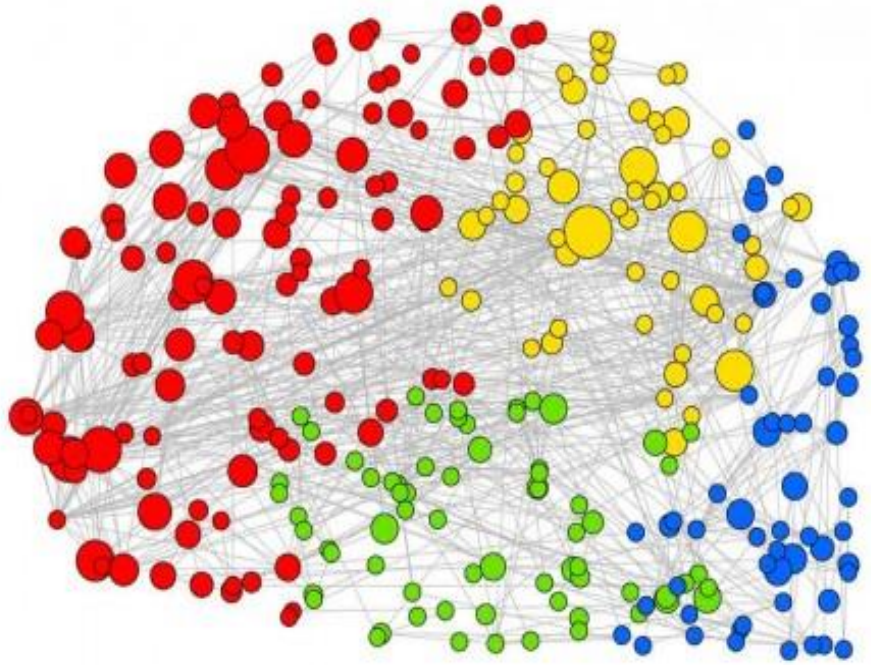
Agenda

- **Introduction- NRC**
- Alzheimer's disease and movement characteristics
- Unresolved issue



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NRC in numbers

- 6 Postdoctor scientists
- 9 PhD students
- 5 Undergraduate students
- 4 Biomedical engineers
- 2 Neuropsychologist
- 1 Biostatistician

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ACOL database

Name	AlzEpi Cohort Observational Library (ACOL) N≈500
Participants	HC, SCD, MCI, AD
Biomarkers	Imaging (sMRI, resting fMRI, DTI) Blood CSF Neuropsychology Fine-movement data Autonomic functions Neurophysiology (24-hour EEG, PSG)
Availability	2014-

- Inclusion criteria
  - Jack 2024- NIA-AA, Petersen 2014, Jessen 2020
- Exclusion criteria
  - antipsychotic therapy in last month
  - extended or non- specific MRI lesions (Laasko)
  - alcohol- drug dependency
  - previous CNS infection
  - known psychiatric disorder
  - epilepsy >10 years before AD

Promoting open science- Openclinica system!

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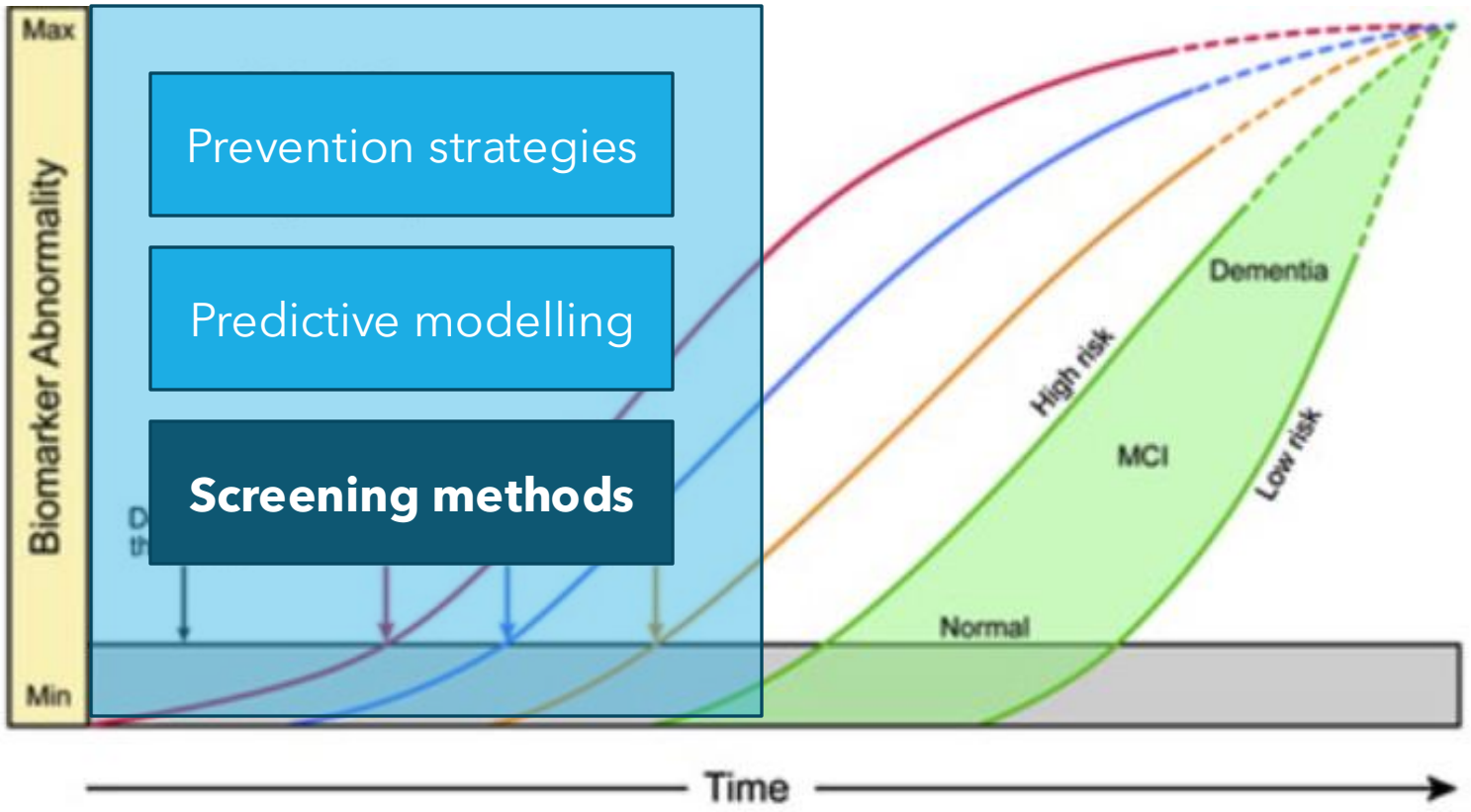
NRC profile



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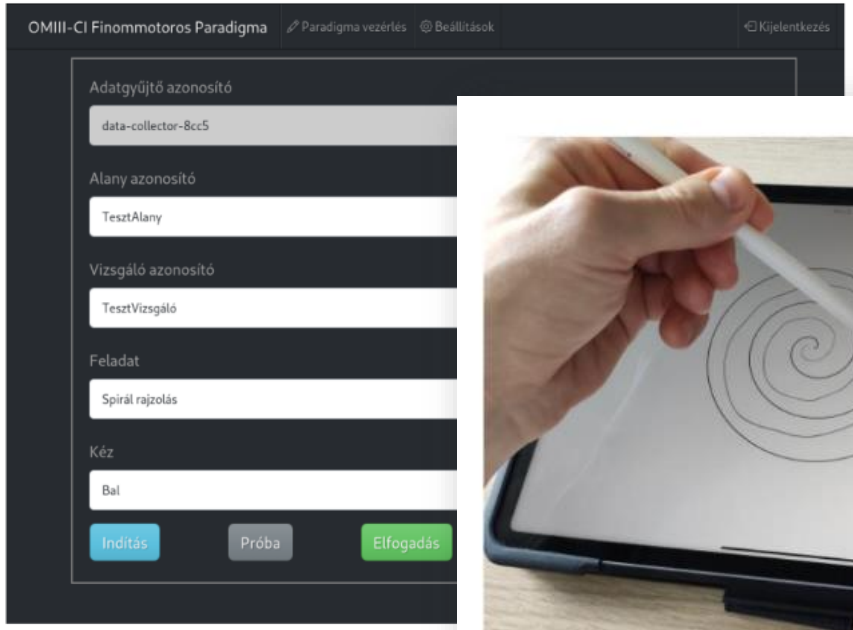
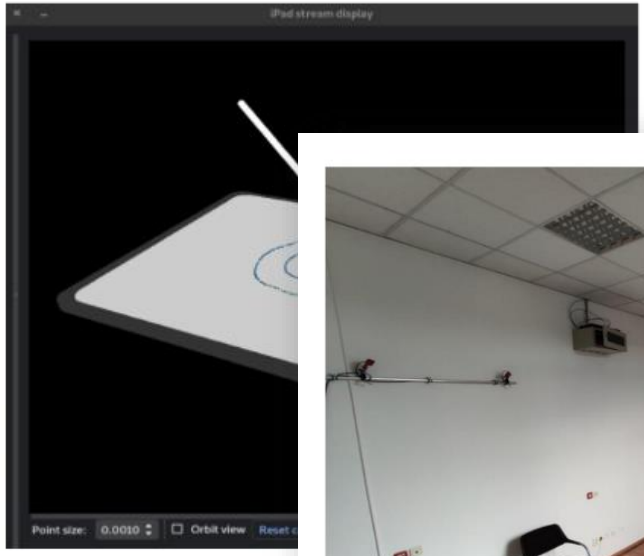
NRC-CI movement lab



1. ábra - Webes adminisztrációs felüle

2. ábra - Tabletes adatgyűjtő



3. ábra - Valós idej

4. ábra - 3D mozgáselemző kamerarendszer (helyszín: OMIII Neurokognitív Kutatóközpont)

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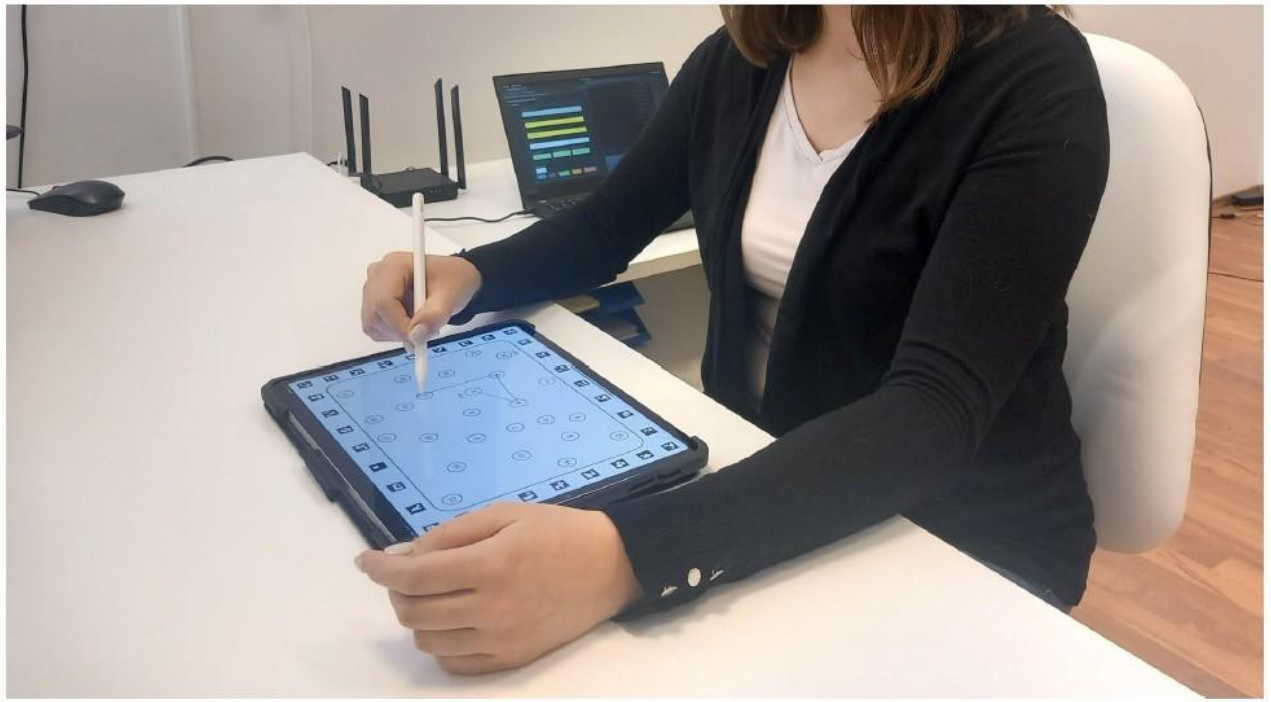
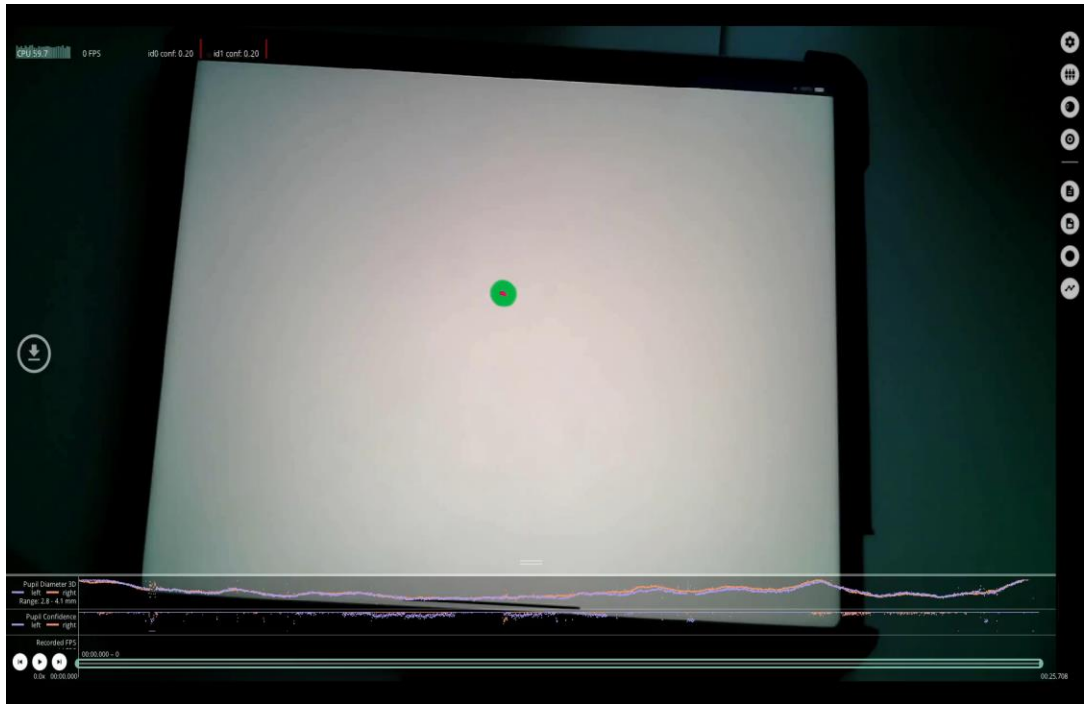
Measurement setup





The system provides a convenient way of assessing fine motor movement parameters.
Current task on the figure: TMT-A with visual markers for fine motor data registration.

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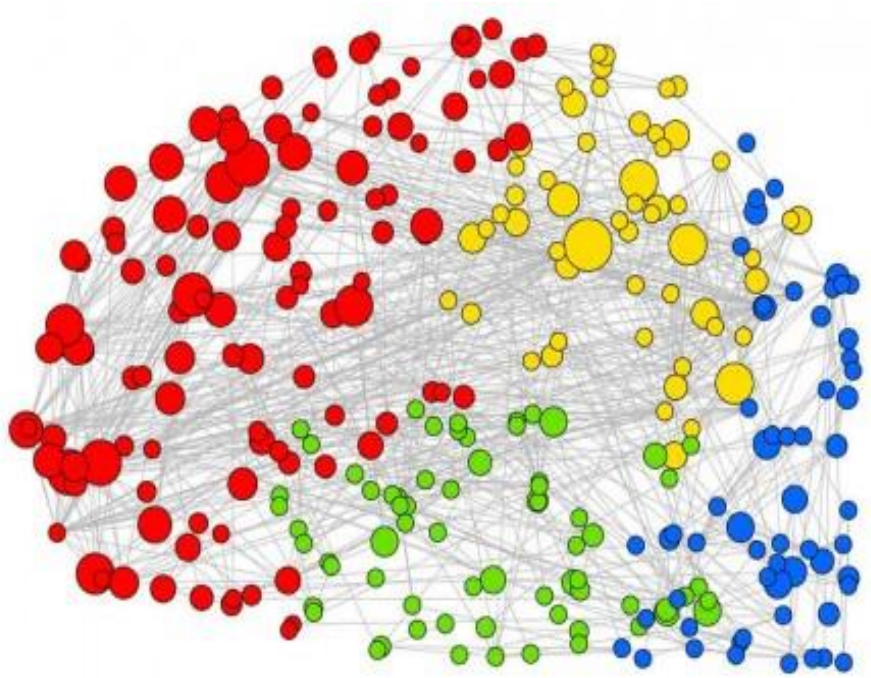

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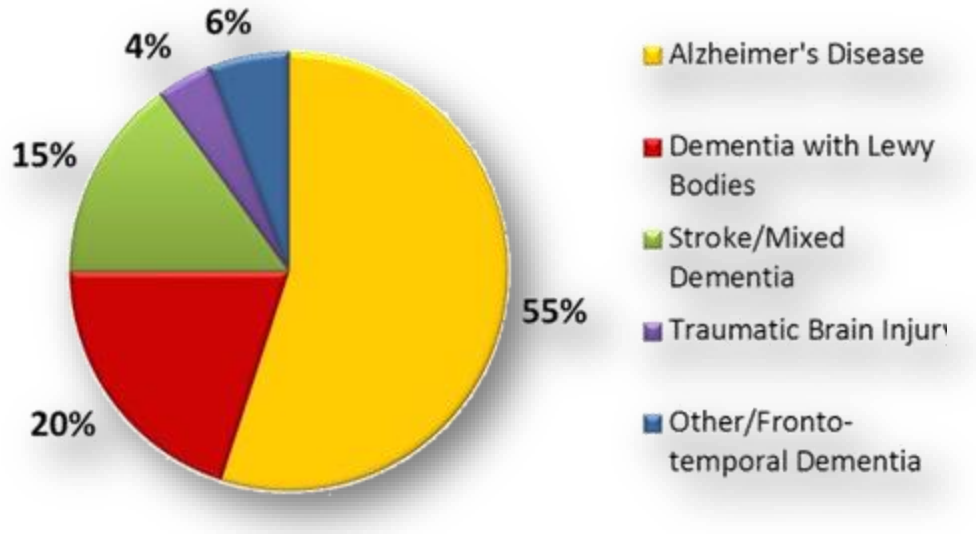
State of art: AD

- AD from NCD: 50-70%
- Prevalence: 47 million, incidence: 4.6 million
- 6. mortality cause
- 1. morbidity cause
- Burden: ~300 billion USD (USA 2022)



Brookmeyer et al., Alz and Dement, 2016; World Alzheimer Report 2022

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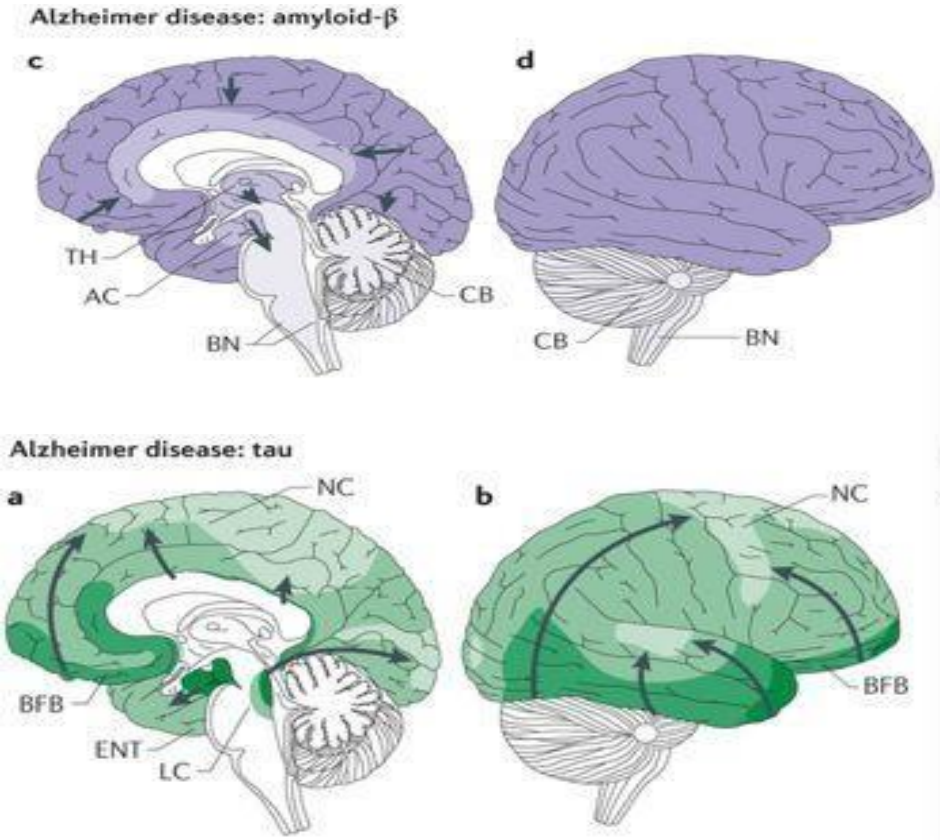
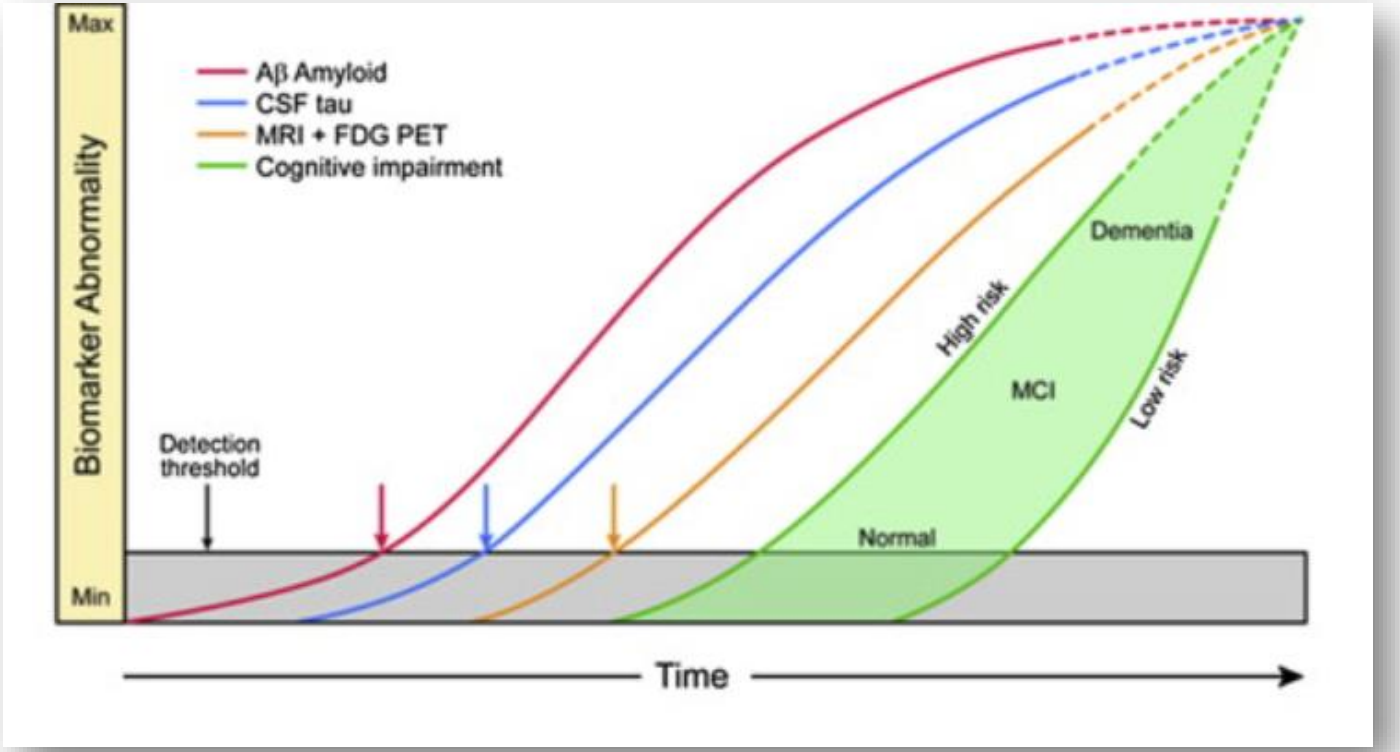
Pathology





Braak and Braak, Acta Neuropathol, 1991; Jack and Holzmann, Neuron, 2013

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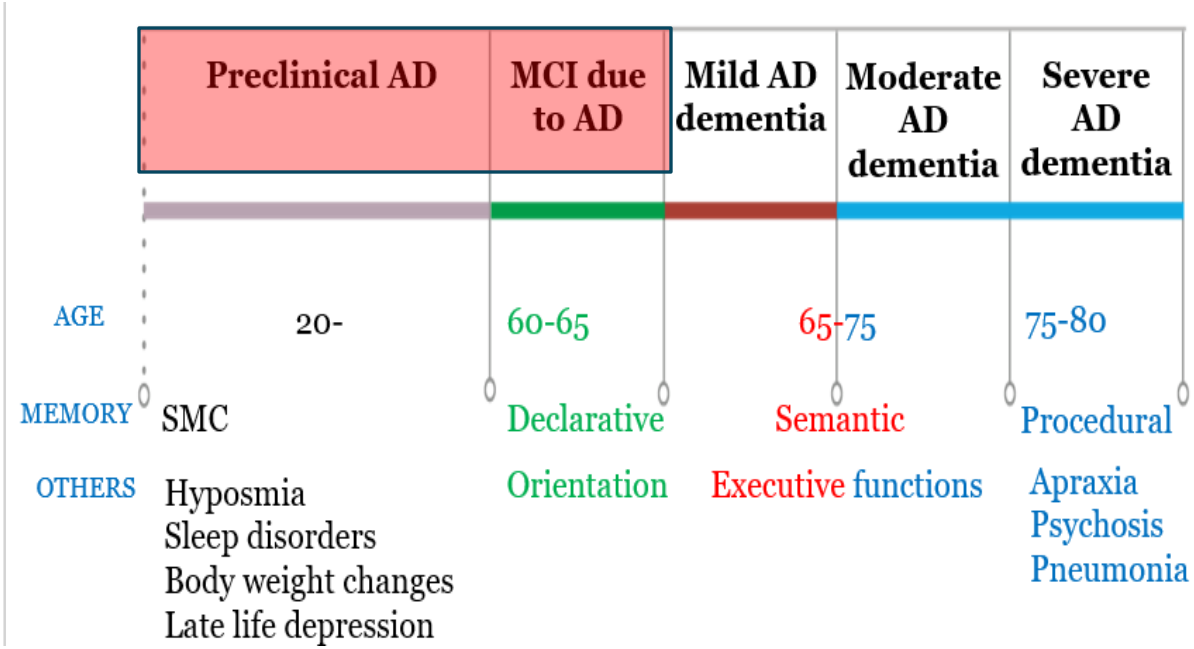
Disease course



Therapeutic window

The importance of early recognition

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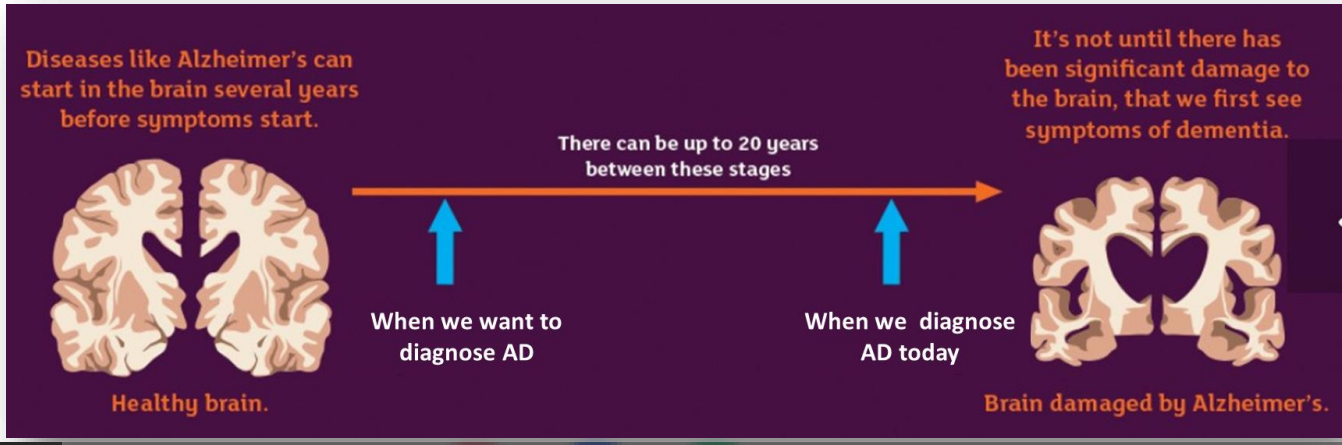
1. Treatable diseases that cause dementia can be identified in time.
2. Comorbidities aggravating dementia can be recognized.
3. Pharmaceutical and non-pharmaceutical treatment can be started in time.
4. The lifestyle and care plan tailored to the patient can be developed in time.



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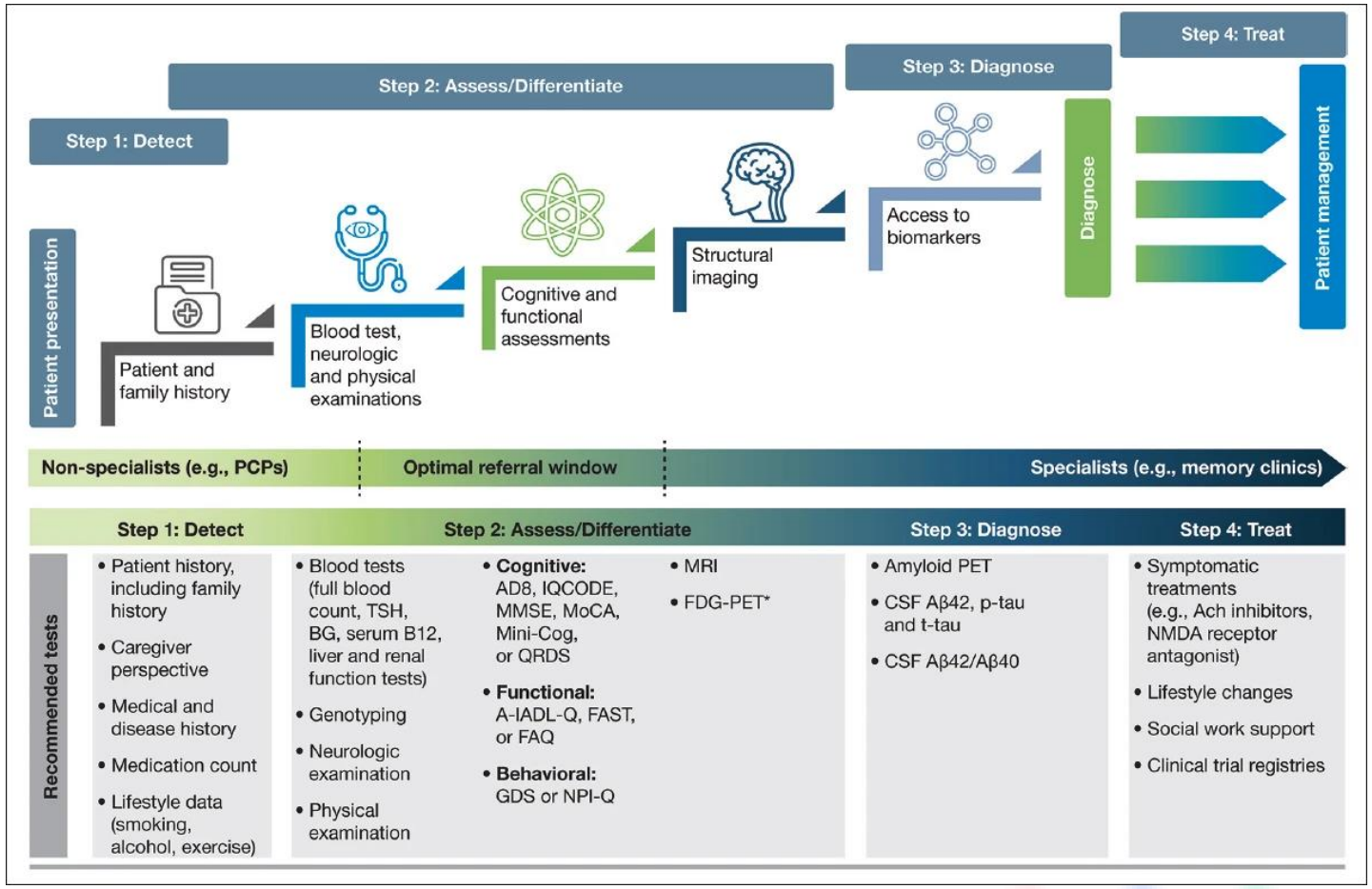
Diagnostic pipeline



Porsteinsson, A.P., Isaacson, R.S., Knox, S. *et al.* Diagnosis of Early Alzheimer's Disease: Clinical Practice in 2021. *J Prev Alzheimers Dis* **8**, 371–386 (2021).

Challenges in the early diagnosis

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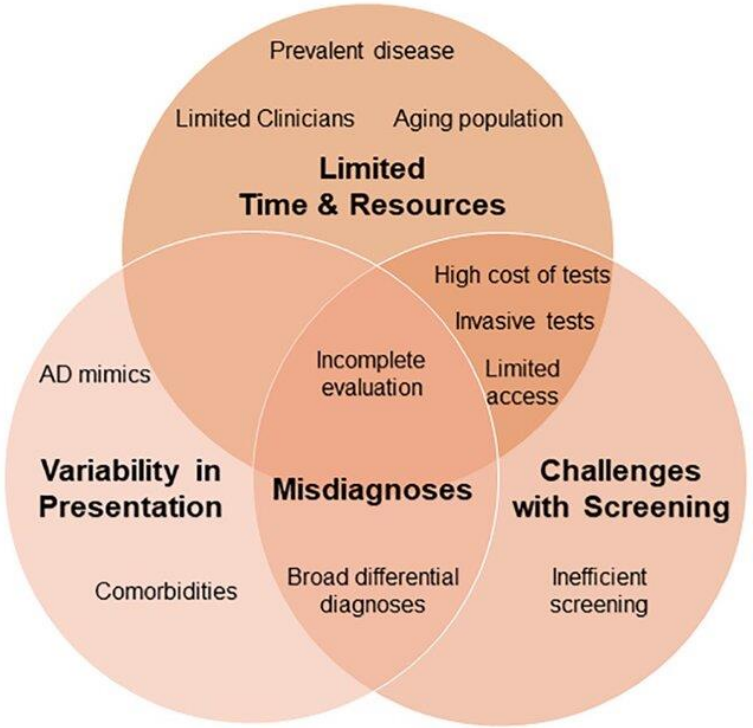
The lack of
- broadly applicable,
- sensitive and specific screening methods that are
- easy-to-use
  - ✓ in clinical settings and
  - ✓ in primary care physician practices.



The currently used methods are
- subjective,
- not standardised,
- time-consuming,
- expensive,

severely limiting the number of patients who get tested for cognitive decline.

Paczynski MM, Day GS. Alzheimer Disease Biomarkers in Clinical Practice: A Blood-Based Diagnostic Revolution. J Prim Care Community Health. 2022.

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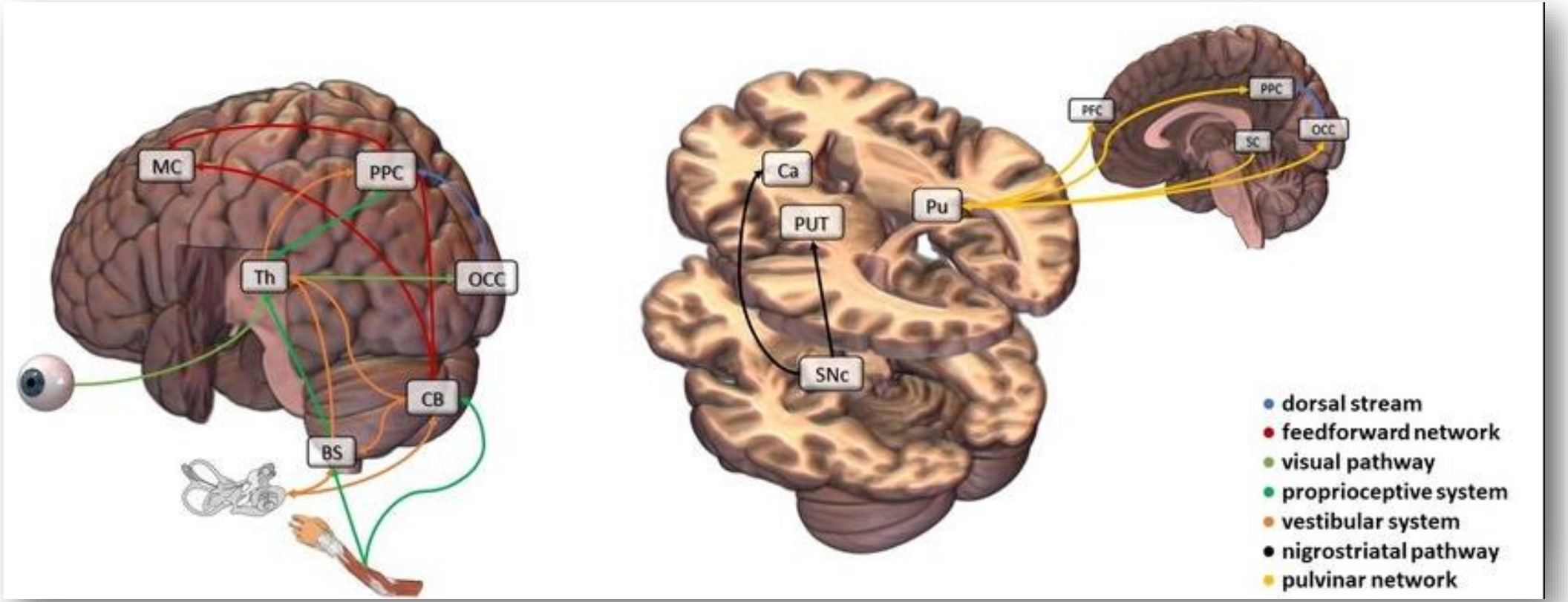
Why movement diagnostics?



Henschke, Pakan. Front Syst Neurosci, 2023; Ilardi et al. J Integ Neurosci 2022

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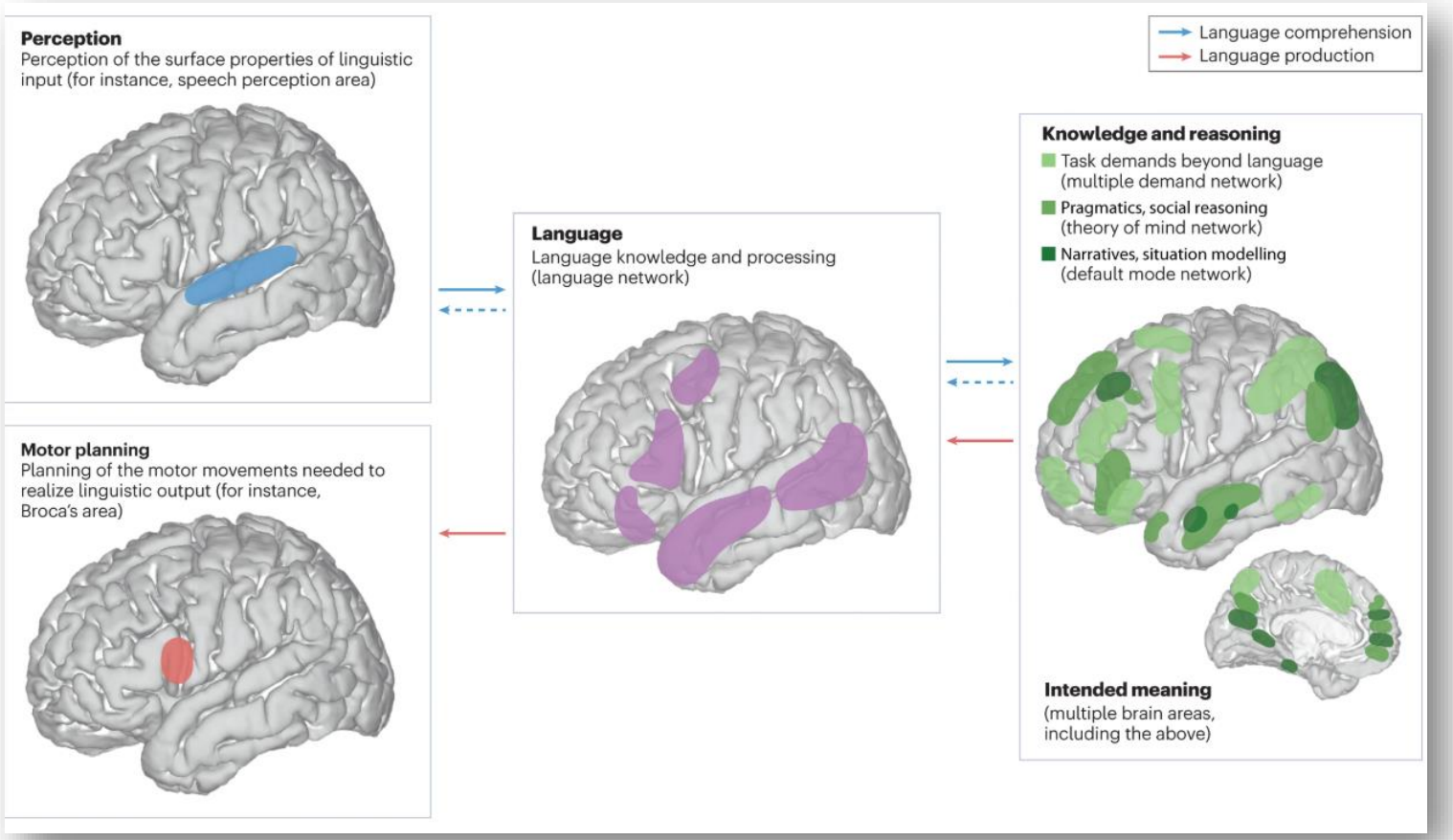
Why speech diagnostics?



Fedorenko et al. Nature Rev Neurosci, 2024

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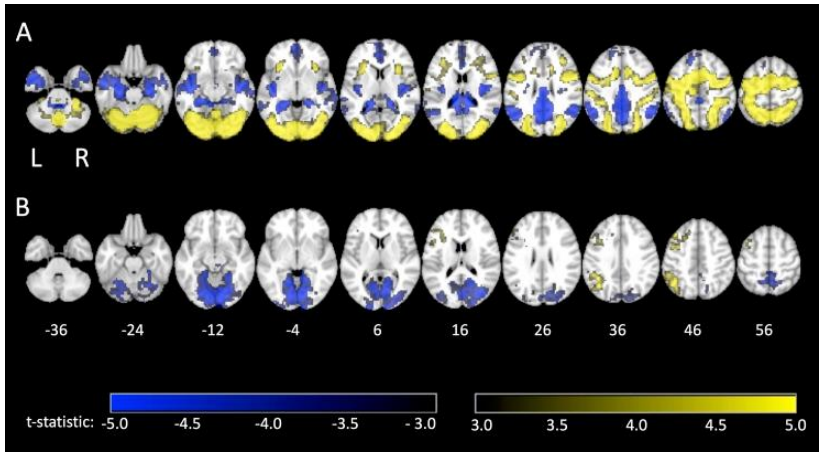
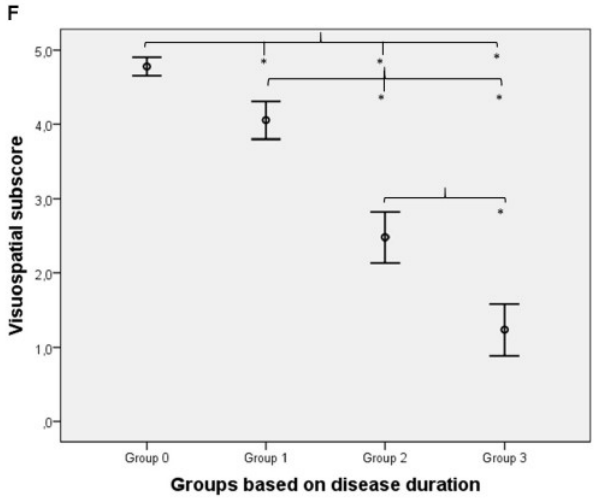
Why visuo-motor diagnostics?

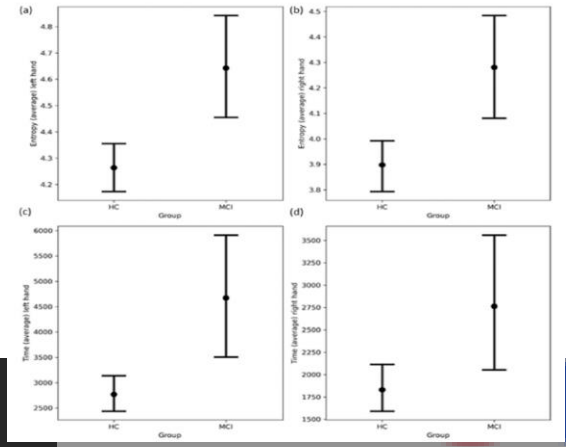
Visuo-motor abilities are already affected at the very early phase of neurodegenerative diseases.

Visuo-motor tests are

- region specific
- easy to perform
- not lanquage specific
- easily digitalized







frontiers in Aging Neuroscience

ORIGINAL RESEARCH

The Assessment of Visuospatial Skills and Verbal Fluency in the Diagnosis of Alzheimer's Disease

Dalida Borbala Berente[1,2], Anita Kamondi[2,3] and Andras Attila Horvath[2,4]*

scientific reports

OPEN

Differentiation of patients with mild cognitive impairment and healthy controls based on computer assisted hand movement analysis: a proof-of-concept study

Andras Attila Horvath[1,2✉], Dalida Borbala Berente[2,3], Balazs Vertes[4], David Farkas[4,5], Gabor Csukly[3,6], Tom Werber[7], Janos Andras Zsuffa[8,7], Mate Kiss[9] & Anita Kamondi[2,3]

Hand writting

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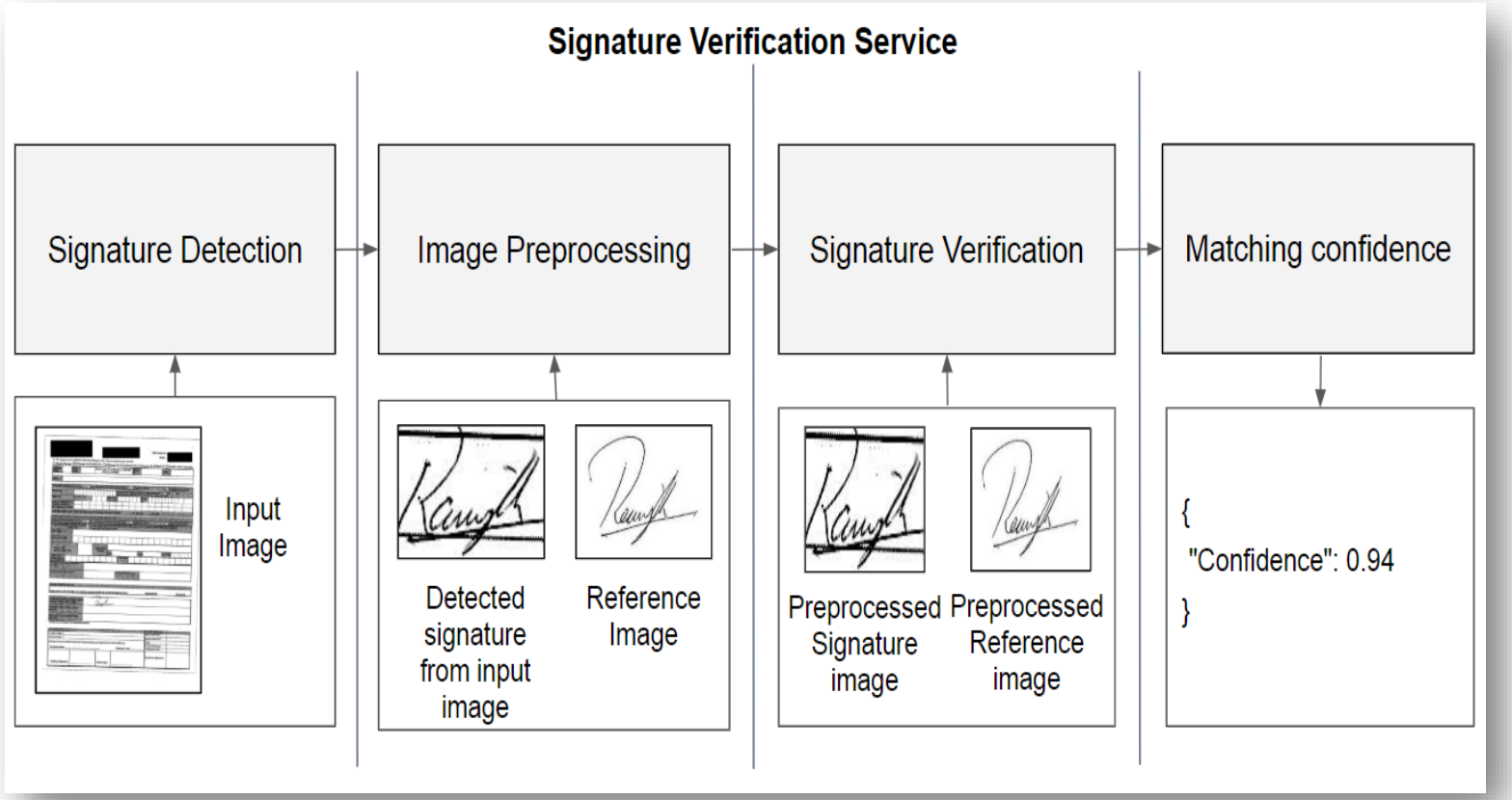

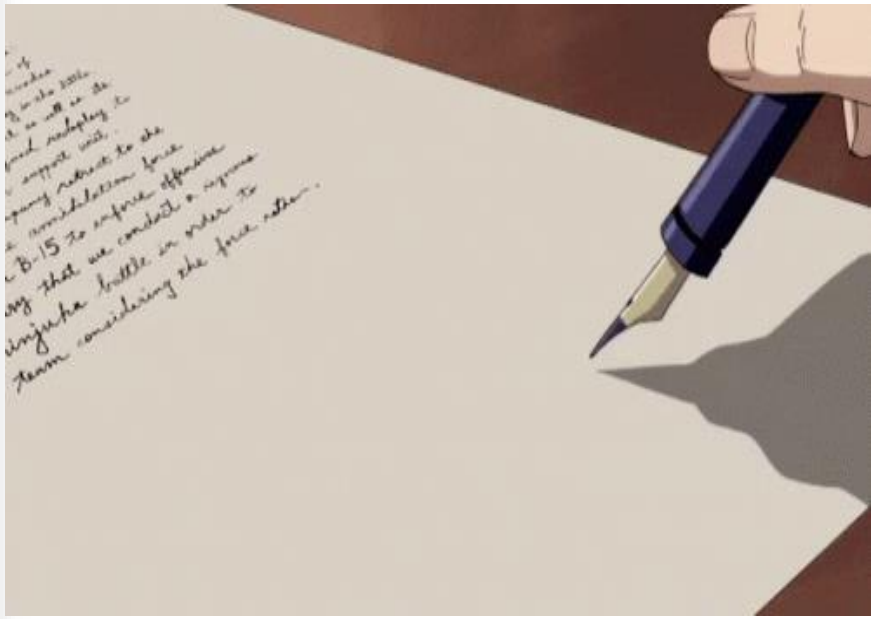

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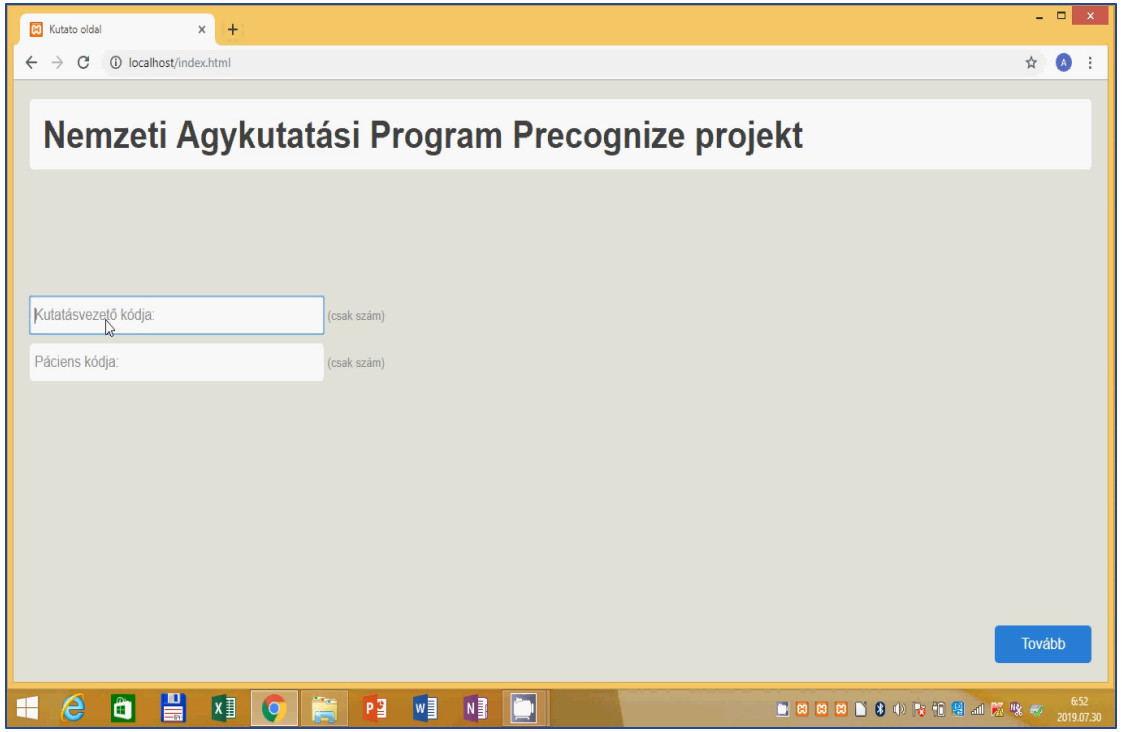
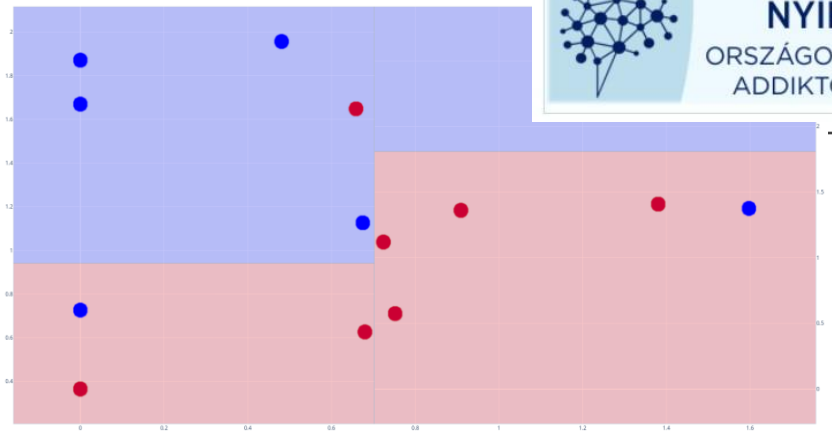
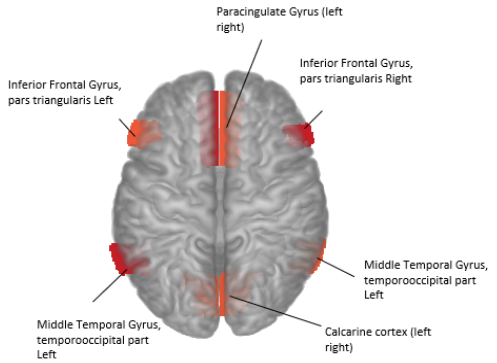
Early results

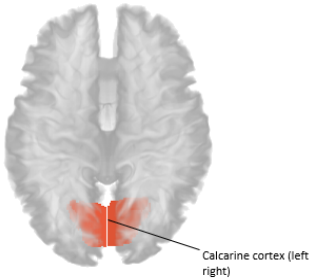




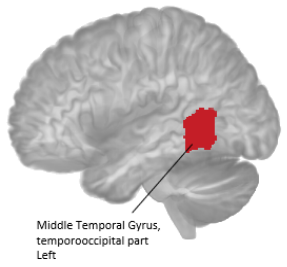
Fractuinal Amplitude of Low Frequency Fluctuations



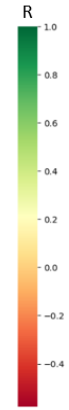
Entropy-right hand



Time-right hand



Velocity-right hand



Horvath el al., 2022; Hanczar et al., 2022; Berente el al., 2024- unpublished

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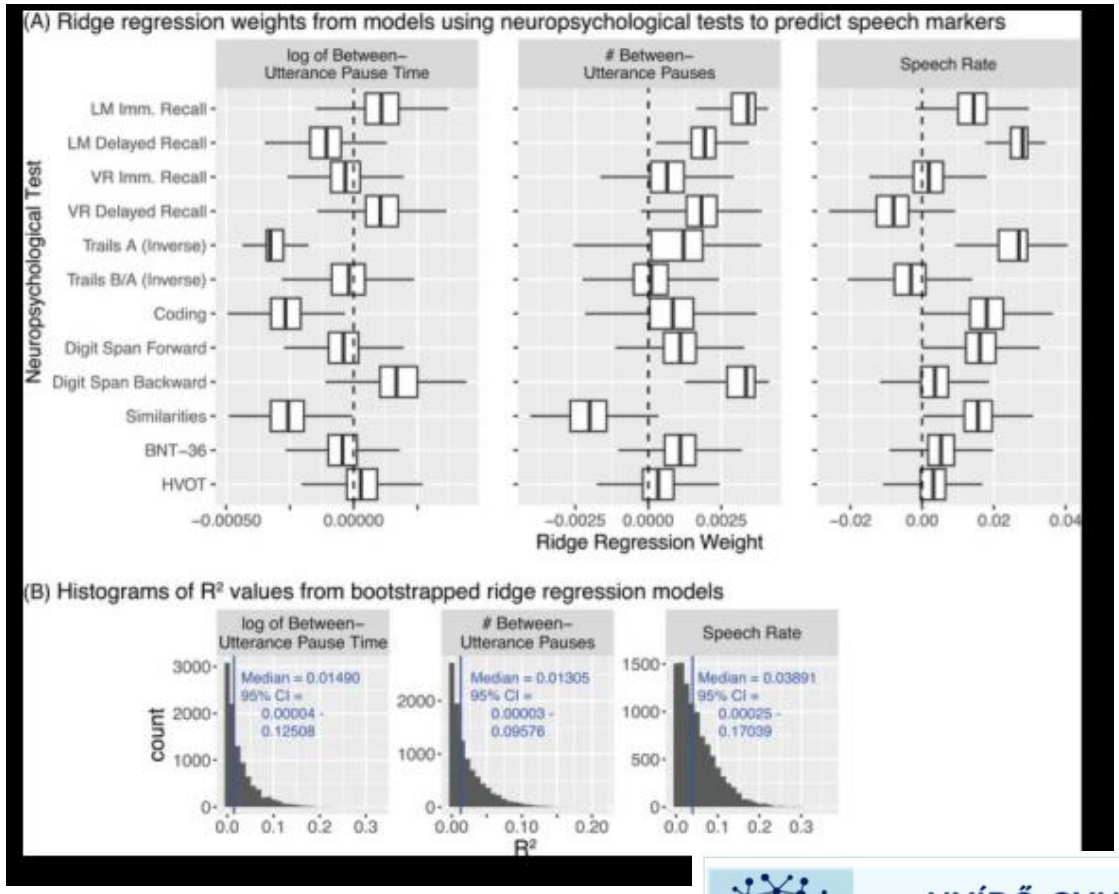
Cross-validated classification

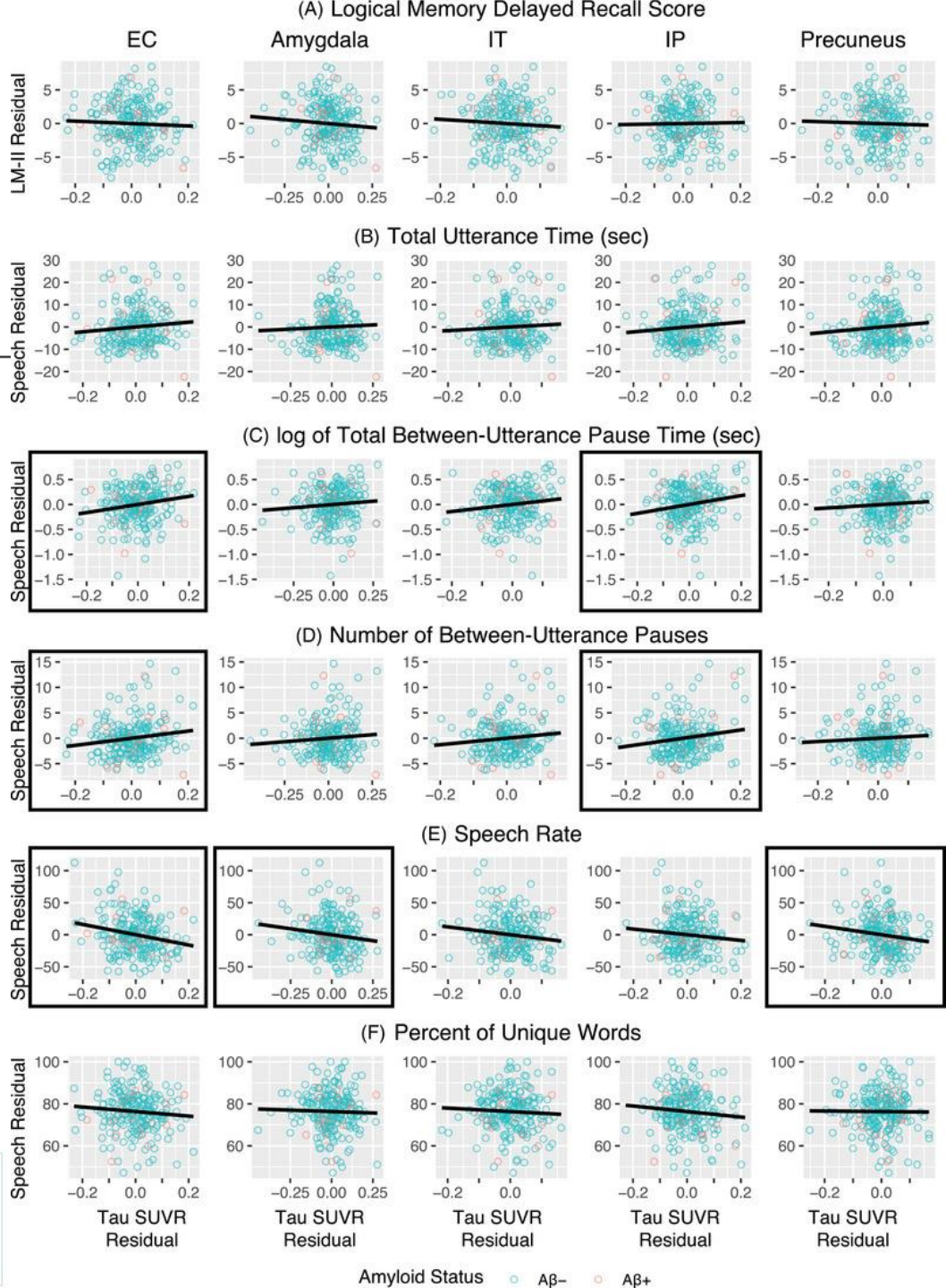
Task	*Sensitivity*	*Specificity*
Spiral	52.1% ± 27.3%	71.4% ± 30.2%
TMT-A	79.5% ± 20.4%	61.5% ± 17.7%
Benson fig. copy	88.3% ± 12.3%	85.8% ± 10.0%
Phone number	77.1% ± 26.9%	42.4% ± 29.7%
Sentence	71.0% ± 28.2%	51.5% ± 30.5%

Table 1: **Preliminary cross-validated classification metrics for the available data.** Given the small number of target class samples (N = 7), a 4-vs-3 splitting scheme was applied in all possible combinations of MCI/Dementia subjects as train and test subsets, resulting in a total of 35 folds. Control subject data was randomly assigned to train and test sets in each fold, following the same 4-to-3 ratio. Feature vectors were averaged per task for each subject and the classification models were assessed for sensitivity and specificity. Results show promising classification metrics but also the need of increasing MCI/Dementia subject ratio for building robust models.

108 subjects, 92 control, 8 MCI and 8 dementia
AlzEpi Cohort Observational Library (ACOL database)

Speech and dementia





Young et al. Alzheimer Dement, 2024

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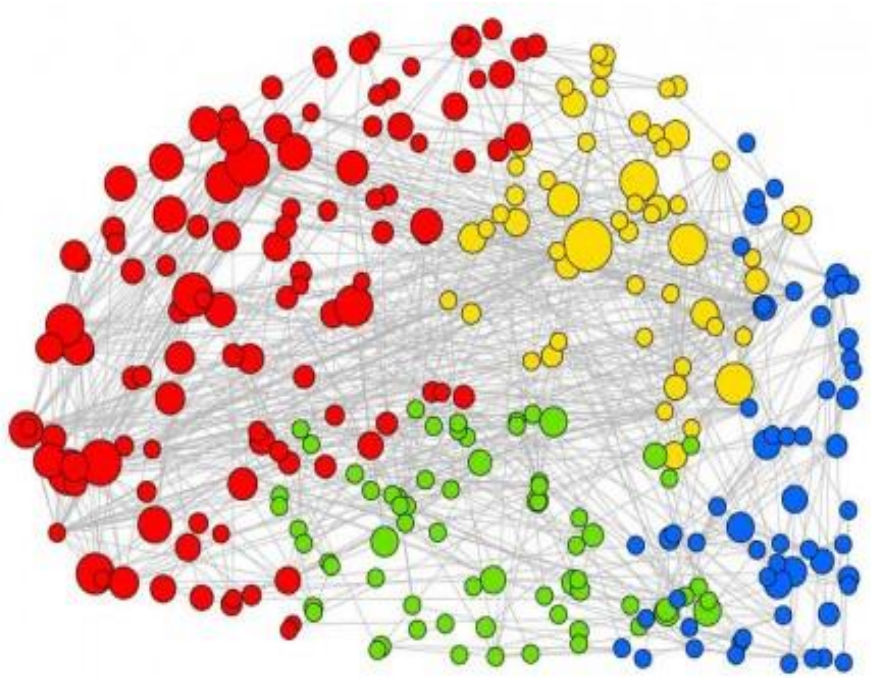

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Kinematics of hand writting

Table 3. Handwriting features				
Kinematic Parameters				
Movement characteristics during handwriting				
Velocity	Measures the speed of the pen movement	motor control issues	lower, slower	(Cilia et al., 2022; Garre-Olmo et al., 2017; Kim et al., 2020; Kobayashi et al., 2022; M. Kachouri, 2021; Perla Werner, 2006; Qi et al., 2023)
Acceleration	The rate of change of velocity	difficulties in initiating and controlling movement		(Cilia et al., 2022)
Jerk	The rate of change of acceleration. It measures the smoothness of the handwriting	neuromotor dysfunction and reduced motor control		
Pressure	The force applied by the pen on the tablet surface	impaired motor function and proprioceptive feedback issues	greater, higher variance, more unstable	(Cilia et al., 2022; Kobayashi et al., 2022; M. Kachouri, 2021; Qi et al., 2023)
Azimuth	Describes the orientation and movement dynamics of the pen	Fine motor control, planning		
Altitude	Refers to the height of the pen from the writing surface and may indicate variations in pen and stroke thickness	Spatial awareness and visual-spatial processing	lowest, however least reliable than pressure	(Cilia et al., 2021; M. Kachouri, 2021)
Curvature variance	Indicate changes in the direction or curvature of strokes varies along its length (also contribute indirectly to spatial characteristics)	Motor coordination and cognitive processing	line segment was longer	(Jiali Chai, 2023)
Stability	Measures the proportion of constant or unchanged curvature (also contribute indirectly to spatial characteristics)	Motor control, planning and execution	higher variance	(Jiali Chai, 2023; Qi et al., 2023)

Kőrösi et al. 2024- unpublished

Spatial characteristics of hand writting

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Spatial parameters				
Spatial or geometric characteristics, and measure the physical dimensions and arrangement of the handwriting				
Length of path	The total distance covered by the pen	difficulties in motor planning and spatial organization	shorter, smaller imagine size, larger ratio	(Jiali Chai, 2023; Kim et al., 2020; Yu & Chang, 2019)
Size	The dimensions of letters, words, and overall handwriting	Indicates motor execution and spatial awareness	shorter strokes, smaller drawn/written images, larger variance	(Jiali Chai, 2023; Kim et al., 2020; M. Kachouri, 2021; Yu & Chang, 2019)
Spacing	The space between letters and words	difficulties in motor control and visual-spatial processing		
Alignment	Consistency and accuracy in maintaining straight lines and margins	impaired motor coordination and visual-spatial deficits		
Stroke thickness	Width or boldness of the lines produced by the pen during handwriting. It indicates how much graphical output is deposited on the writing surface.	Impairments affecting attention, motor planning, and spatial awareness can lead to irregularities in stroke thickness		
Stroke Height/Width	Stroke height shows the vertical dimension of a stroke (e.g., how tall a letter is), while stroke width refers to the horizontal dimension (e.g., how wide a stroke is)	Indicates stable motor control and coordination, visual-spatial processing and executive function	smaller, higher variability	(Kim et al., 2020; Perla Werner, 2006; Qi et al., 2023; Yu & Chang, 2019)

Kőrösi et al. 2024- unpublished

Temporal characteristics of hand writting

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Temporal parameters				
Refer to the timing aspects of handwriting, and measure how long different parts of the handwriting process take				
Writing time	Total time taken to complete a writing task	Reflects cognitive processing speed and motor execution	longer, more time to need	(Garre-Olmo et al., 2017; Huang et al., 2019; Jiali Chai, 2023; Kim et al., 2020; Perla Werner, 2006; Qi et al., 2023)
Pen-up time (in-air)	Time when the pen is not in contact with the tablet	Suggest hesitancy or planning difficulties	longer time in the air	(Cilia et al., 2021; Perla Werner, 2006; Yu & Chang, 2019)
Pen-down time (on-paper)	When the writing instrument contacts the surface of the tablet.	Variability in it can indicate inconsistent motor control	shorter time, more hesitation in the air	(Cilia et al., 2021; Perla Werner, 2006; Yu & Chang, 2019)
Transition time	Refers to the time taken to move the pen or stylus from one stroke to the next without the pen touching the writing surface (pen-up phase)	Longer transition times can indicate hesitation, planning difficulties, or cognitive slowing	longer pause time, more hesitation	(Kim et al., 2020; Kobayashi et al., 2022; Yu & Chang, 2019)
Initiation Latency	Measures the delay between the completion of one stroke and the initiation of the next stroke	Cognitive slowing or difficulties in task initiation and can reflect issues with motor planning and execution	longer	(Kim et al., 2020; Yu & Chang, 2019)
Consistency	Consistent transition times across different sequences	Indicate stable motor control, execution and spatial awareness		
Variability	Fluctuations or irregularities in transition times	Motor coordination or cognitive processing		

Kőrösi et al. 2024- unpublished

Dynamic characteristics of hand writting

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Dynamic parameters				
Reflect the changes and variabilities during handwriting				
Stroke number	The number of individual strokes	Increased number can indicate difficulty in executing smooth, continuous movements	increased, higher – making more mistakes,	(Jiali Chai, 2023; Kim et al., 2020; Qi et al., 2023)
Stroke duration	Time taken to complete individual strokes	Variability in it can reflect difficulties in motor control and timing		
Stroke frequency	The number of strokes per unit time			
Fluency	The smoothness and flow of writing, assessed through the consistency of strokes	Reduced fluency can be a sign of impaired motor coordination and cognitive processing speed		

Kőrösi et al. 2024- unpublished

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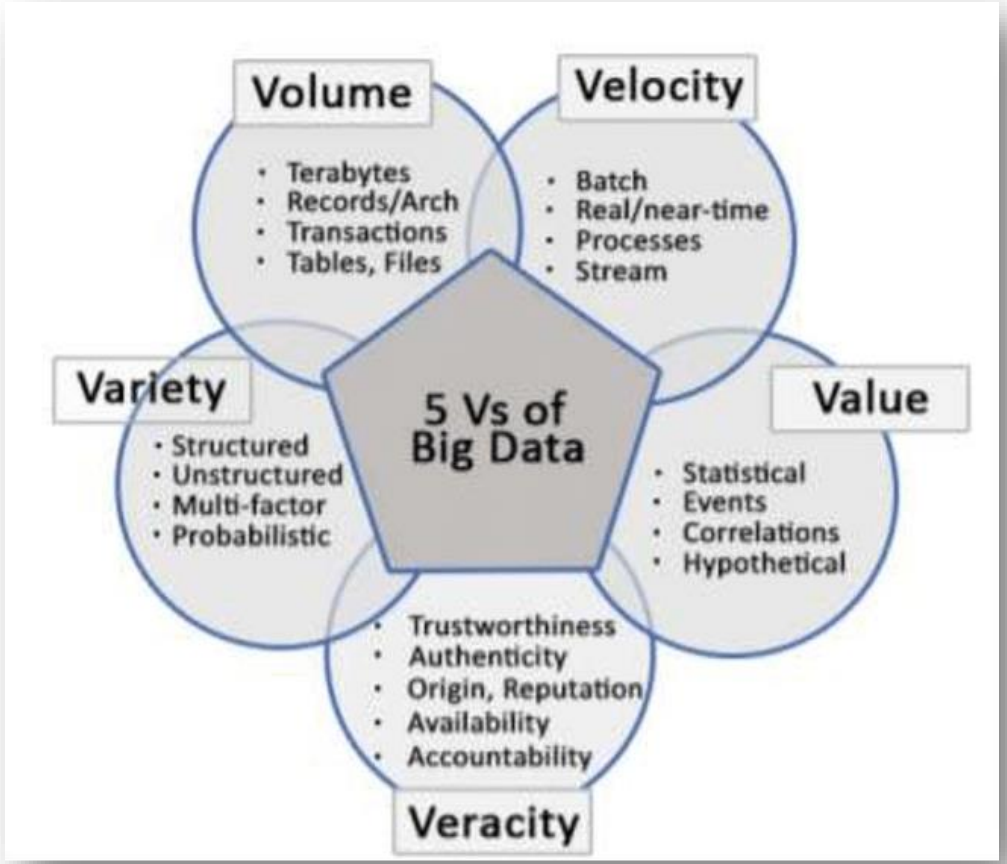
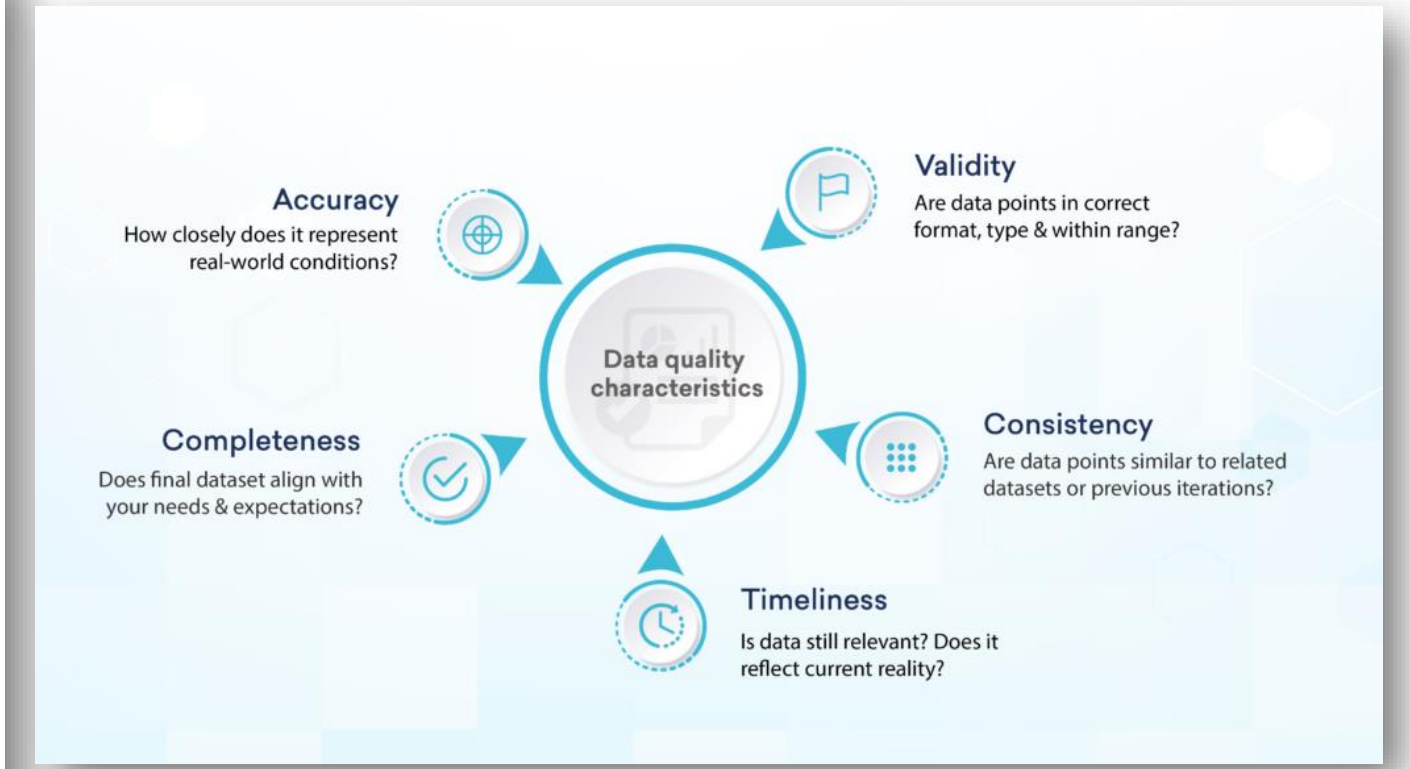
Key remarks





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