Medical/Bio Research Topics I: Week 10 (09.05.2024)

Development of Brain Imaging-based Artificial Intelligence Models (1): Data and Prediction Problems

뇌영상 기반 인공지능 모델 개발 연습 (1): 데이터 및 예측 문제

Hands-on Machine Learning (1): Predicting Memory Performance

Memory

- Fundamental brain function that encompasses the processes of encoding, storing, and retrieving information
- Plays a crucial role in various cognitive processes, such as learning, reasoning, problem-solving, and decision-making

Process of memory formation

Encoding

- Perceiving information from the environment and transforming it into a format that can be stored in the brain
- May involve sensory input becoming associated with existing knowledge, emotions, or sensory experiences

Consolidation

- Stabilizing encoded information
- Involves the reorganization of information

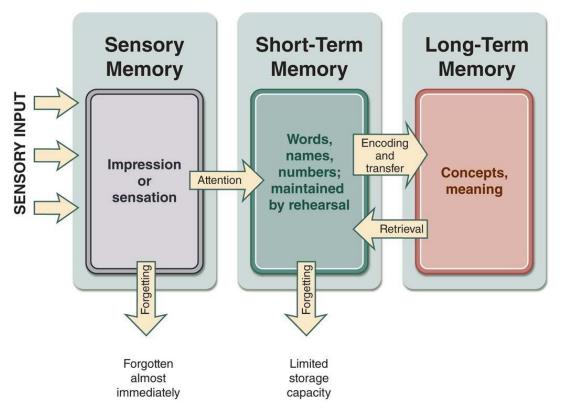
Storage

- Maintaining encoded information over time
- Short-term or long-term
- Retrieval (or recall)
 - Accessing and recalling stored information when it is needed
 - Influenced by various factors, including the context in which the information was learned and the similarity of that context when the information is recalled

Memory Types

- Based on duration
 - Sensory memory: up to a few seconds
 - Ability to retain impressions of sensory information after the original stimuli have ended
 - Short-term memory (or working memory): up to minutes
 - Ability to hold information temporarily for processing
 - Working memory is a more active version of short-term memory that involves the manipulation of the information being held in short-term memory

- Long-term memory: from hours to years or even decades
 - Ability to store information over prolonged periods
 - More stable than short-term memory



[https://getgoally.com/blog/short-term-vs-long-term-memory-kids/]

- Based on the nature of information or awareness
 - Declarative (explicit) memory: conscious recollection
 - Episodic memory
 - Remembering personal experiences and autobiographical events
 - Semantic memory
 - Remembering general facts, concepts, and knowledge about the world
 - Non-declarative (implicit) memory: unconscious learning
 - Procedural memory
 - Acquiring skills and procedures
 - Conditioning
 - Associative learning
 - Priming
 - Influence of past experience on current behaviour

- Based on the type of information
 - Verbal memory
 - Remembering words, texts, and language
 - Visual memory
 - Remembering objects, faces, and visual patterns
 - Spatial memory
 - Remembering locations, routes, and spatial relationships

- Based on the sensory modality
 - Auditory memory
 - Remembering sounds and music
 - Olfactory memory
 - Remembering smells
 - Gustatory memory
 - Remembering tastes
 - Tactile memory
 - Remembering textures and tactile sensations

- Based on the brain systems involved
 - Hippocampal-dependent memory
 - Episodic, spatial, and contextual memories
 - Striatal-dependent memory
 - Habits, skills, and stimulus-response associations
 - Amygdala-dependent memory
 - Emotional memories and fear conditioning
 - Cerebellar-dependent memory
 - Motor skills and procedural memories

Memory Assessments

- Involve various neuropsychological tests and experimental paradigms designed to evaluate different aspects of memory
- Utilized in both clinical and research settings
- Often require consideration of other cognitive domains, such as attention, language, and executive functioning, which can influence memory performance in interpreting results

Working memory

- Digit span test (Wechsler Adult Intelligence Scale)
 - Participants must repeat a sequence of numbers forward, backward, or in a rearranged order, as presented by the examiner
- Spatial span test (Wechsler Memory Scale)
 - Participants must tap or point to a sequence of spatial locations (e.g., blocks on a board or squares on a screen) in the same or reverse order as demonstrated by the examiner

– N-back task

 Participants must monitor a series of stimuli (e.g., letters, numbers, or shapes) and indicate when the current stimulus matches the one presented N positions back in the sequence

Episodic memory

- Logical memory test (Wechsler Memory Scale)
 - Participants must recall verbatim two short stories immediately after hearing them, and again after a delay
 - To assess verbal episodic memory
- Rey auditory verbal learning test
 - Participants must learn and recall a list of unrelated words over multiple trials, with delayed recall and recognition components
 - To assess verbal episodic memory

California verbal learning test

- Participants must learn and recall a list of words from different semantic categories over multiple trials, with delayed recall and recognition components
- To assess verbal episodic memory and semantic clustering

Rey complex figure test

- Participants must copy a complex geometric figure, and then reproduce it from memory after a delay
- To assess visuospatial episodic memory

Semantic memory

- Vocabulary subtest (Wechsler Adult Intelligence Scale)
 - Participants must define or provide the meaning of a series of words presented orally or in writing
 - To assess semantic memory and general knowledge
- Boston naming test
 - Participants must name or identify objects, animals, or famous people depicted in line drawings
 - To assess semantic memory and confrontation naming abilities

Seoul Neuropsychological Screening Battery (SNSB)

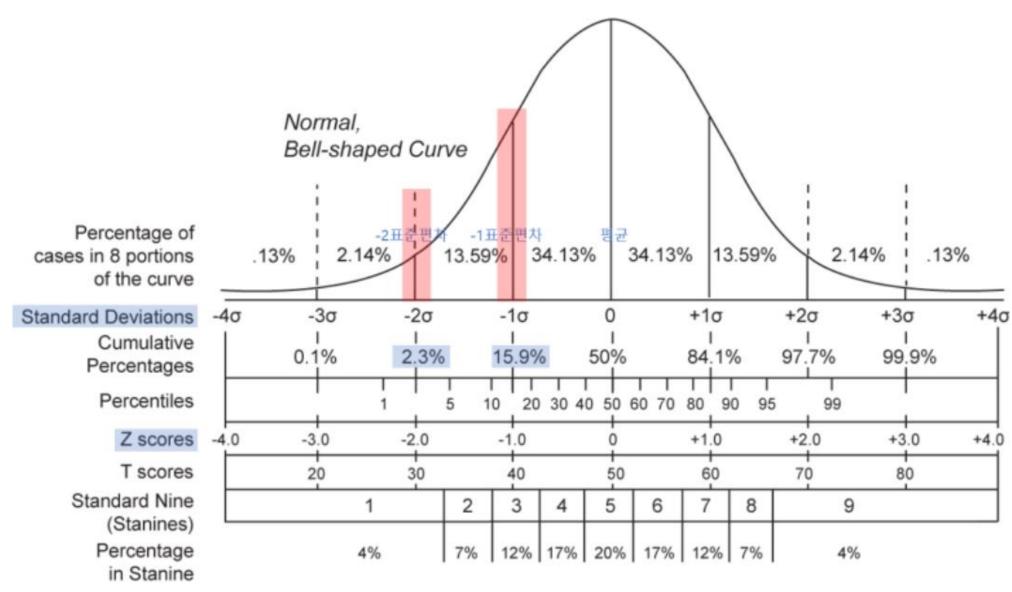
- Comprehensive neuropsychological test battery developed with its cultural adaptation for the Korean population
- Assesses various domains of cognitive functions
 - Attention
 - Language and related functions
 - Visuospatial functions
 - Memory
 - Frontal/executive functions

- Memory assessments in the SNSB
 - [Verbal episodic memory] Seoul verbal learning test
 - Immediate and delayed free recalls, depending on the time interval
 - Recognition
 - [Visuospatial episodic memory] Ray complex figure test
 - Immediate and delayed free recalls, depending on the time interval
 - Recognition

Memory	
[18-1] SVLT-E:IR (0-36)	The word list in the test consists of 12 items divided into 3 categories (flowers, housekeeping tools, school supplies), and each category contains 4 words. After the examiner reads out all 12 words to the subject, the examiner asks the subject to recall the words again. The test performs a total of 3 times.
[18-2] SVLT-E:DR (0-12)	The test is done about 20 min after the SVLT-E:IR. The examiner asks the subjects to recall the words learned in the SVLT-E:IR without clues.
[18-3] SVLT-E:recognition (0-24)	The test is done right after the SVLT-E:DR. The examiner reads out 24 words (12 target words and 12 non-target words) one by one and asks the subject to judge whether the word is included in the SVLT-E:IR or not. The score is True Positive+(12–False Positive).
[16-2] RCFT:IR (0-36)	The test is done right after the RCFT:copy. The scoring is the same as the RCFT:copy scoring method.
[16-3] RCFT:DR (0-36)	The test is done about 20 min after the RCFT:DR. The scoring is the same as the RCFT:copy scoring method.
[16-4] RCFT:recognition (0-24)	The test is done right after the RCFT:DR. The examiner shows 24 figure fragments (12 target fragments and 12 non-target fragments) and asks the subjects to judge whether the figure piece is part of the RCFT:copy or not. The score is True Positive+(12–False Positive).



Seoul verbal learning test: immediate recall



Distribution of scores on the SNSB

Brain Regions Involved in Memory

- Based on complex interactions among multiple brain regions
- Key brain regions:
 - Hippocampus
 - Formation, consolidation, and retrieval of long-term episodic and spatial memories
 - Prefrontal cortex
 - Encoding and retrieval of episodic memories and working memory
 - Strategic control of memory processes

Posterior parietal cortex

- Integration of spatial and episodic information, retrieval of autobiographical memories, and processing of contextual information
- Medial temporal lobe (including the hippocampus and surrounding cortical regions)
 - Formation and consolidation of declarative (episodic and semantic) memories

Amygdala

Modulation of memory consolidation, especially for emotional or arousing events

Cerebellum

 Acquisition and retention of procedural memories, particularly for motor skills and implicit learning

- Basal ganglia (including the striatum)
 - Formation and retrieval of procedural memories
 - Modulation of memory processes

Entorhinal cortex

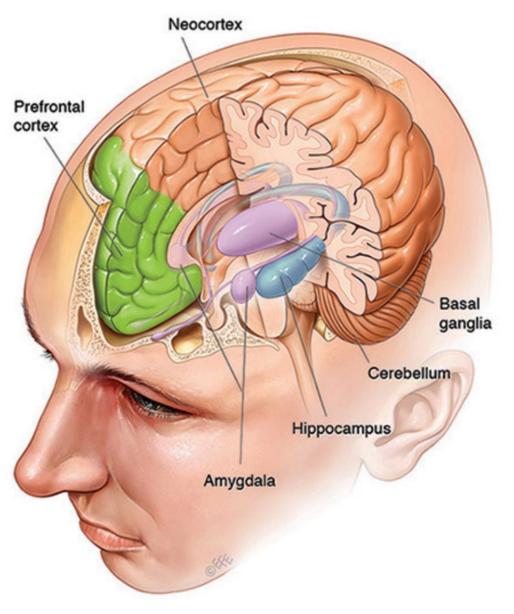
 Transfer of information between the neocortex and hippocampus during encoding and retrieval

Perirhinal cortex

 Formation and retrieval of semantic memories, particularly object recognition and processing of complex visual stimuli

Parahippocampal cortex

- Processing of spatial and contextual information related to episodic memories
- Encoding and retrieval of scene and environmental memories



[https://qbi.uq.edu.au/brain-basics/memory/where-are-memories-stored]

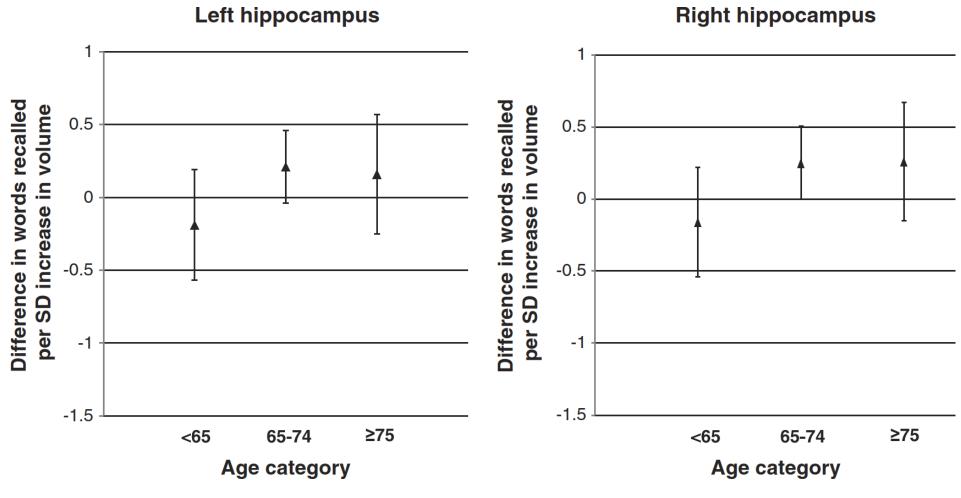
Brain regions involved in memory

Influence of Ageing on Memory

- Normal ageing is often accompanied by a decline in certain types of memory abilities, particularly those related to episodic and working memory
 - Episodic memory decline
 - Working memory reduction
 - Semantic memory preservation
 - Procedural memory stability
 - Retrieval slowing

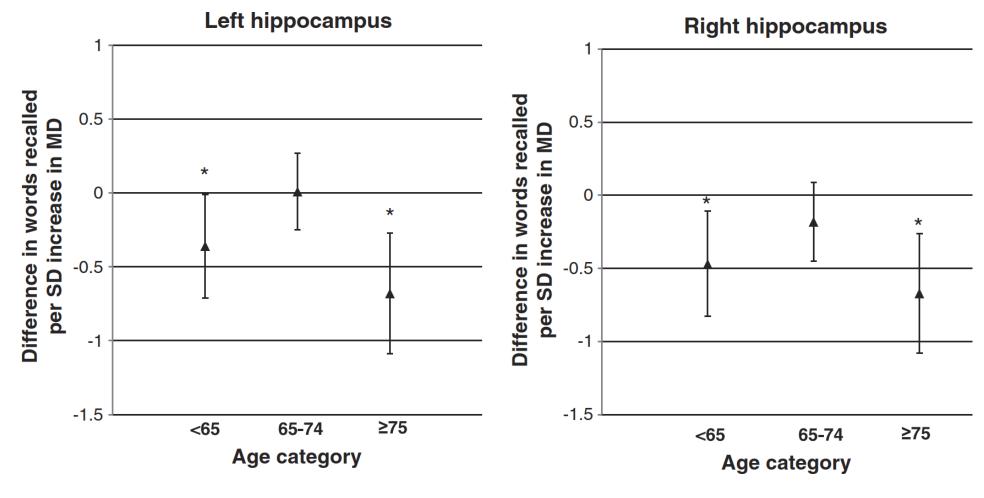
- Various changes occurring in the brain can impact memory and cognitive functioning
 - Age-related decline in episodic memory is thought to be associated with changes in the hippocampus and other medial temporal lobe structures
 - Age-related changes in brain structure and function, such as reductions in grey and white matter volume, changes in neurotransmitter systems, and alterations in functional connectivity, can contribute to memory difficulties in older adults

- The extent and rate of memory decline with age can vary considerably among individuals
 - Factors such as education level, cognitive reserve, lifestyle, and overall health can influence the trajectory of age-related memory changes
- Pathological conditions like Alzheimer's disease or other forms of dementia can lead to more severe and accelerated memory impairments that go beyond the normal effects of ageing



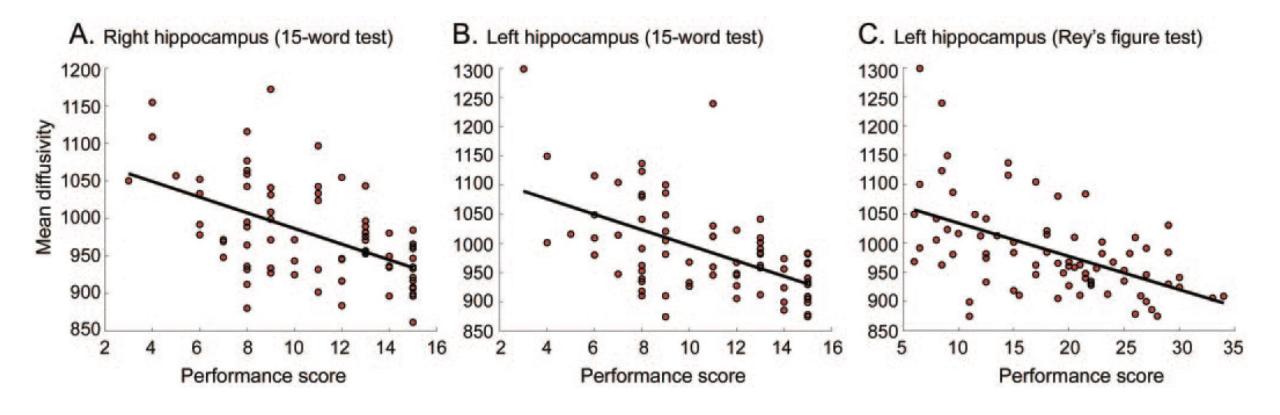
[Heijer et al., 2012]

Memory performance (episodic memory: delayed recall) ≁ regional volume (hippocampus)



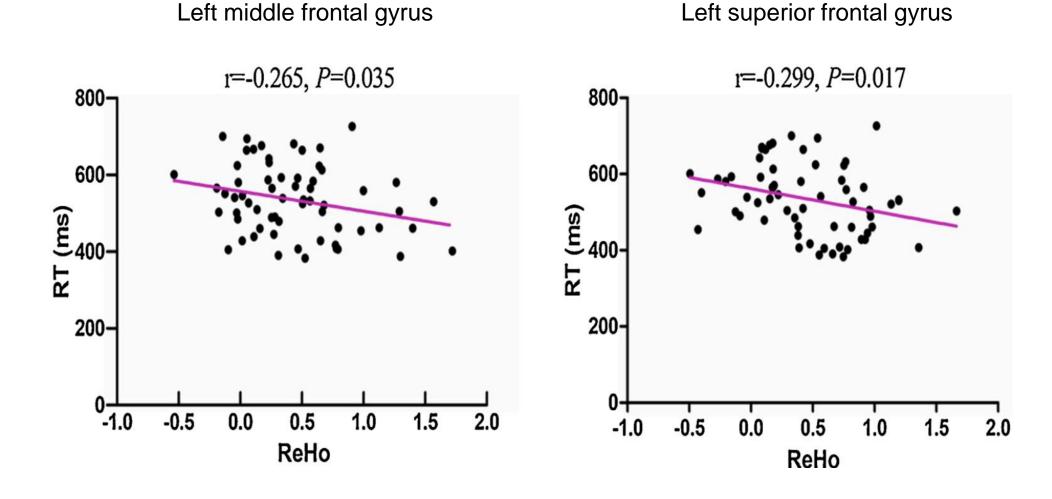
[Heijer et al., 2012]

Memory performance (episodic memory: delayed recall) ~ mean diffusivity (hippocampus)



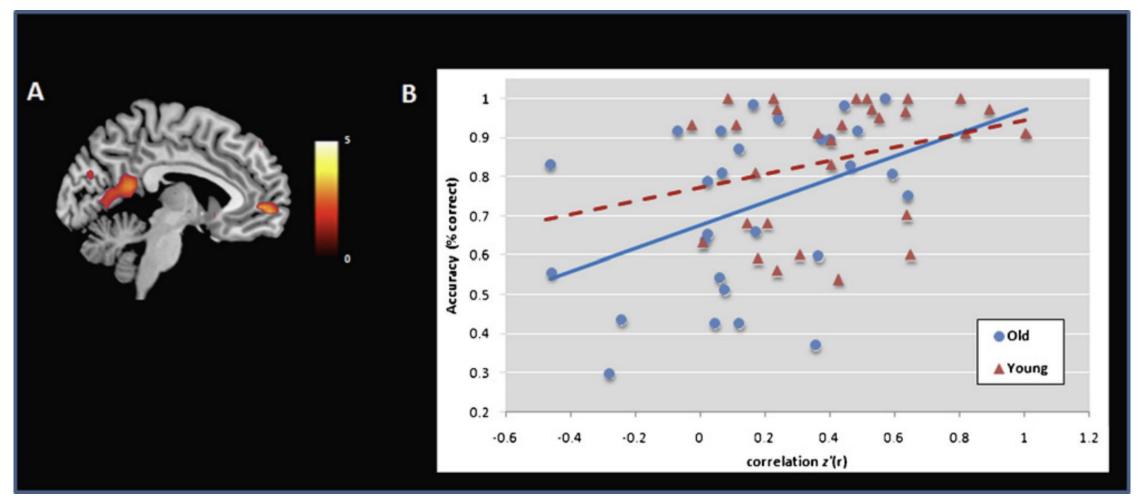
[Carlesimo et al., 2010]

Memory performance (episodic memory: delayed recall) ~ mean diffusivity (hippocampus)



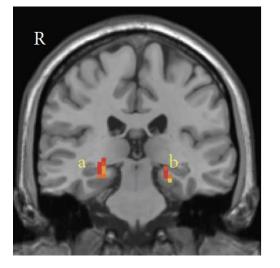
[Xie et al., 2021]

Memory performance (episodic memory: recognition) ~ regional homogeneity

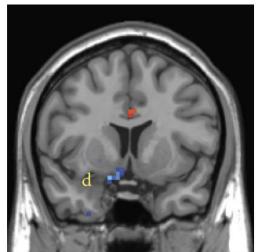


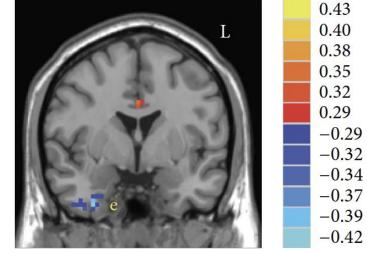
[Sambataro et al., 2010]

Memory performance (working memory: 2-back task) ~ default mode network (between posterior cingulate gyrus and medial prefrontal cortex)









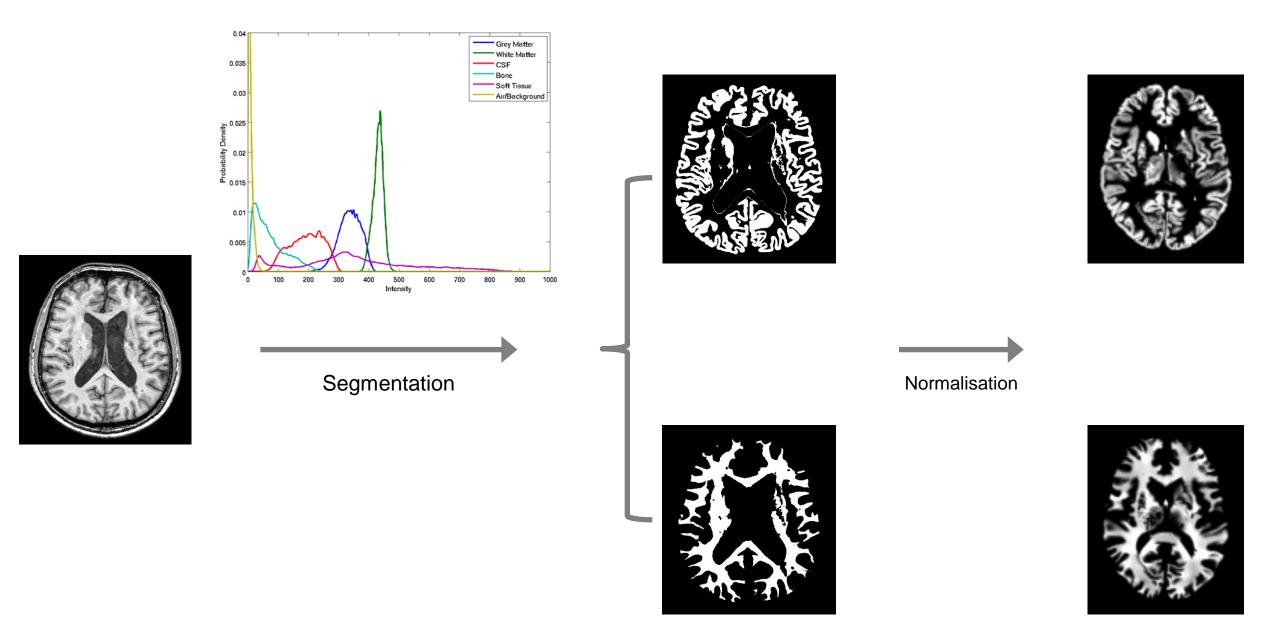
[Ren et al., 2015]

Memory performance (episodic memory: cued recall) ~ amplitude of low frequency fluctuations (parahippocampal gyrus)

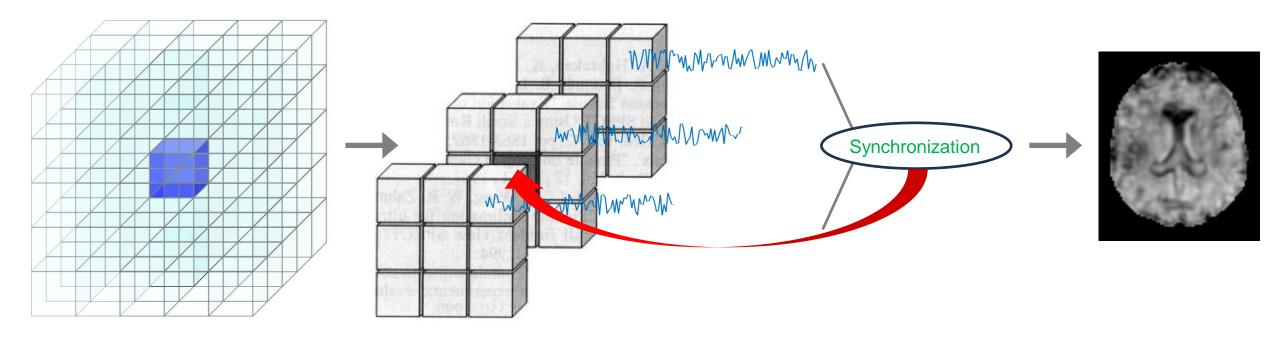
Data and Features

- Locally acquired data (n = 90)
 - Structural, resting state functional, and diffusion-weighted MRI
 - Demographic information including age, sex, and years of education
 - Memory performance scores

- Training dataset: n = 80
 - Images
 - Grey matter map: train/GM/001-080.nii.gz
 - White matter map: train/WM/001-080.nii.gz
 - Regional homogeneity map: train/ReHo/001-080.nii.gz
 - Posterior cingulate gyrus (PCG)-based correlation map: train/PCGcorr/001-080.nii.gz
 - Fractional anisotropy map: train/FA/001-080.nii.gz
 - Mean diffusivity map: train/MD/001-080.nii.gz



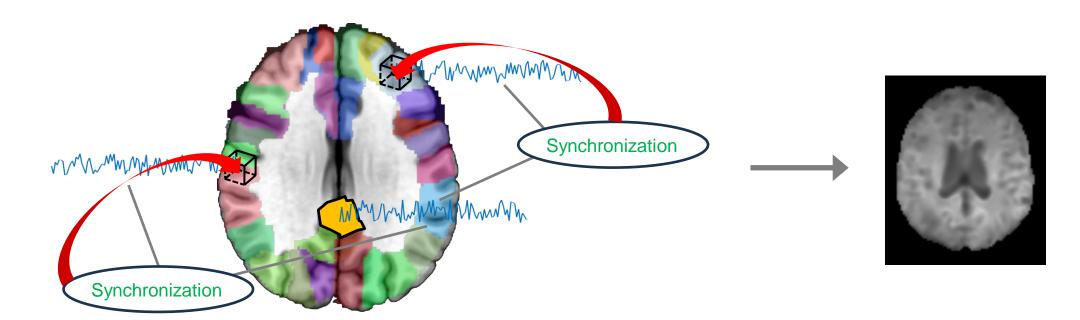
Grey matter and white matter maps



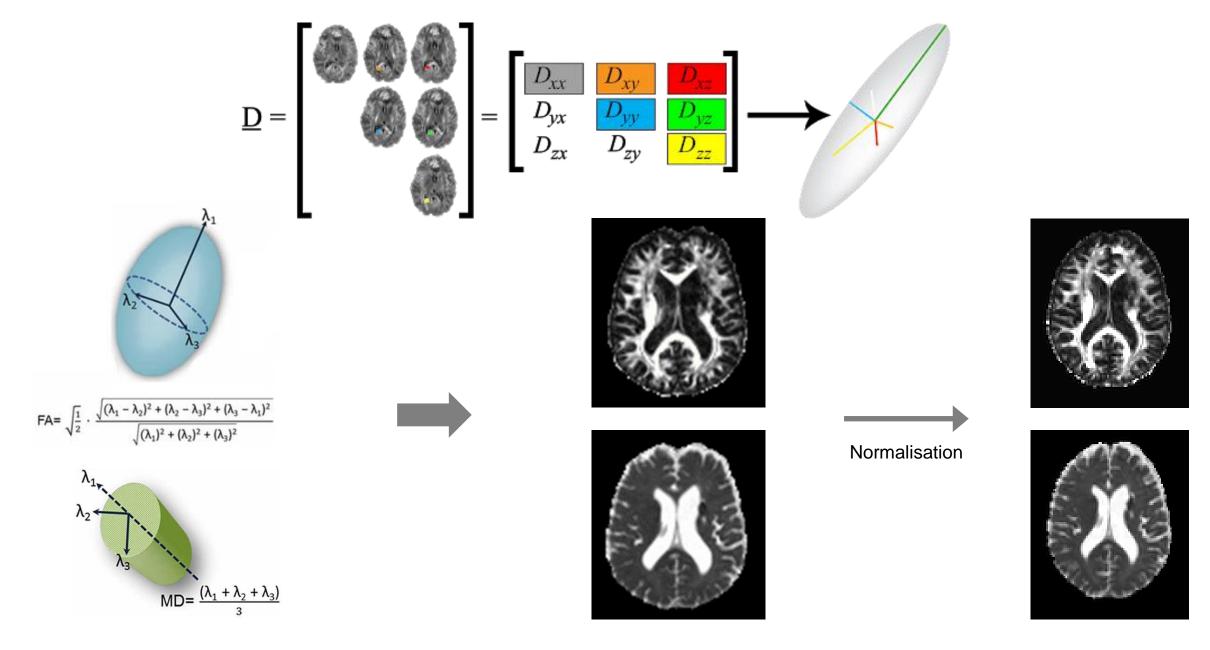
Centre voxel

Nearest neighbours

Regional homogeneity map



Seed: posterior cingulate gyrus



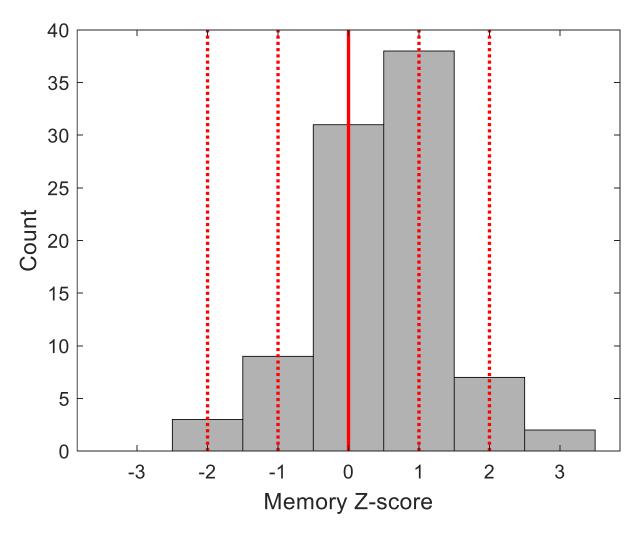
Fractional anisotropy and mean diffusivity maps

- Grey matter features: train/GM.csv
- White matter features: train/WM.csv
- Regional homogeneity features: train/ReHo.csv
- PCG-based correlation features: train/PCGcorr.csv
- Fractional anisotropy features: train/FA.csv
- Mean diffusivity features: train/MD.csv

- Test dataset: *n* = 10
 - Images
 - Grey matter map: test/GM/001-010.nii.gz
 - White matter map: test/WM/001-010.nii.gz
 - Regional homogeneity map: test/ReHo/001-010.nii.gz
 - PCG-based correlation map: test/PCGcorr/001-010.nii.gz
 - Fractional anisotropy map: test/FA/001-010.nii.gz
 - Mean diffusivity map: test/MD/001-010.nii.gz

- Grey matter features: test/GM.csv
- White matter features: test/WM.csv
- Regional homogeneity features: test/ReHo.csv
- PCG-based correlation features: test/PCGcorr.csv
- Fractional anisotropy features: test/FA.csv
- Mean diffusivity features: test/MD.csv

- Subjects (n = 90)
 - Age: 72.2±5.5 years
 - Sex: 75 females and 15 males
 - Years of education: 10.5±3.6 years
 - Memory performance assessed by the SNSB
 - Raw score: 0.277±0.489
 - Z-score: 0.444±0.889



Memory performance

Hands-on Machine Learning (2): Predicting Sex

Sex and Gender

Sex

- Usually described by the terms "males" and "females"
- Typically refers to the biological and physiological characteristics that define males and females
- Determined by biological factors, primarily chromosomal (XX for females, XY for males) and anatomical differences

Gender

- Usually described by the terms "men" and "women"
- Often refers to the socially constructed roles, behaviours, activities, and attributes that a society considers appropriate for individuals based on their sex
- Related to how individuals perceive themselves and what they call themselves, which can be influenced by societal norms and personal experiences
- Both sex and gender exist on a spectrum, such that individuals may identify and express themselves in various ways that do not conform to traditional binary categories

Brain Regions Implicated in Sex Differences

- Sex differences in brain structure and function, with many findings subject to ongoing debate and research
 - There is significant individual variability within each sex, and findings from group studies may not apply to all individuals
 - The interplay between biological and environmental factors may shape sex differences in brain regions
 - Sex differences in brain regions may not necessarily translate into clear-cut behavioural differences

	Levene's test for equality of variances		t-test fo	r equali	95% CI of the mean				
	F	Significance (2-tailed)	t	df	Significance	Mean difference	SE difference	Lower	Upper
Whole cortical volume	0.116	0.735	5.180	58	0.000	76561.23	14780.44	46974.97	106147.50
Left cortical hemisphere	0.018	0.895	5.023	58	0.000	38805.93	7725.01	23342.65	54269.22
Right cortical hemisphere	0.047	0.829	5.145	58	0.000	38320.30	7448.02	23411.47	53229.13
Left frontal cortical lobe	0.009	0.927	4.191	58	0.000	12919.23	3082.67	6748.60	19089.87
Right frontal cortical lobe	0.003	0.959	3.909	58	0.000	12004.97	3070.83	5858.04	18151.89
Left occipital cortical lobe	0.175	0.677	4.037	58	0.000	5413.17	1340.82	2729.22	8097.12
Right occipital cortical lobe	0.188	0.666	3.689	58	0.000	6106.97	1655.27	2793.59	9420.35
Left parietal cortical lobe	0.010	0.919	1.871	58	0.066	4696.90	2510.98	-329.37	9723.17
Right parietal cortical lobe	0.297	0.588	3.226	58	0.002	7875.47	2440.97	2989.33	12761.60
Left temporal cortical lobe	0.022	0.883	6.133	58	0.000	14377.30	2344.27	9684.74	19069.86
Right temporal cortical lobe	0.735	0.395	5.048	58	0.000	10571.00	2093.94	6379.53	14762.47

[Carne et al., 2006]

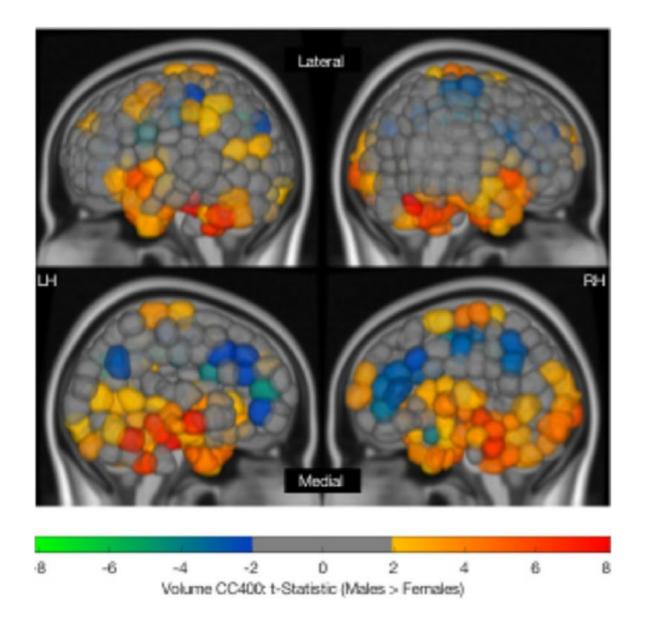
LEFT HEMISPHERE

RIGHT HEMISPHERE

													Covariate			TIV
	Raw	VBM8	Proportion	Covariate regression	PCP	Residual	TIV matched		R	law	VBM8	Proportion	regression	PCP	Residuals	
Precentral L	0.72		-0.24					_	Precentral_R 0.	.69	-0.32	-0.34				
Frontal Sup L	0.66	-0.38	-0.38	-0.30	-0.27	-0.25		1.4 Fronta		.76	-0.32	-0.26				
Frontal Sup Orb L	0.79	-0.48	-0.41	-0.40	-0.35	-0.34	-0.42			.77	-0.44	-0.32	-0.34	-0.33	-0.31	-0.38
Frontal Mid L	0.71	-0.30	-0.24	-0.23	-0.21					.87	0.00					
Frontal Mid Orb L	0.97	-0.22		-0.22						.85	-0.28	0.00			,, ,	
Frontal Inf Oper L	1.06	-0.53	-0.44							.56	-0.43	-0.33				
Frontal Inf Tri L	0.72	-0.35	-0.32						ital_Inf_Tri_R 0.	.79	-0.30	-0.22				
Frontal Inf Orb L	1.09	-0.27						Front		.83	-0.27					
Rolandic Oper L	1.00	-0.21						Rola		.89						
Supp Motor Area L	0.91	-0.23			2			1.0 Supp_N		.97						
Olfactory L	1.20	0.20								.93						
Frontal_Sup_Medial_L	0.73	-0.29	-0.26							.91						
Frontal Med Orb L	0.70	0.20	0.20	-0.25	-0.23			Frontal		.86	-0.23		-0.23	-0.24	-0.22	
Rectus L	0.70			-0.25	-0.20			0.8	Rectus R 0.	.92						
Insula L	0.55	-0.21						0.0	Insula R 1.	.09						
				0.24	-			Cin	gulum Ant R 0.	.68	-0.37	-0.27	-0.22			
Cingulum_Ant_L	0.54	-0.24		-0.21		_		Cine		.93	-0.29	-0.26				
Cingulum_Mid_L	0.74	-0.28						0.6 Cing		.93	,	0.20				
Cingulum_Post_L	0.49	0.55	0.50	—		\vdash		U.O Hin	pocampus R 0.	.91	-0.60	-0.45				
Hippocampus_L	1.14	-0.55	-0.50				0.05	ParaHii		.18	3.00	00				
ParaHippocampal_L	0.28						0.35	i aiai ii		.39		0.30	0.30	0.29	0.29	0.61
Amygdala_L	0.96			0.27	0.22	0.23	0.41		Calcarine R 0.	.70		0.50	0.50	0.23	0.23	0.01
Calcarine_L	0.96							0.4		.95						
Cuneus_L	1.15									.30			0.27	0.24	0.05	0.46
Lingual L	0.68	-0.30						0-			0.40	0.07			0.25	0.46
Occipital Sup L	0.85		-0.25					000	cipital_Sup_R 0.	.55	-0.40	-0.37	-0.34	-0.27	-0.26	0.00
Occipital Mid L	0.87	-0.34	-0.26	-0.23	-0.22	-0.21				.74	-0.52	-0.28	-0.29	-0.25	-0.25	-0.36
Occipital Inf L	0.60							O O		.88						0.11
Fusiform L	0.57									.30		0.22	0.20			0.44
Postcentral L	0.47	-0.37	-0.52	-0.27	-0.22					.59	-0.44	-0.42				
Parietal Sup L	0.66	-0.40	-0.30	0.2.						.66		-0.23				
Parietal Inf L	0.54	-0.59	-0.52	-0.29	-0.21	-0.21				.43	-0.52	-0.52	-0.31	-0.21	-0.22	
SupraMarginal L	0.61	-0.42	-0.32	-0.23	U.L.I	0.21		Sup		.85						
Angular_L	0.74	-0.30	0.02	0.20				0.0		.54	-0.59	-0.39	-0.25			
Precuneus L	0.89	-0.39			6					.06	-0.27					
Paracentral Lobule L	0.49	-0.27	-0.27					Paracent	ral Lobule R 0.	.55	-0.27	-0.24				
Caudate L	0.55	-0.57	-0.45						Caudate R 0.	.60	-0.57	-0.40				
	1.14	-0.57	-0.43	0.40	0.20	0.21	0.20	0.4	Putamen R 1.	.09			0.34	0.26	0.26	0.34
Putamen_L Pallidum L	0.79	-0.31		0.44	0.30	0.31 0.29	0.39 0.44	-0.4		.83	-0.32		0.37	0.25	0.25	
	0.79	-0.31	-0.79	-0.27	0.30	0.29	-0.16			.46	-0.65	-0.67				
Thalamus_L		-0.70	-0.79	-0.21			-0.16			.69						
Heschl_L	0.88							Tem		.78	-0.44	-0.32				
Temporal_Sup_L	0.96			 						.98						
Temporal_Pole_Sup_L	0.92	0.50	0.07							.87	-0.65	-0.37				
Temporal_Mid_L	0.96	-0.52	-0.27							.10	3.00	0.24	0.29	0.21	0.23	0.33
Temporal_Pole_Mid_L	0.93									.15	-0.37	U.E.	0.20	V.= 1	0.20	5.00
Temporal_Inf_L	1.15	-0.23								.94	-0.23		0.28			
Cerebelum_Crus1_L	1.12			0.31	0.23	0.25	0.34			.69	-0.23	-0.27	0.20			
Cerebelum_Crus2_L	0.68	-0.35	-0.30							.57	-0.44	-0.21				
Cerebelum_3_L	0.49									.97	-0.25		0.26		1	
Cerebelum_4_5_L	0.85	-0.34								.07	-0.25		0.20			0.24
Cerebelum 6 L	1.05	-0.33										-0.38				0.24
Cerebelum 7b L	0.87									.53	-0.45	-0.38				
Cerebelum 8 L	0.99									.00	-0.24					
Cerebelum 9 L	0.60	-0.33						-1.2 Ce		.67	-0.31					
Cerebelum 10 L	0.29	-0.35	-0.46	-0.33	-0.21	-0.22	-0.45	Cere		.46	-0.23	-0.31				
Vermis 1 2	0.57	0.00	0,,0	0.00	V.= .		00			.45		-0.29				
Vermis 4 5	0.72	-0.40	-0.25					V 100		.67	-0.58	-0.43				
		-0.40	-0.59	 				-1.4	Vermis 8 0.	.68	-0.49					
Vermis 7	0.47								Vermis 10 0.	.50		-0.28				

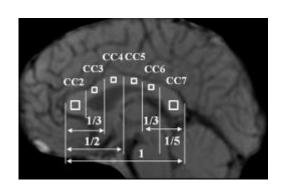
[Sanchis-Segura et al., 2019]

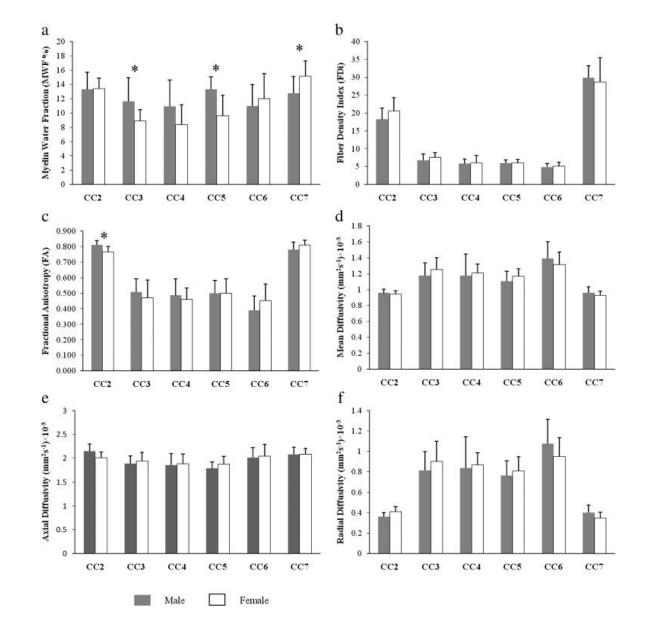
Adjusted regional volume: males vs. females



[Dhamala et al., 2020]

Regional volume: grey matter volume-matched males vs. females



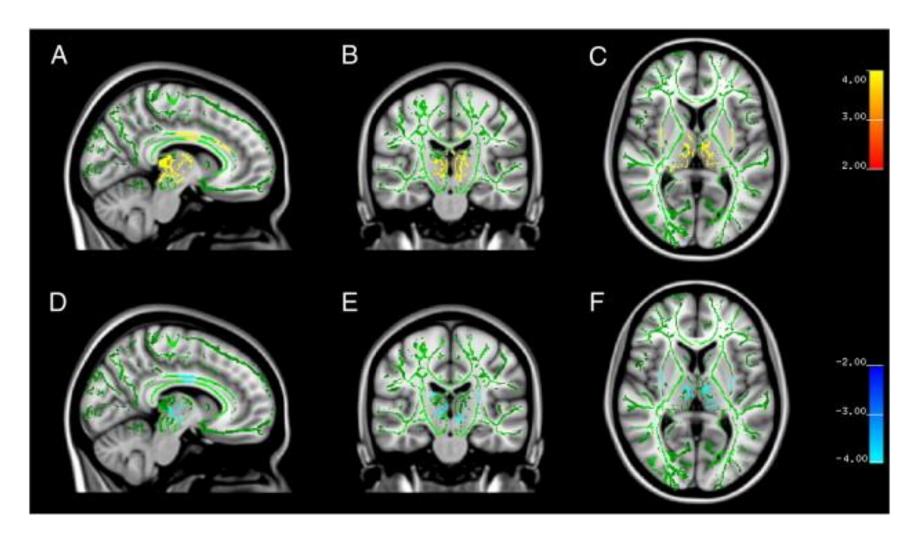


[Liu et al., 2010]

White matter microstructure (corpus callosum): males vs. females

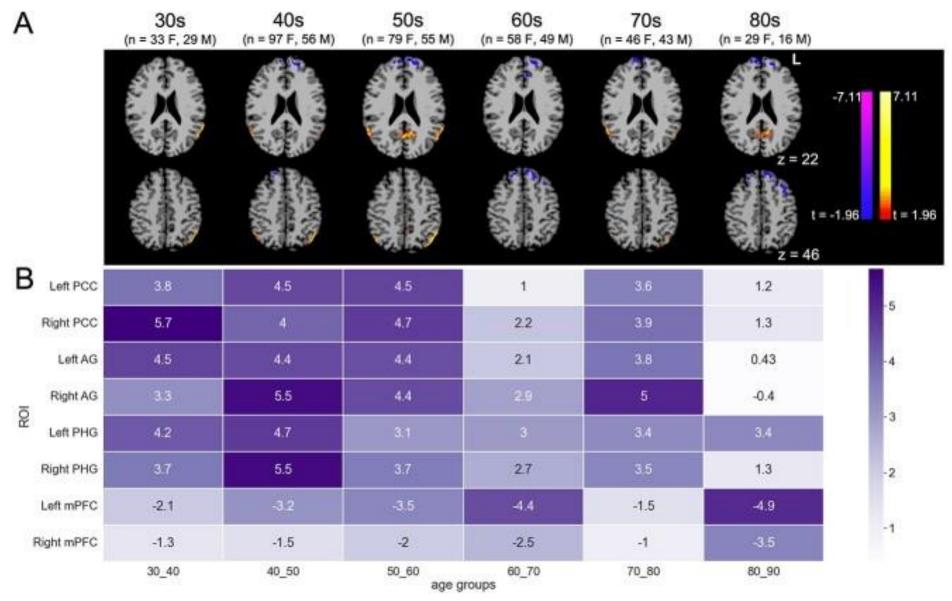
Fractional anisotropy

Radial diffusivity



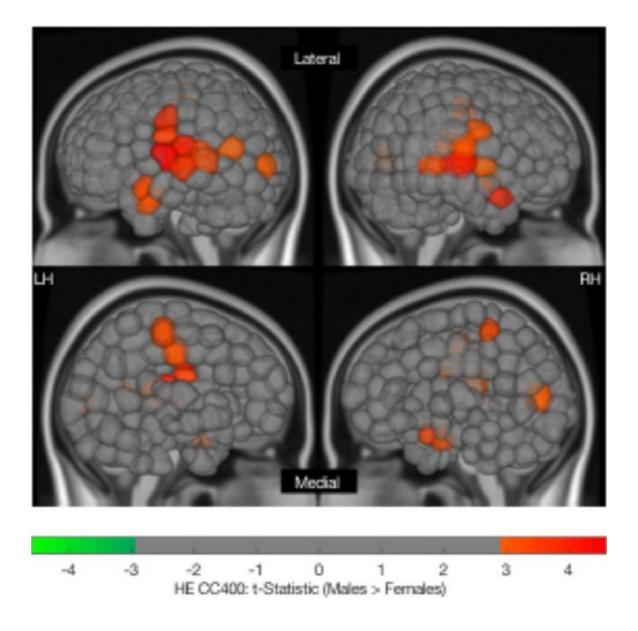
[Menzler et al., 2011]

White matter microstructure: males vs. females



[Ficek-Tani et al., 2023]

Default mode network: females vs. males



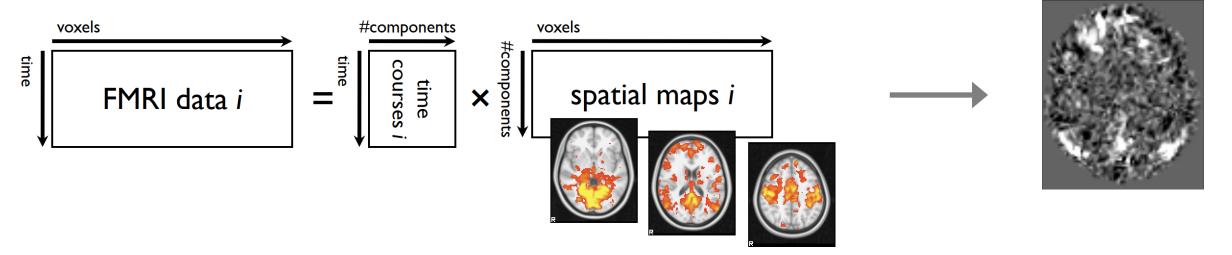
[Dhamala et al., 2020]

Hurst exponent (long-range temporal dependence of time series): males vs. females

Data and Features

- Data from UK Biobank (https://www.ukbiobank.ac.uk/) (*n* = 500)
 - Structural, resting state functional, and diffusion-weighted MRI
 - Demographic information including sex and age

- Training dataset: n = 450
 - Images
 - Grey matter map: train/GM/001-450.nii.gz
 - White matter map: train/WM/001-450.nii.gz
 - Default mode network map: train/DMN/001-450.nii.gz
 - Fractional anisotropy map: train/FA/001-450.nii.gz
 - Mean diffusivity map: train/MD/001-450.nii.gz



Independent component analysis

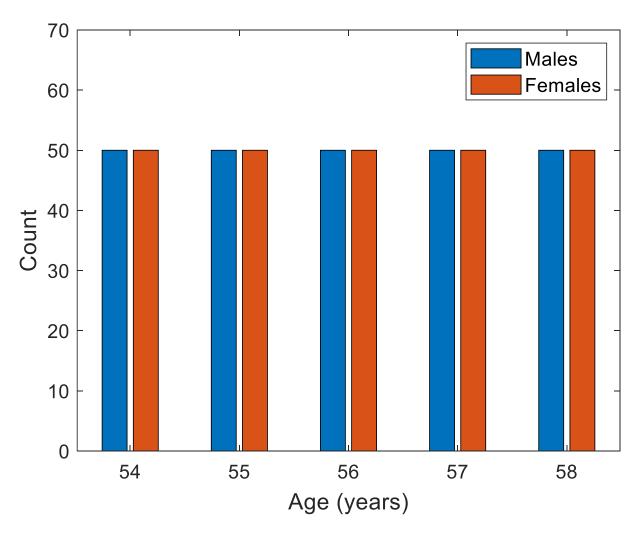
Default mode network map

- Grey matter features: train/GM.csv
- White matter features: train/WM.csv
- Default mode network features: train/DMN.csv
- Fractional anisotropy features: train/FA.csv
- Mean diffusivity features: train/MD.csv

- Test dataset: n = 50
 - Images
 - Grey matter map: test/GM/001-050.nii.gz
 - White matter map: test/WM/001-050.nii.gz
 - Default mode network map: test/DMN/001-050.nii.gz
 - Fractional anisotropy map: test/FA/001-050.nii.gz
 - Mean diffusivity map: test/MD/001-050.nii.gz

- Grey matter features: test/GM.csv
- White matter features: test/WM.csv
- Default mode network features: test/DMN.csv
- Fractional anisotropy features: test/FA.csv
- Mean diffusivity features: test/MD.csv

- Subjects (n = 500)
 - Age and sex: 50 females and 50 males for each age from 54 to 58 years



Sex distribution across ages