

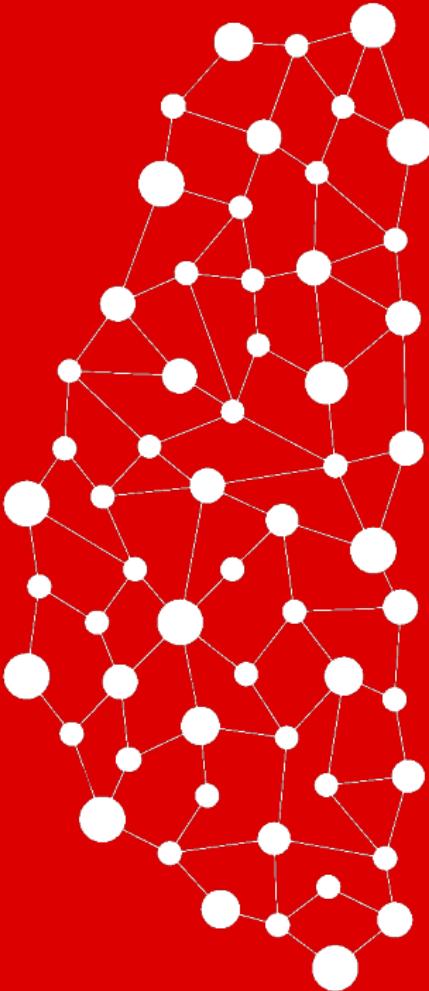
Exploring brain heterogeneity in neuropsychiatric patients with explainable artificial intelligence



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Outline

1. Background and motivation
2. Explainable dementia classification
3. Explainable brain age predictions



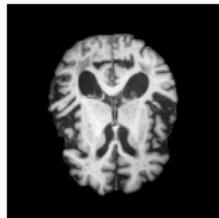
Background: Predictive clinical neuroscience



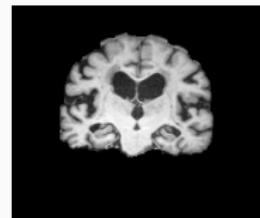
Background: Predictive clinical neuroscience



Side

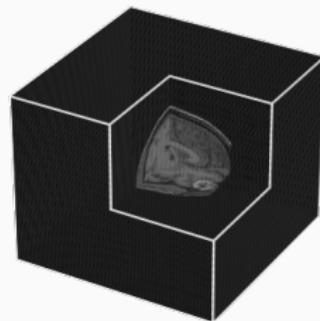


Above



Front

Structural Magnetic
Resonance Imaging (MRI) scans



Background: Predictive clinical neuroscience



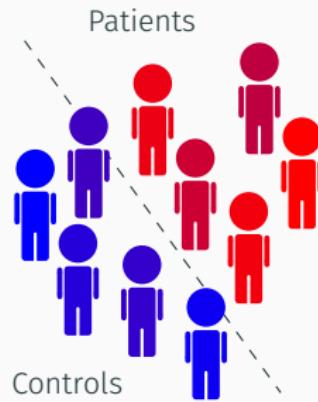
Background: Predictive clinical neuroscience



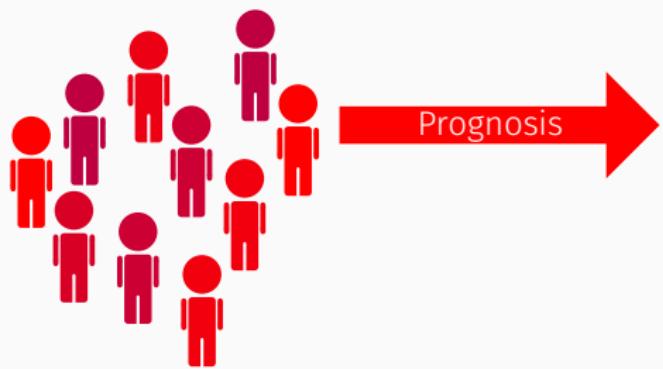
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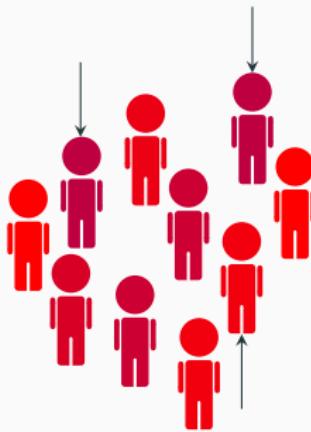
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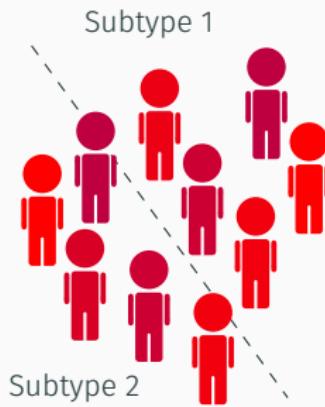
Background: Predictive clinical neuroscience



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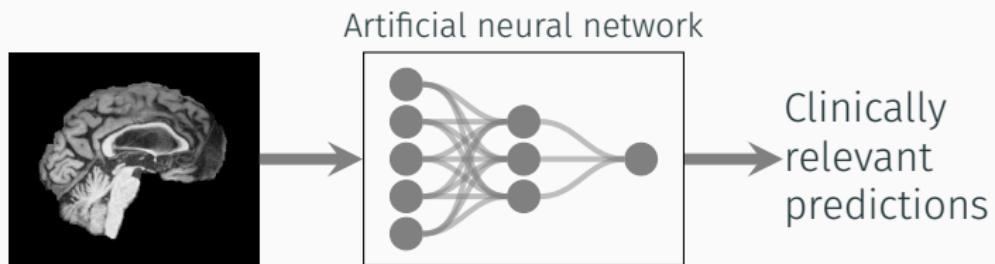
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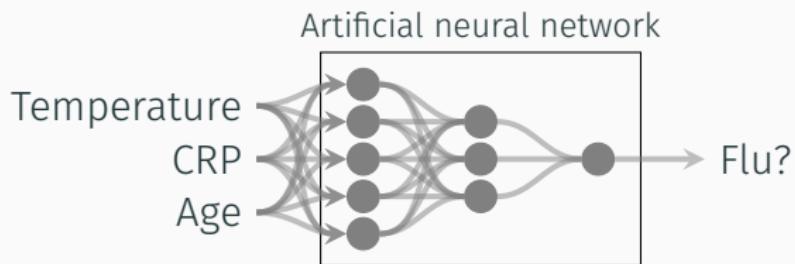
Background: Explainable artificial intelligence



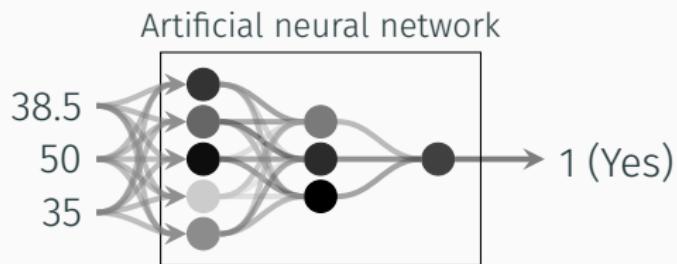
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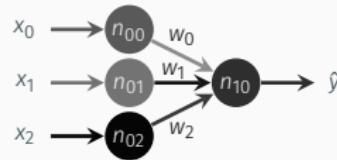
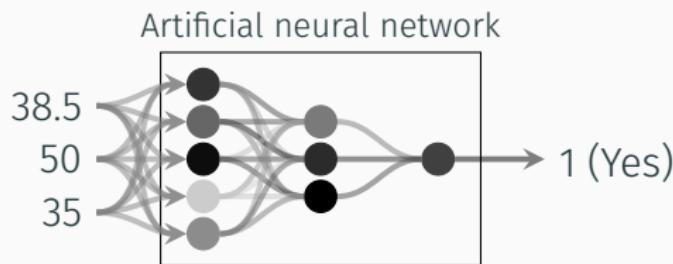
Background: Explainable artificial intelligence



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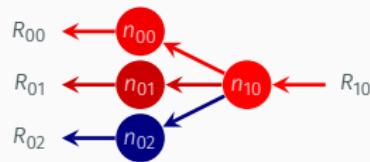
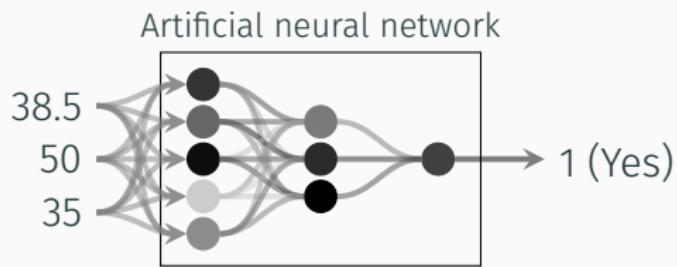
Background: Explainable artificial intelligence



$$\hat{y} = f \left(\sum_i^N w_i \cdot n_{0i} \right)$$



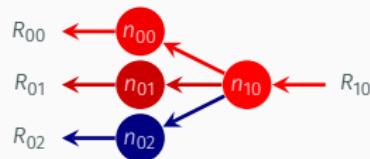
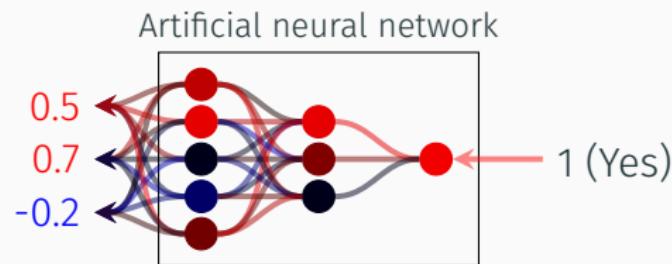
Background: Explainable artificial intelligence



$$R_{0i} = \sum_j \frac{n_{0i} w_i}{\sum_k n_{0k} w_k} R_{1j}$$



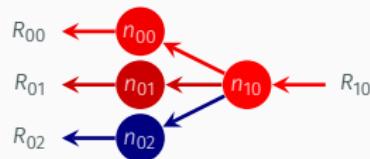
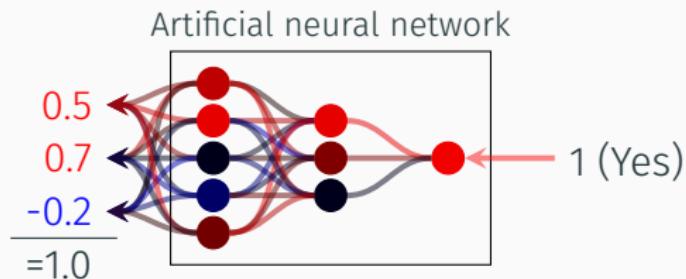
Background: Explainable artificial intelligence



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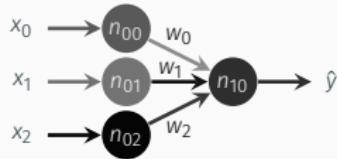
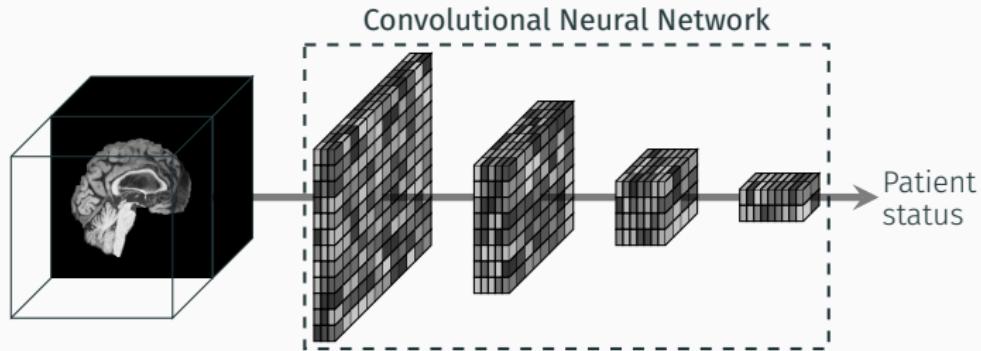
Background: Explainable artificial intelligence



$$R_{0i} = \sum_j \frac{n_{0i} w_i}{\sum_k n_{0k} w_k} R_{1j}$$



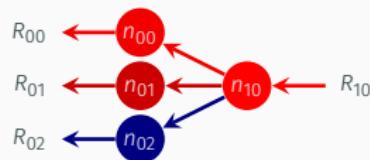
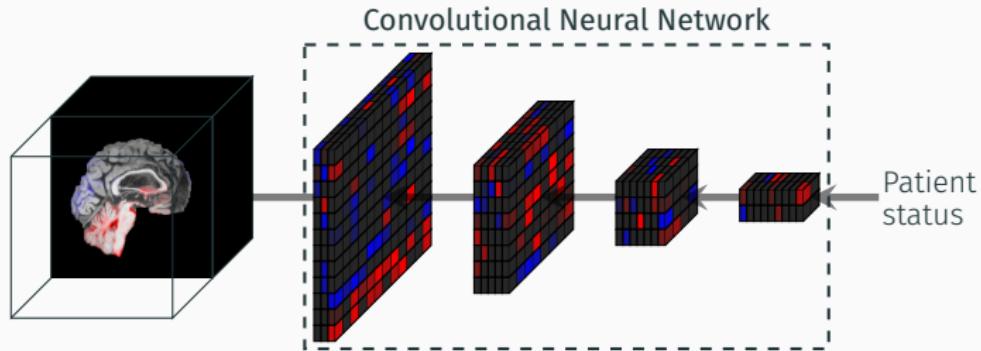
Background: Explainable artificial intelligence



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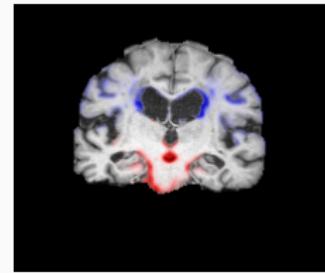
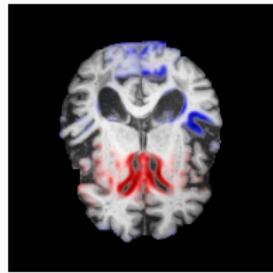
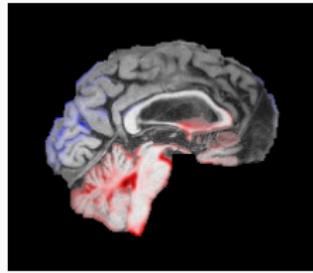
Background: Explainable artificial intelligence



$$R_{0i} = \sum_j \frac{n_{0i} w_i}{\sum_k n_{0k} w_k} R_{1j}$$



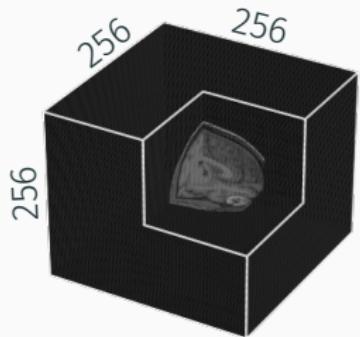
Background: Explainable artificial intelligence



Background: Conceptualization



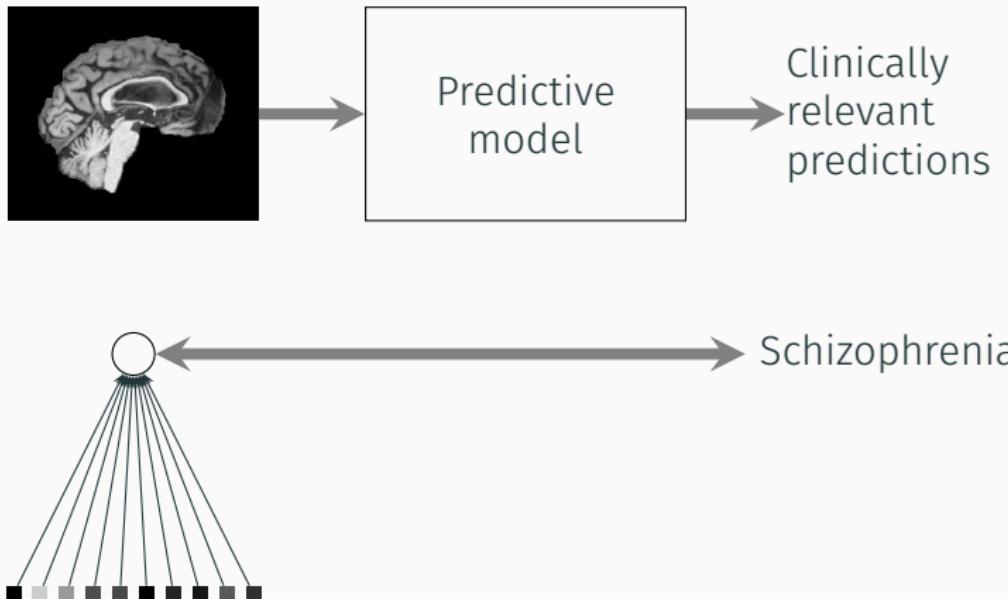
Background: Conceptualization



Background: Conceptualization



Background: Conceptualization



Background: Conceptualization

"Despite considerable heterogeneity at the regional level, deviations were often coupled to common functional circuits and networks"

Regional, circuit and network heterogeneity of brain abnormalities in psychiatric disorders
Segal, A. et al., *Nature Neuroscience* (2023)



Background: Conceptualization



Background: Conceptualization



Background: Conceptualization



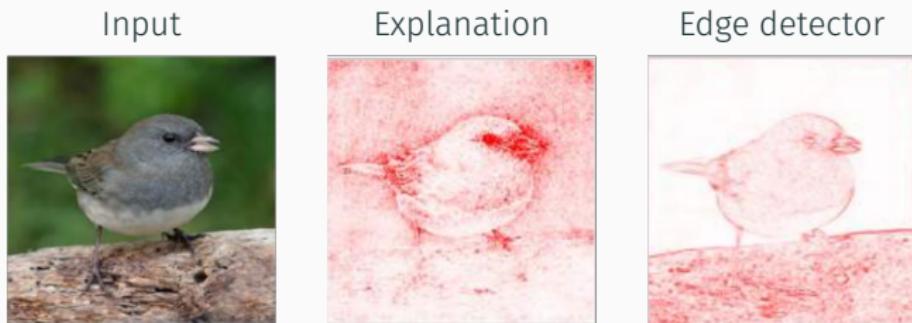
Background: Conceptualization

"We propose explanation space as a powerful embedding to facilitate detection of latent disease subtypes, [...]. Transforming from feature space to explanation space should not be seen in competition to dimensionality reduction, but rather as a complimentary processing step"

Inferring disease subtypes from clusters in explanation space
Schulz, MA. et al., *Scientific Reports* (2020)



Background: Conceptualization



Sanity Checks for Saliency Maps
Adebayo, J. et al., *preprint at arXiv* (2018)

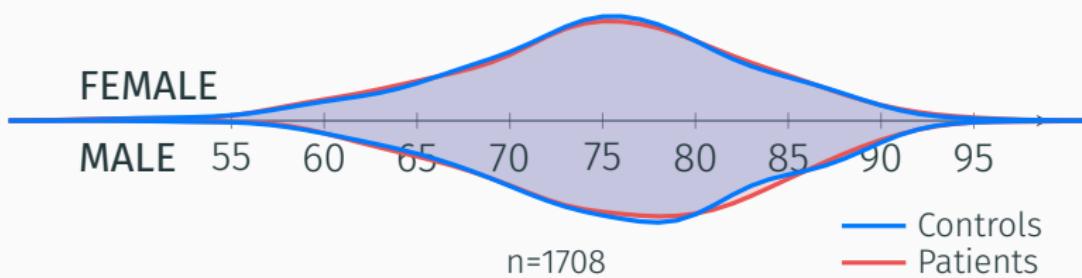


Explainable dementia classification

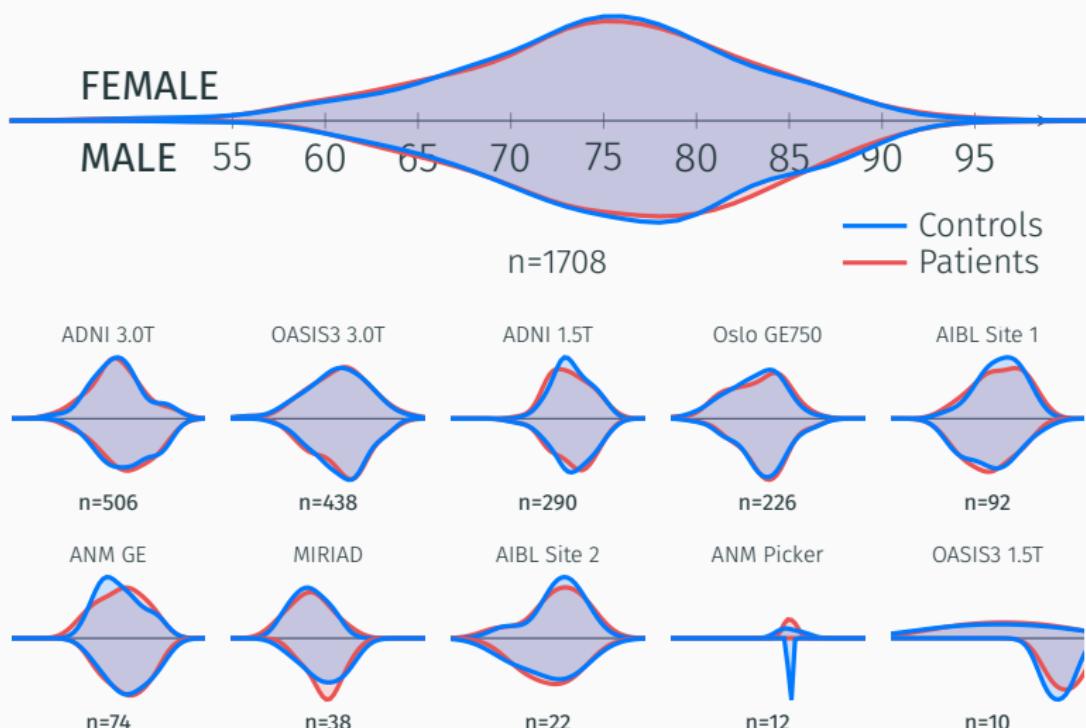


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Explainable dementia classification: Dataset



Explainable dementia classification: Dataset

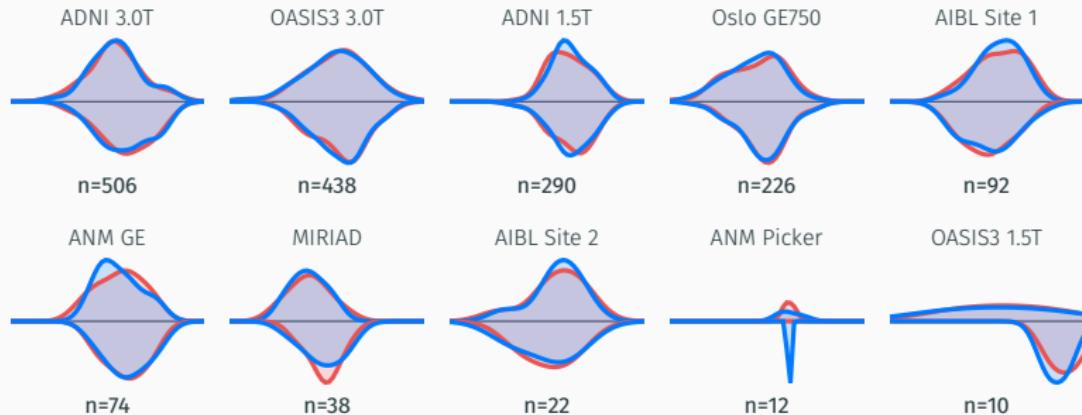


Explainable dementia classification: Dataset

ADNI:
Probable
Alzheimer's disease

OASIS3:
Dementia

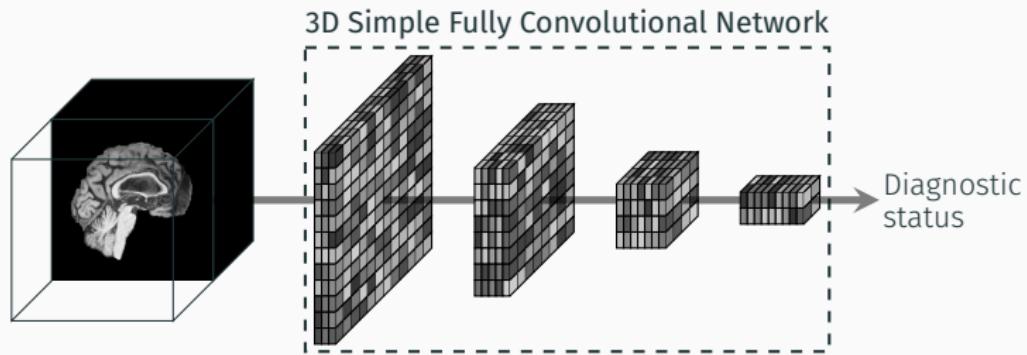
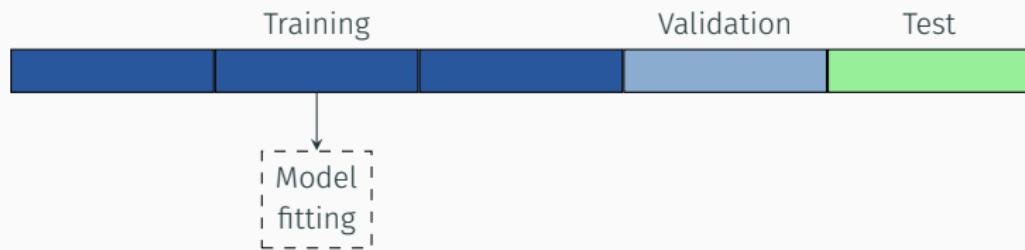
Oslo:
Alzheimer's disease,
Vascular dementia,
Unspecified dementia



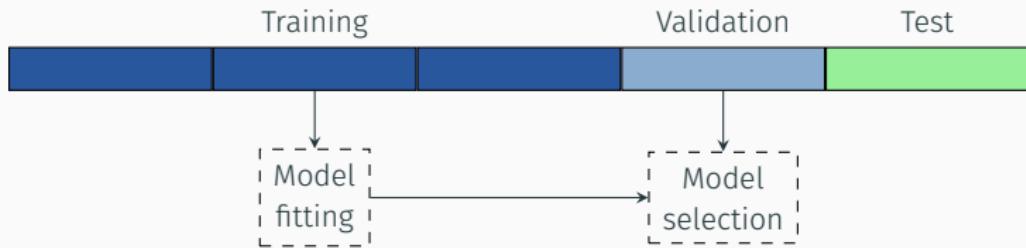
Explainable dementia classification: Modelling



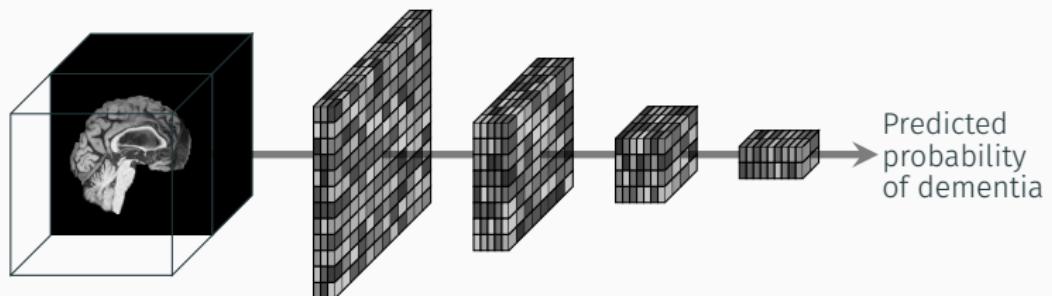
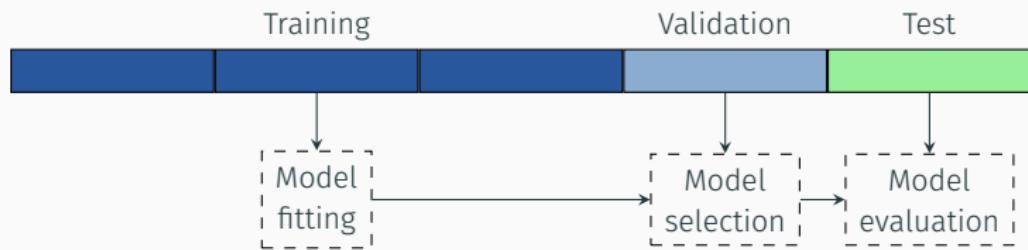
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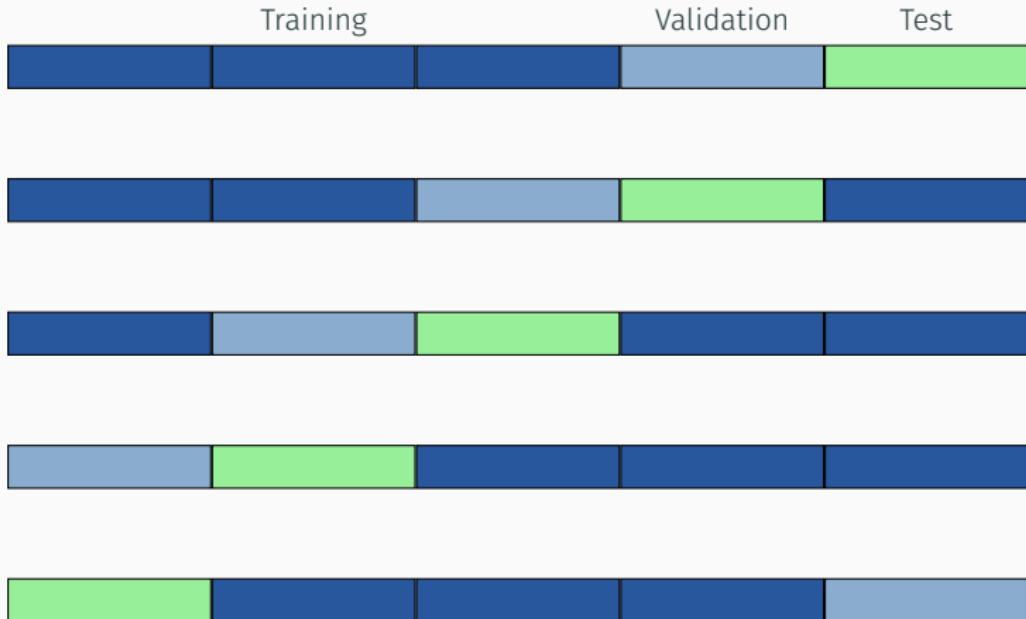
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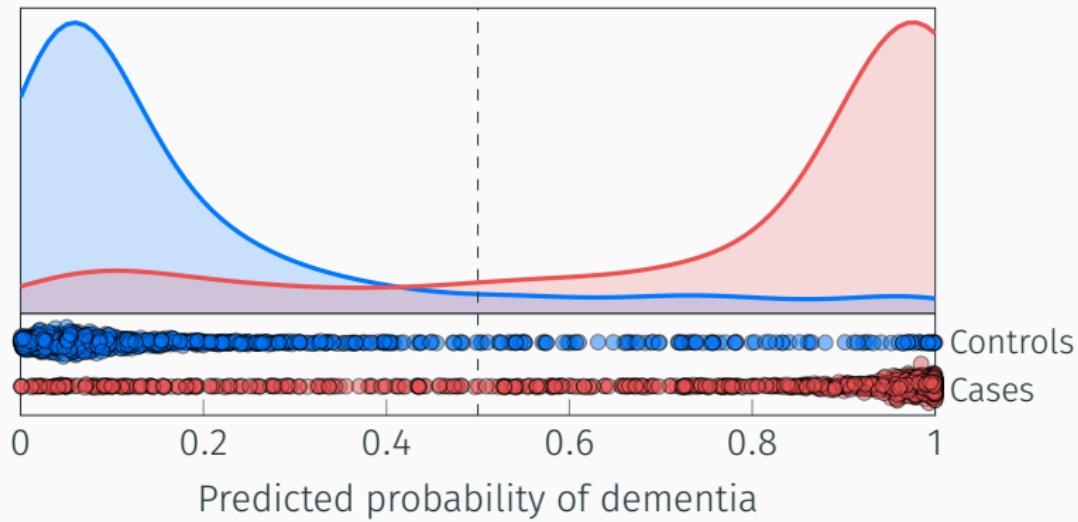
Explainable dementia classification: Modelling



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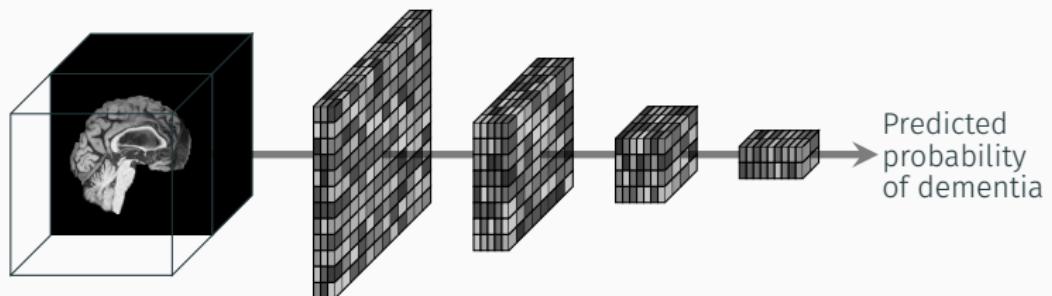
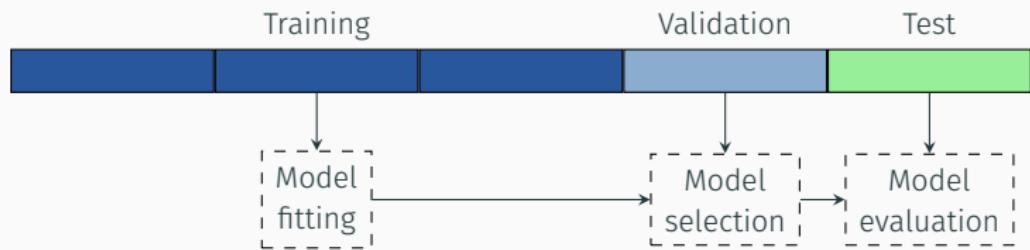


Explainable dementia classification: Modelling

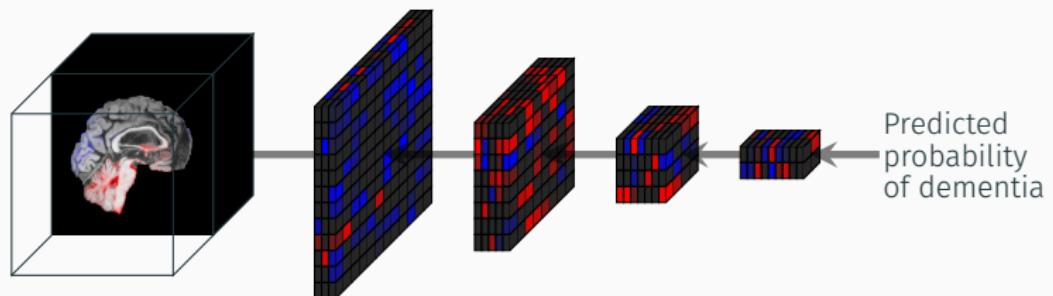
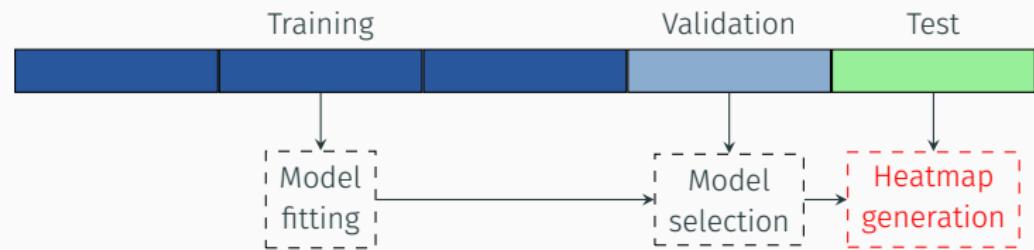


AUC=0.91, balanced accuracy=85%

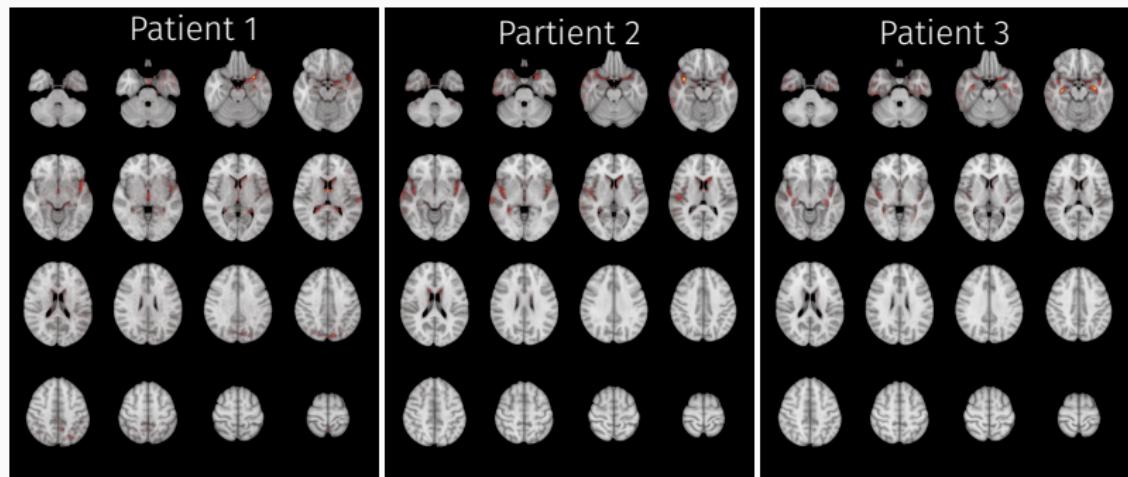
Explainable dementia classification: Modelling



Explainable dementia classification: Modelling

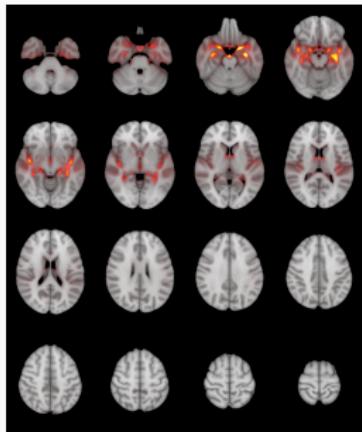


Explainable dementia classification: Validation



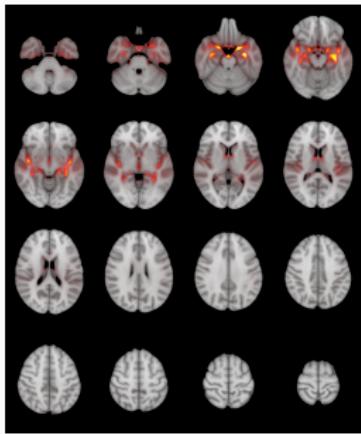
Explainable dementia classification: Validation

LRP

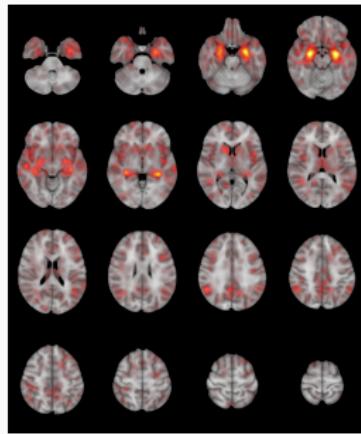


Explainable dementia classification: Validation

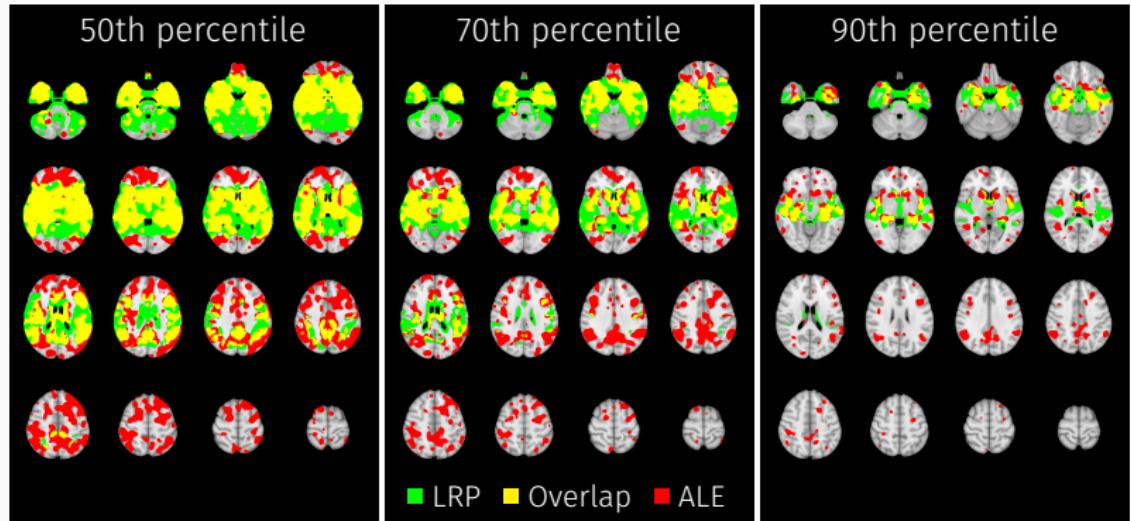
LRP



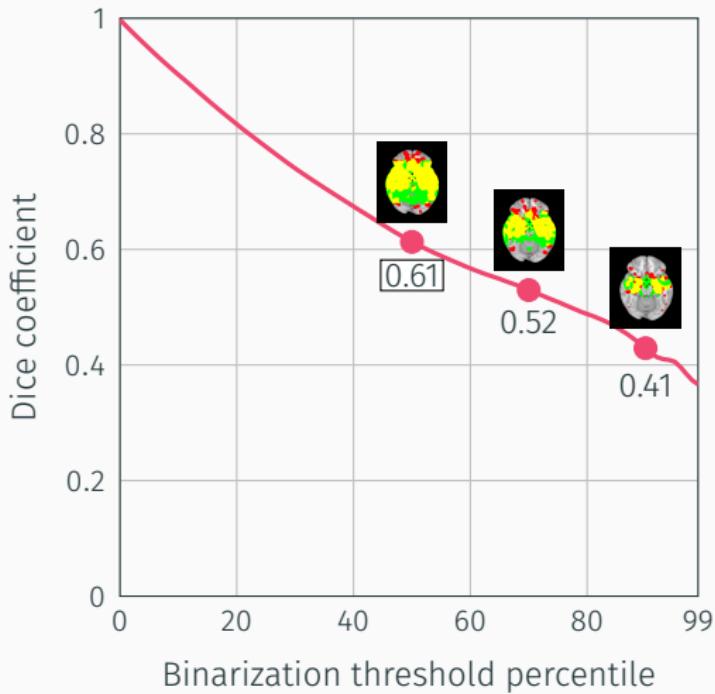
GingerALE



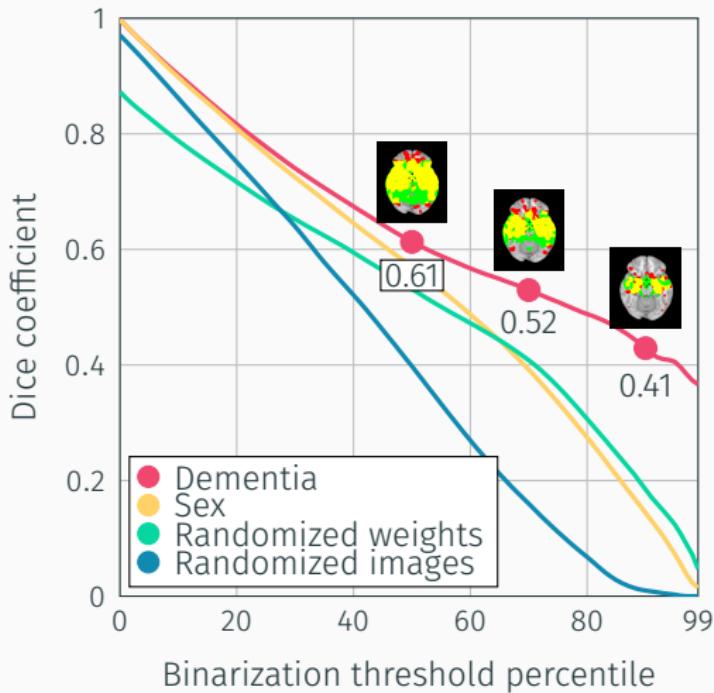
Explainable dementia classification: Validation



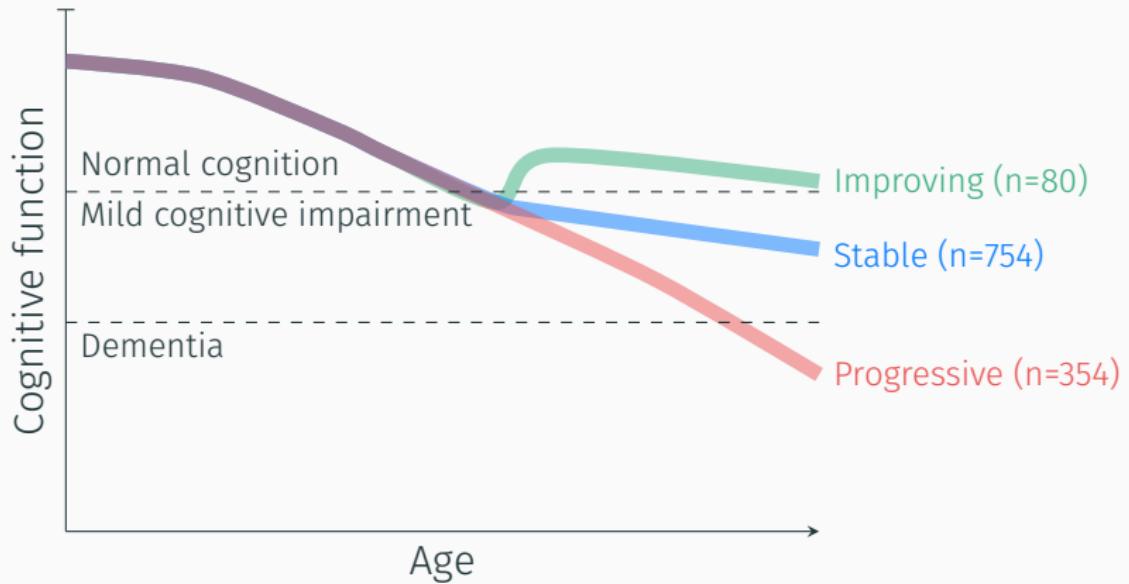
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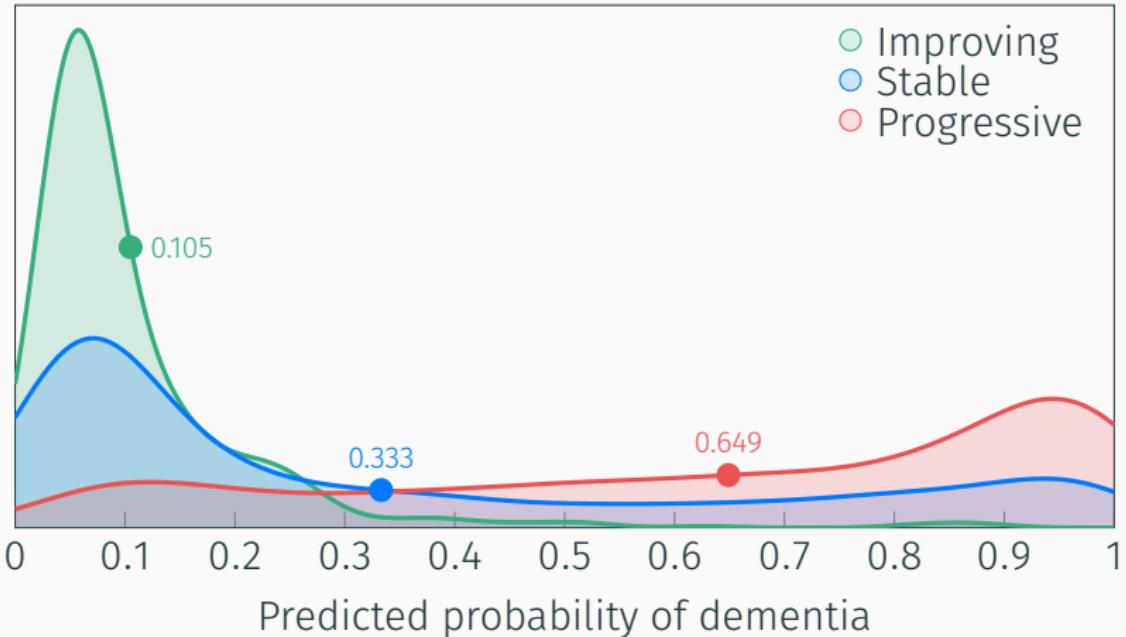
Explainable dementia classification: Validation



Explainable dementia classification: Application

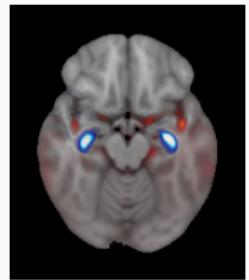
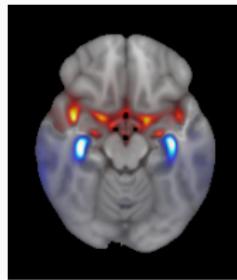
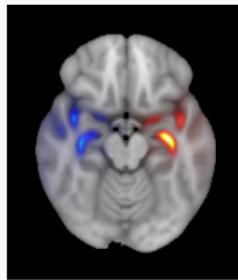
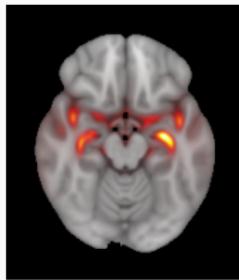


Explainable dementia classification: Application



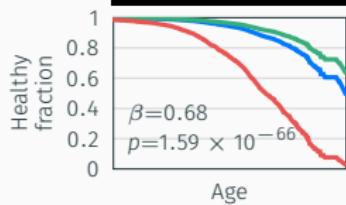
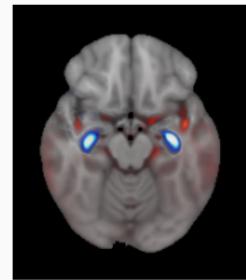
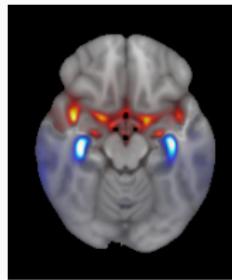
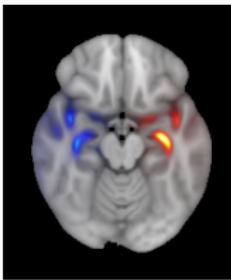
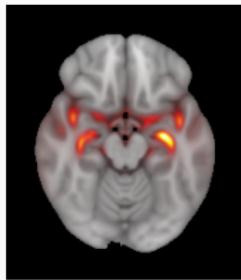
Explainable dementia classification: Application

Component 0 Component 1 Component 2 Component 3

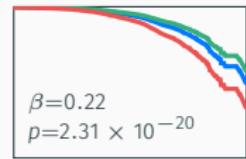
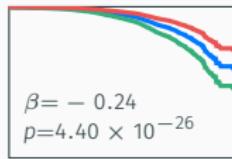


Explainable dementia classification: Application

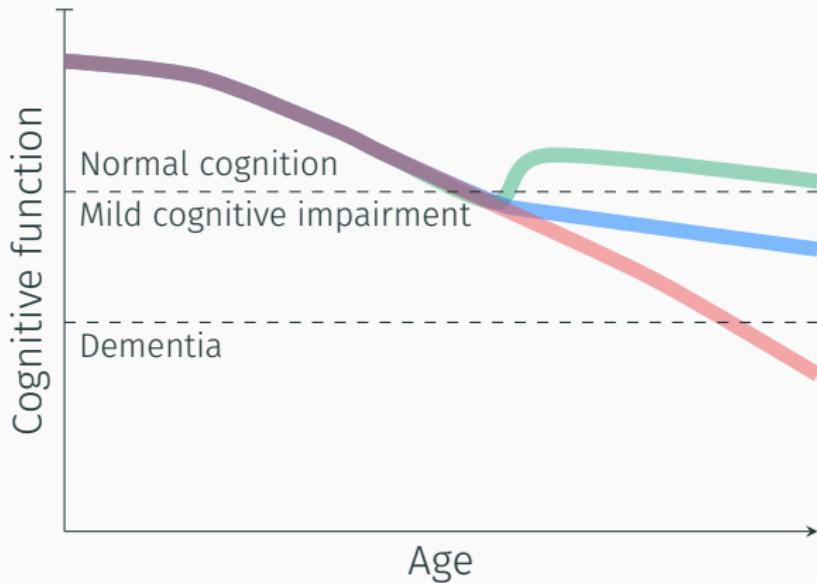
Component 0 Component 1 Component 2 Component 3



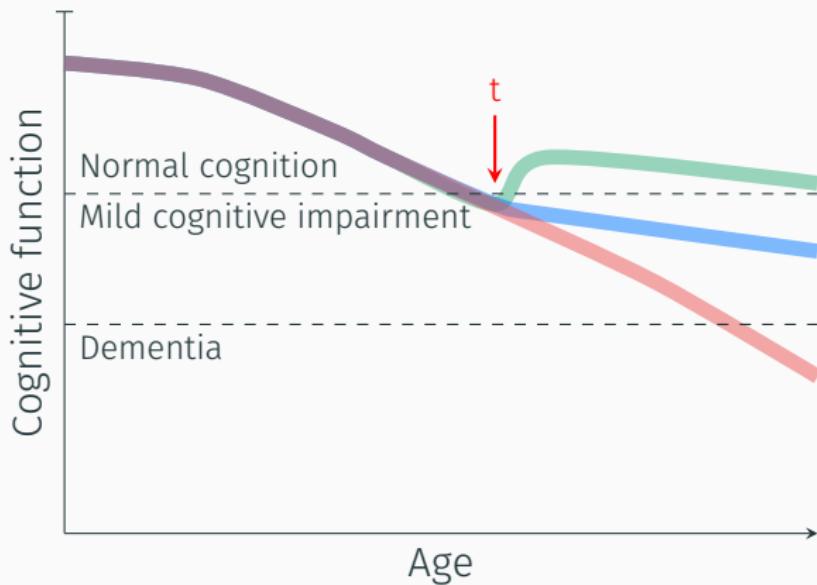
Percentiles
— 5th
— 50th
— 95th



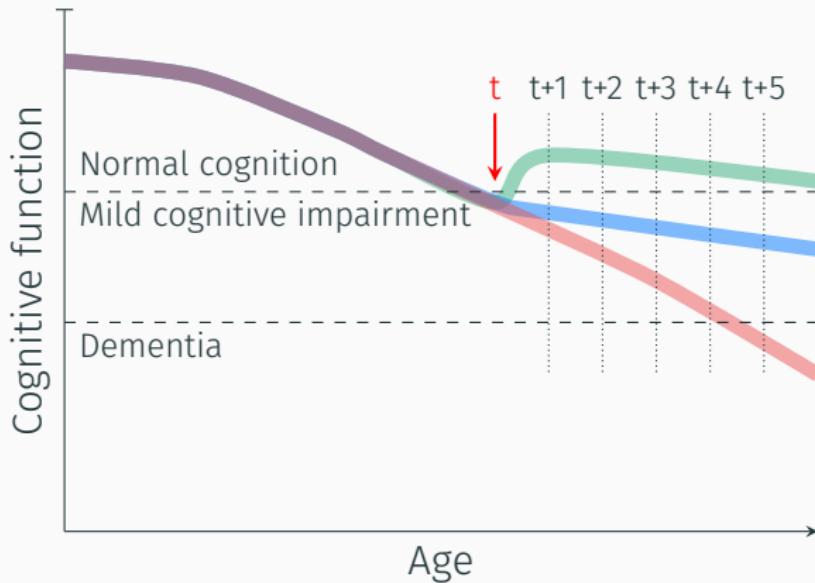
Explainable dementia classification: Application



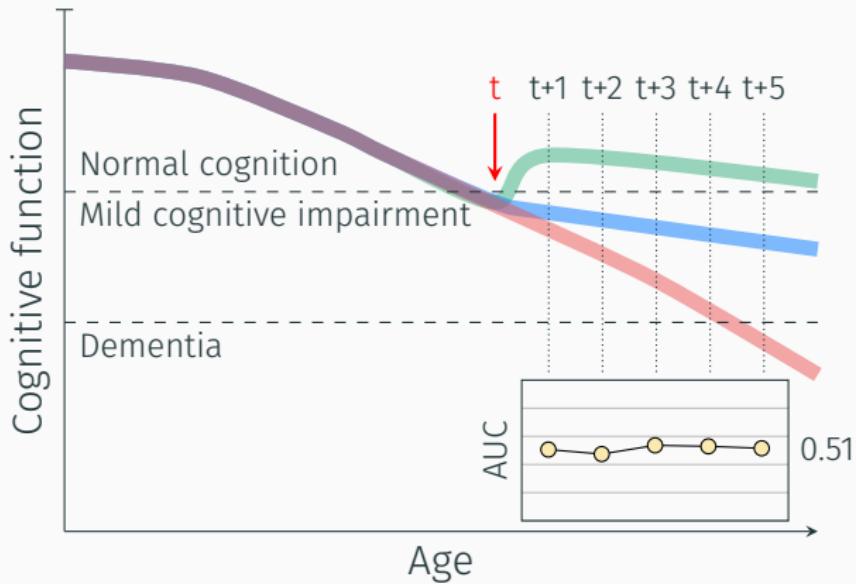
Explainable dementia classification: Application



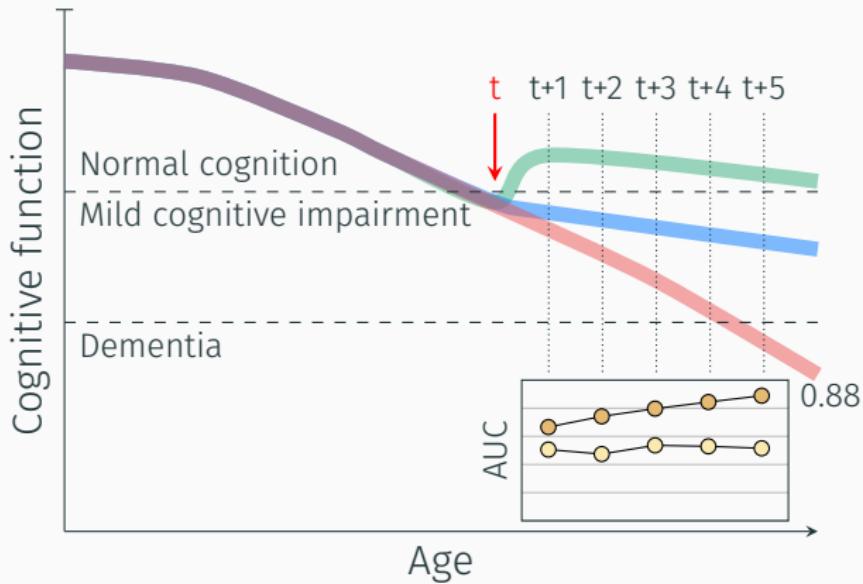
Explainable dementia classification: Application



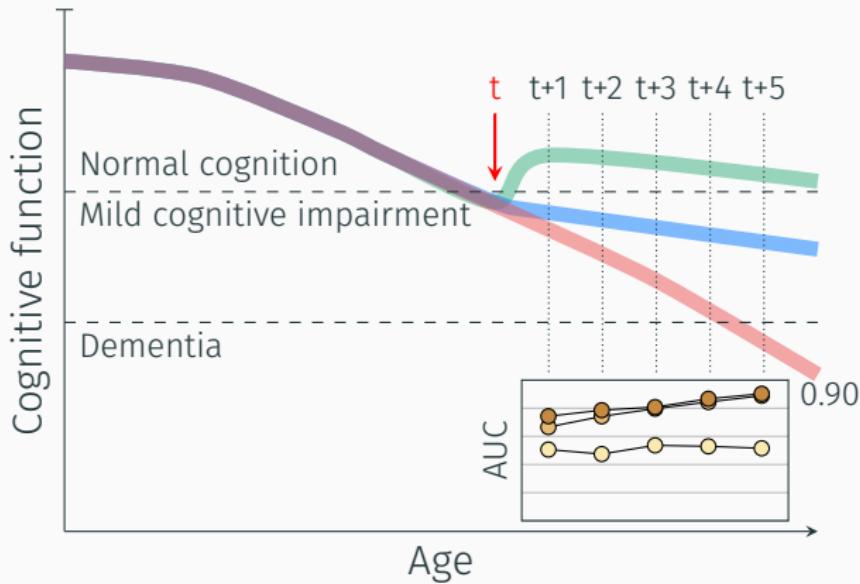
Explainable dementia classification: Application



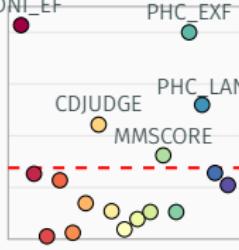
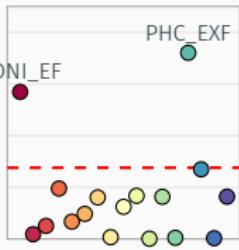
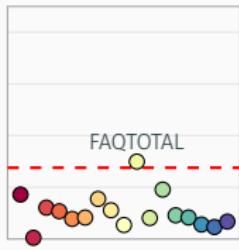
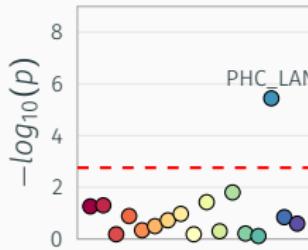
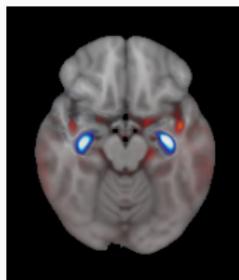
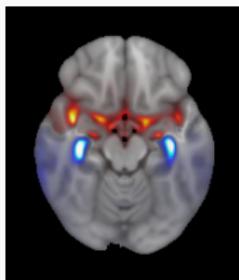
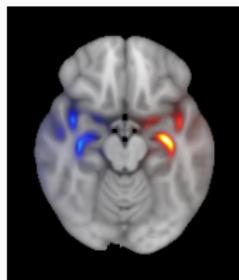
Explainable dementia classification: Application



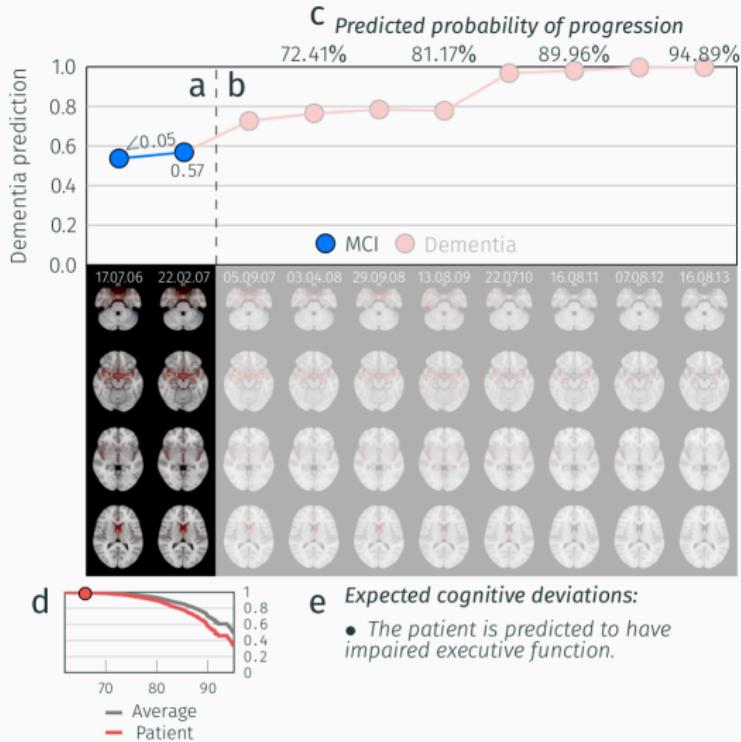
Explainable dementia classification: Application



Explainable dementia classification: Application



Explainable dementia classification: Application



Explainable dementia classification: Summary

We used explainable artificial intelligence to characterize brain aberrations associated with dementia as seen in neuroimaging data at the level of the individual patient

- Visual patterns in the heatmaps were associated with future progression and clinical manifestation of the disease
- The absolute majority of the signal carried by the heatmaps for subsequent predictive tasks was also present in the singular predictions

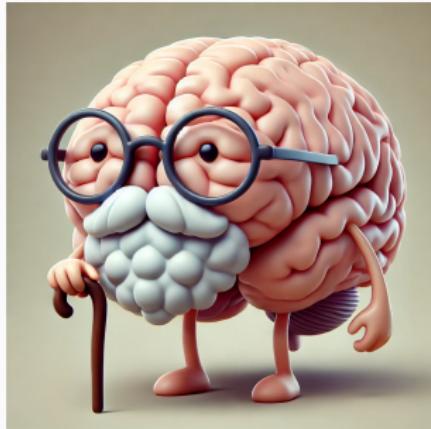


Explainable brain age



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Explainable brain age: Motivation



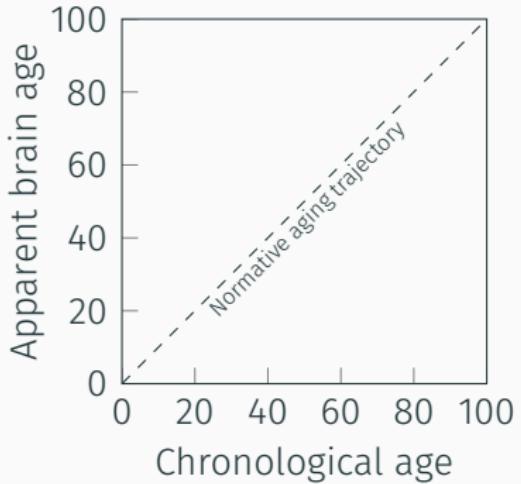
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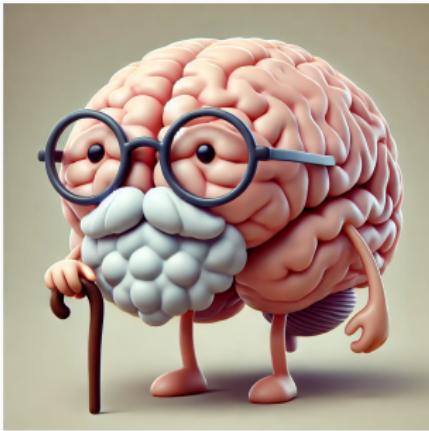
Explainable brain age: Motivation



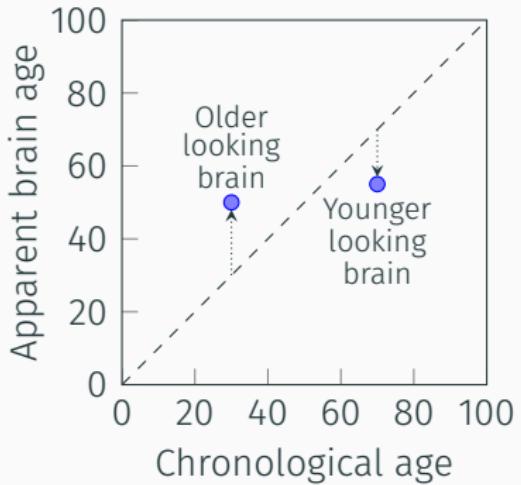
Generated by Dall-E 3



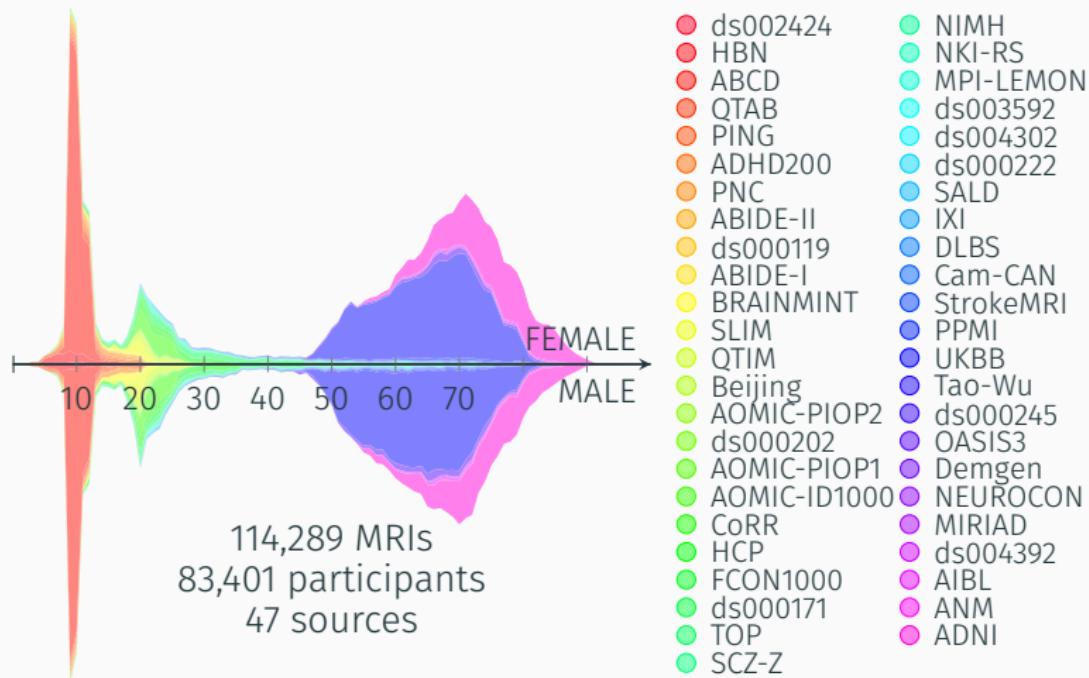
Explainable brain age: Motivation



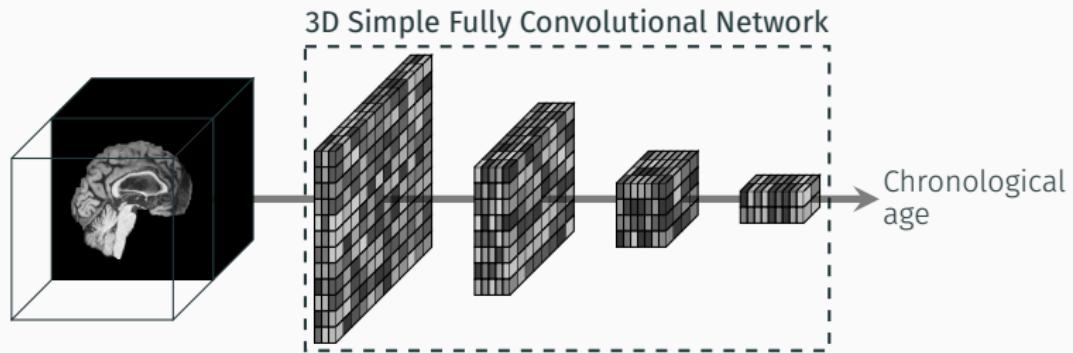
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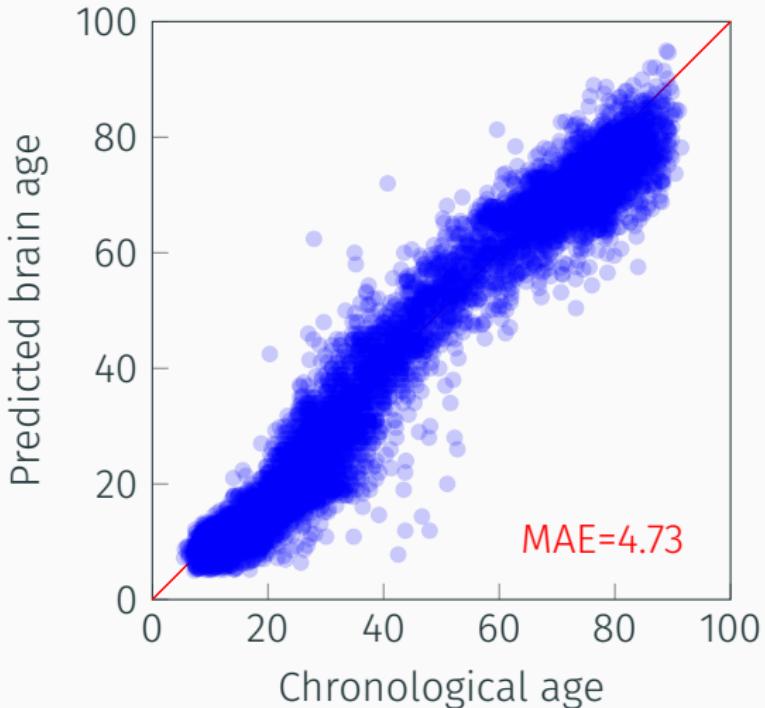
Explainable brain age: Motivation



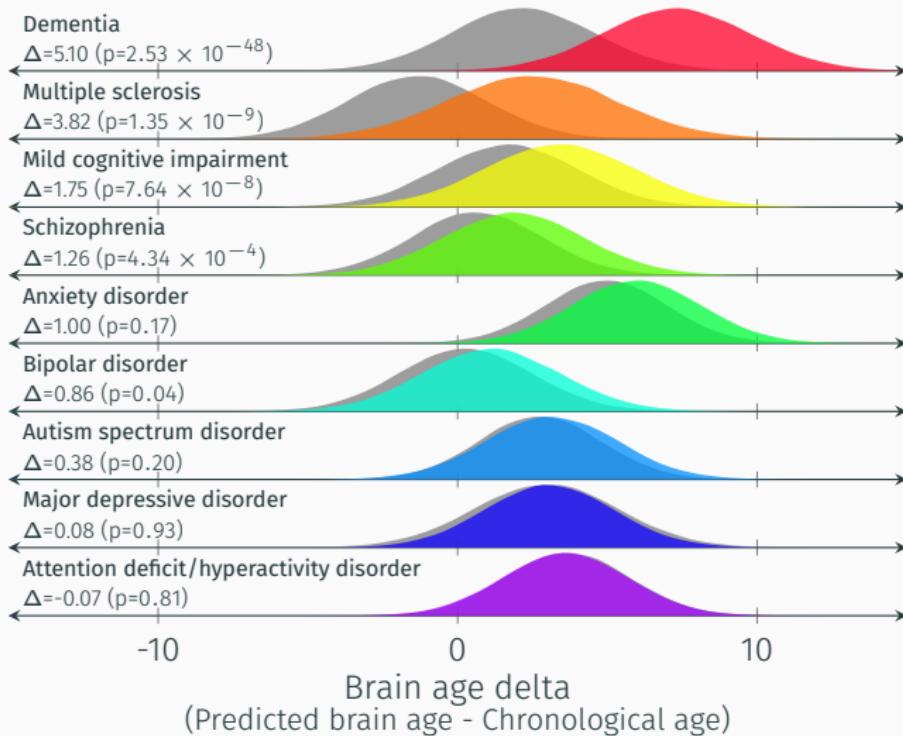
Explainable brain age: Motivation



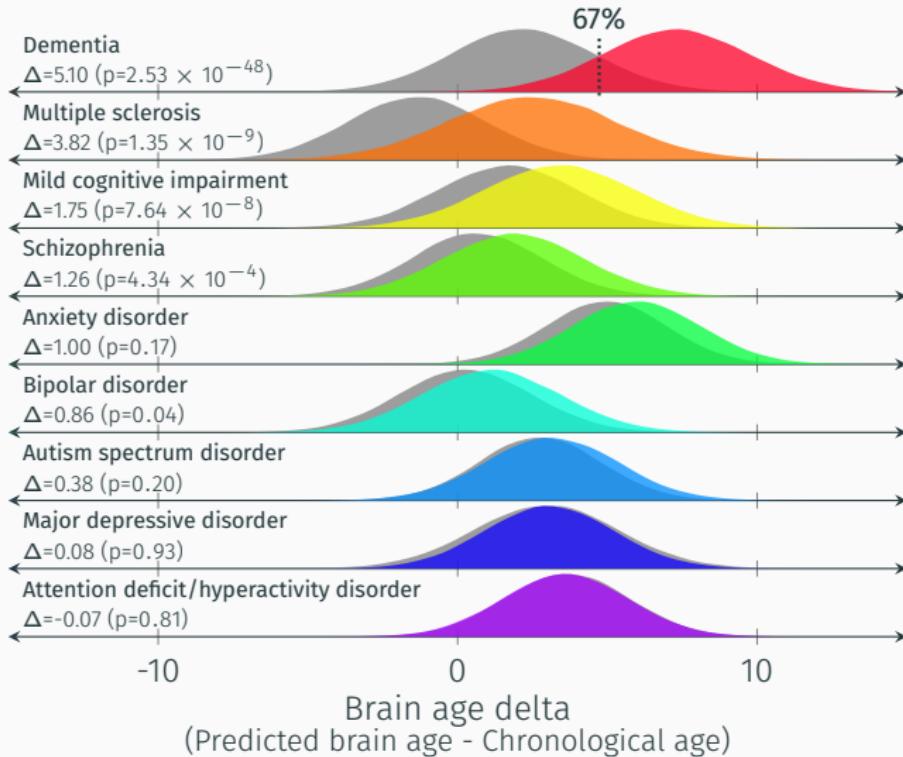
Explainable brain age: Motivation



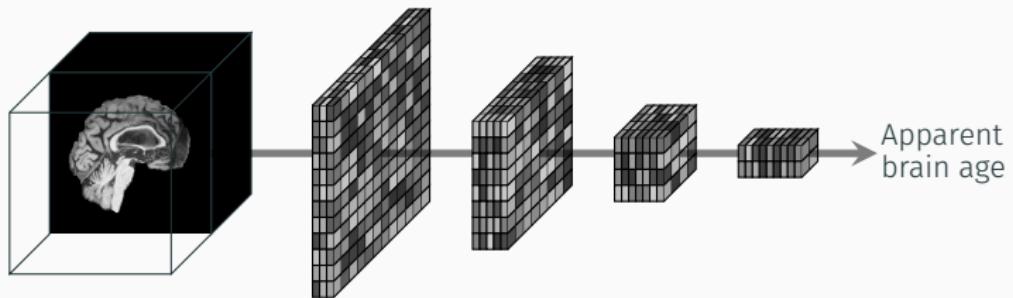
Explainable brain age: Motivation



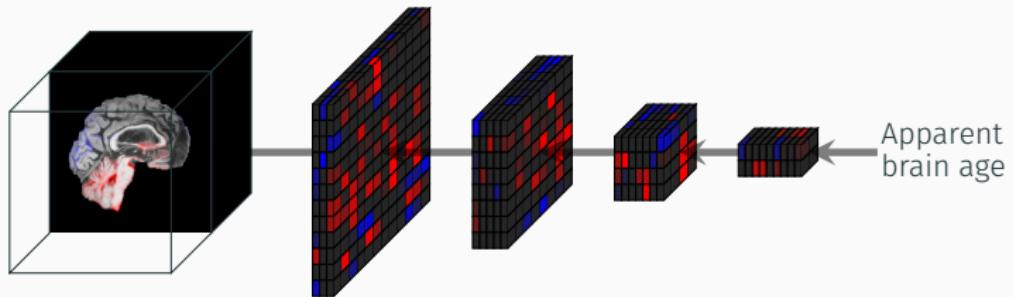
Explainable brain age: Motivation



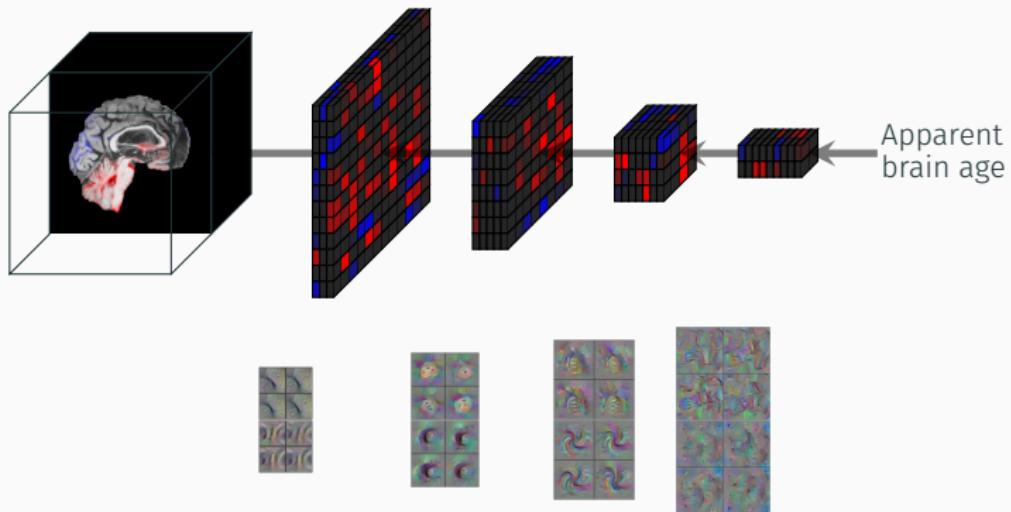
Explainable brain age: Methods



Explainable brain age: Methods



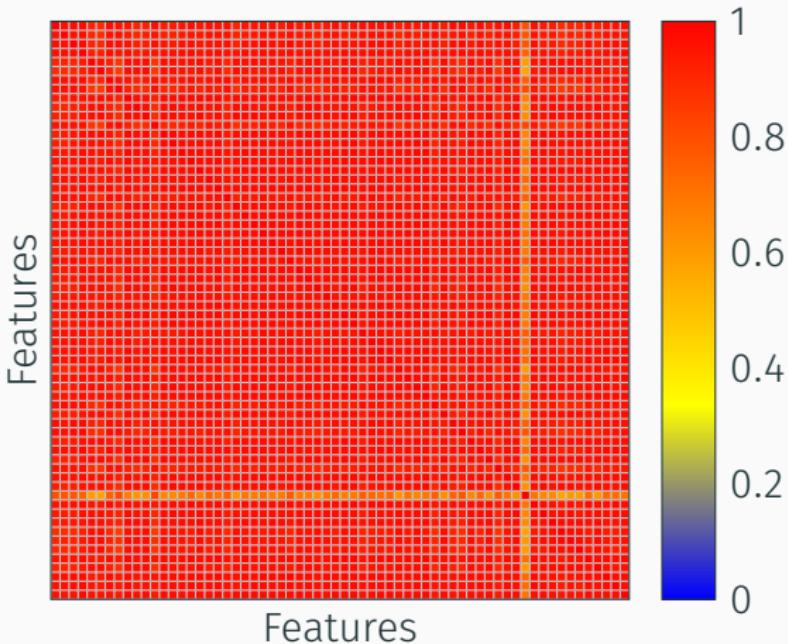
Explainable brain age: Methods



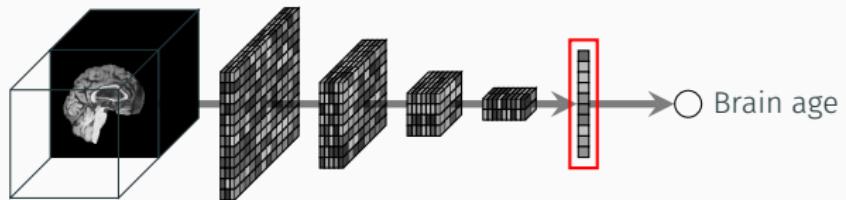
Understanding Neural Networks Through Deep Visualization
Yosinski, J. et al., preprint at arXiv (2015)



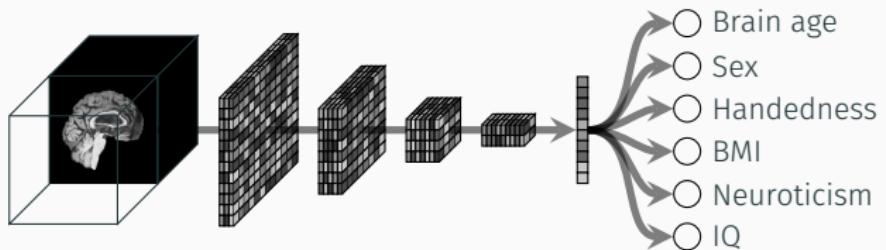
Explainable brain age: Methods



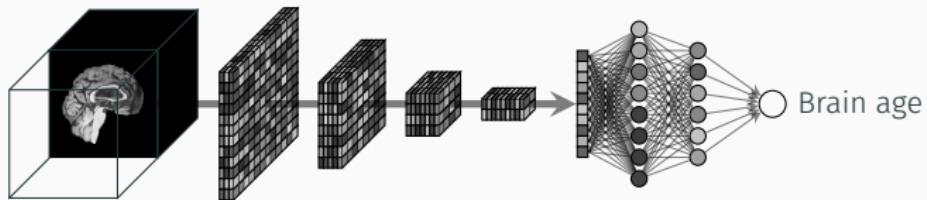
Explainable brain age: Methods



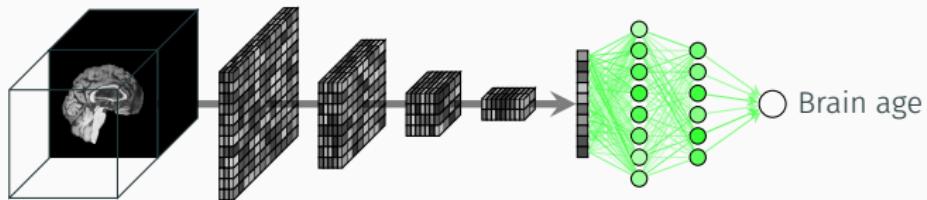
Explainable brain age: Methods



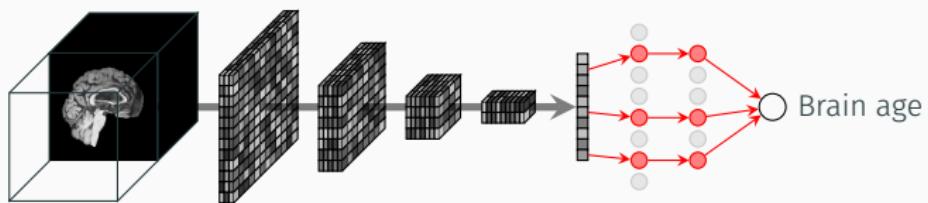
Explainable brain age: Methods



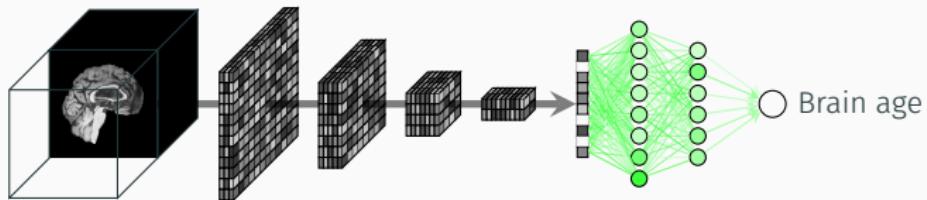
Explainable brain age: Methods



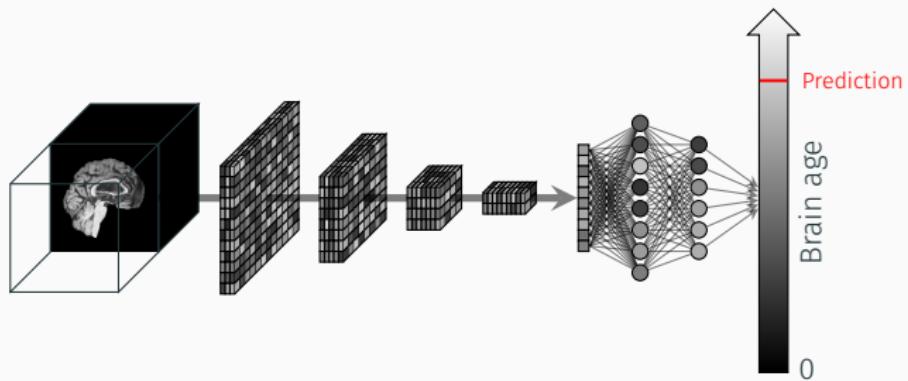
Explainable brain age: Methods



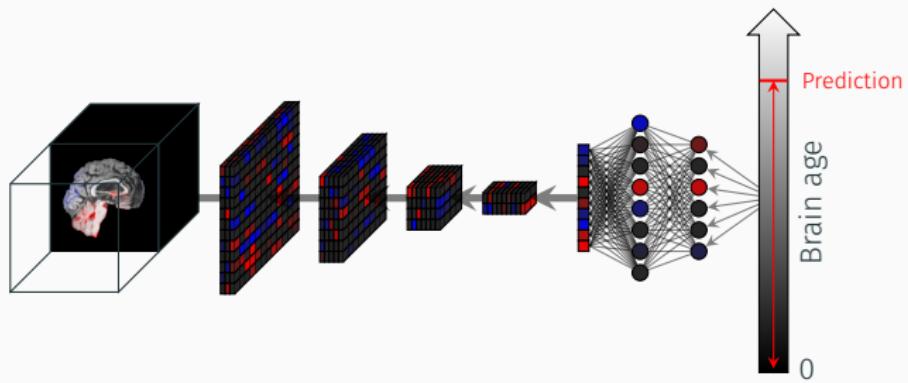
Explainable brain age: Methods



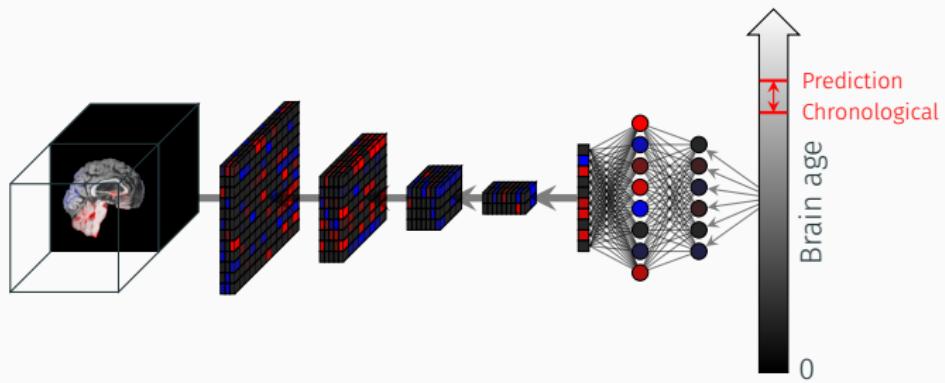
Explainable brain age: Methods



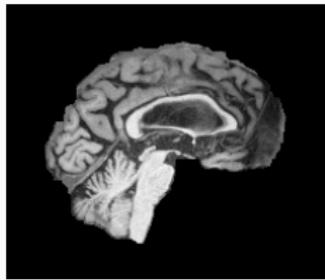
Explainable brain age: Methods



Explainable brain age: Methods

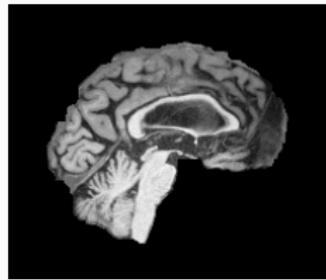


Explainable brain age: Methods



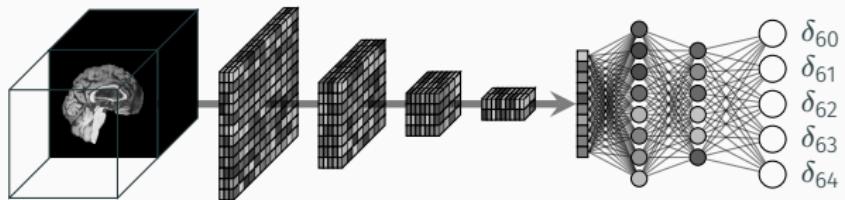
Age
62

Explainable brain age: Methods

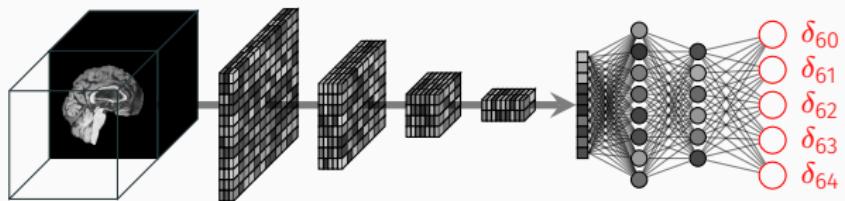


δ_{60}	δ_{61}	δ_{62}	δ_{63}	δ_{64}
2	1	0	-1	-2

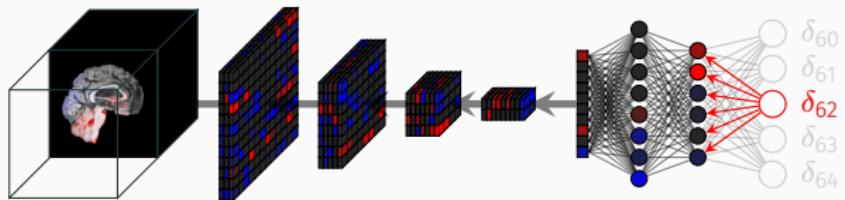
Explainable brain age: Methods



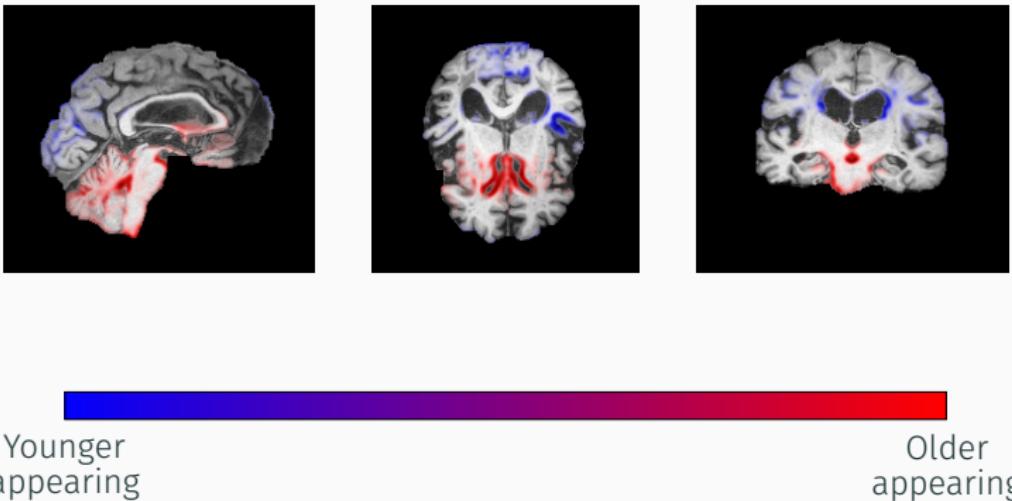
Explainable brain age: Methods



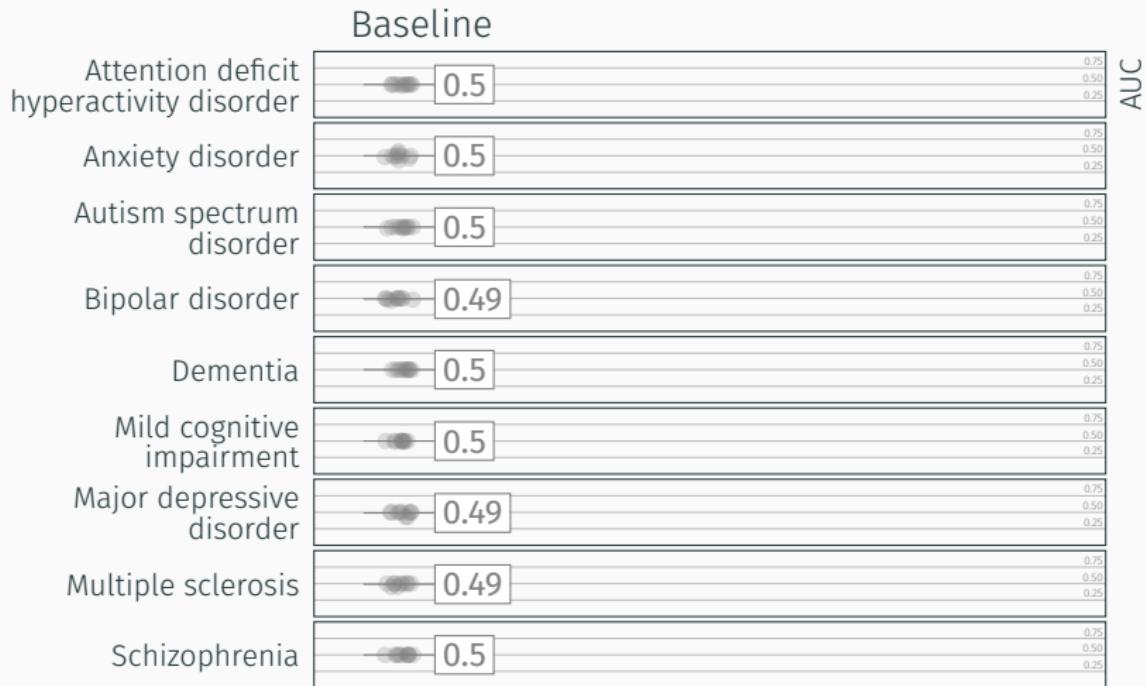
Explainable brain age: Methods



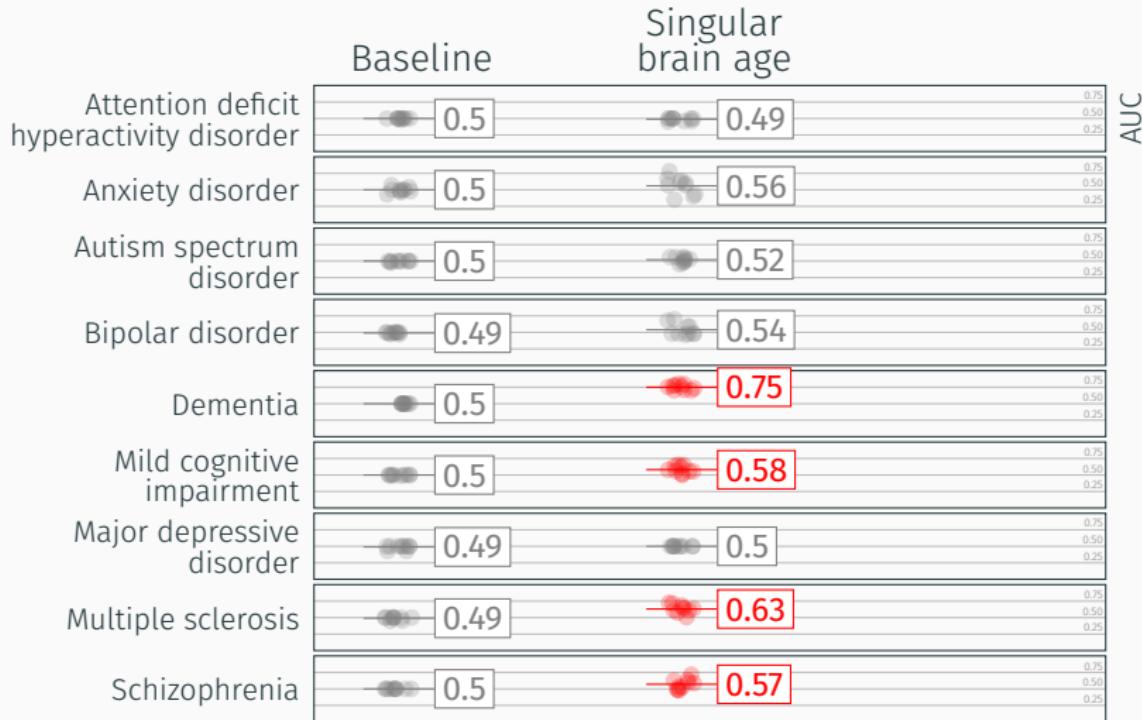
Explainable brain age: Results



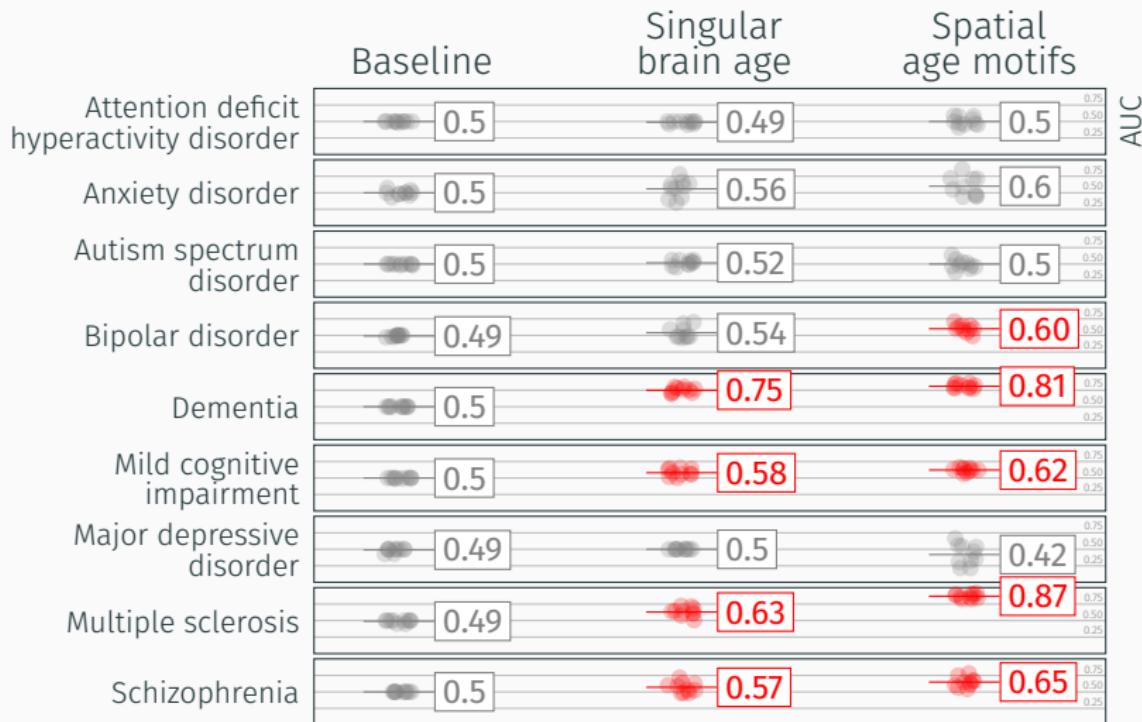
Explainable brain age: Results



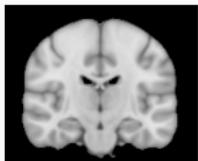
Explainable brain age: Results



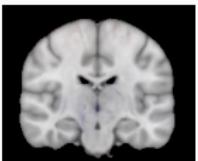
Explainable brain age: Results



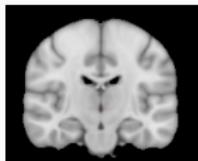
Explainable brain age: Results



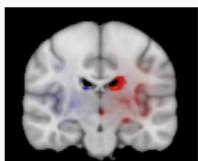
Attention deficit
hyperactivity disorder



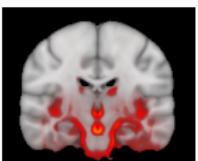
Anxiety
disorder



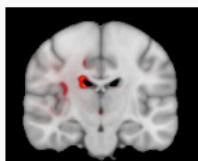
Autism spectrum
disorder



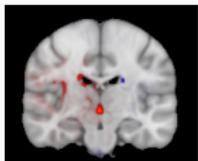
Bipolar
disorder



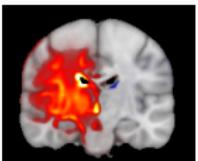
Dementia



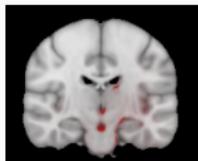
Schizophrenia



Major depressive
disorder

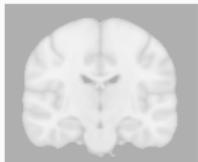


Multiple
sclerosis

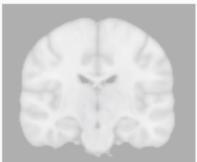


Mild cognitive
impairment

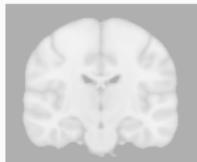
Explainable brain age: Results



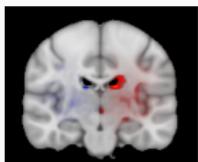
Attention deficit
hyperactivity disorder



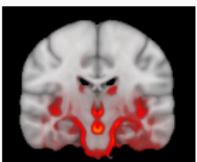
Anxiety
disorder



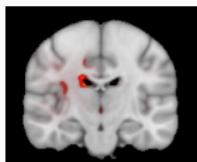
Autism spectrum
disorder



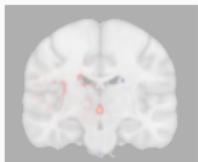
Bipolar
disorder



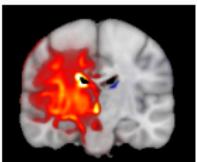
Dementia



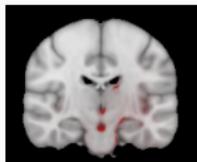
Schizophrenia



Major depressive
disorder



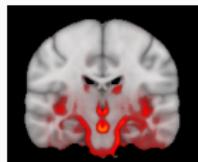
Multiple
sclerosis



Mild cognitive
impairment



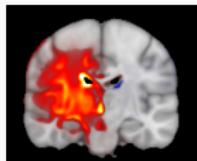
Explainable brain age: Results



Dementia

- Temporal pole
- Left amygdala
- Parahippocampal gyrus

Explainable brain age: Results

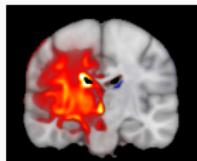


Multiple
sclerosis

- Right pallidum
- Right thalamus
- Right putamen



Explainable brain age: Results

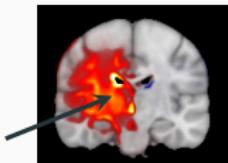


Multiple
sclerosis

- Right pallidum
- Right thalamus
- Right putamen



Explainable brain age: Results

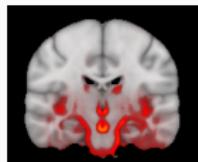


Multiple
sclerosis

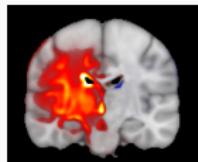
- Right pallidum
- Right thalamus
- Right putamen



Explainable brain age: Results



Dementia



Multiple
sclerosis



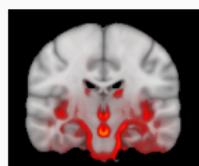
Explainable brain age: Results

	AUC	
	Singular brain age	Spatial age motifs
Dementia	0.75	0.81
Multiple sclerosis	0.63	0.87



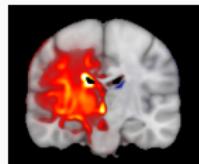
Explainable brain age: Results

AUC



Dementia

Singular brain age	Spatial age motifs
0.75	0.81 0.06

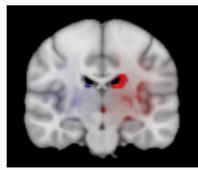


Multiple
sclerosis

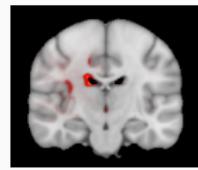
0.63	0.87 0.24
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Explainable brain age: Results

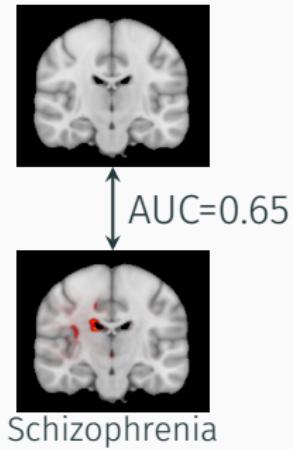
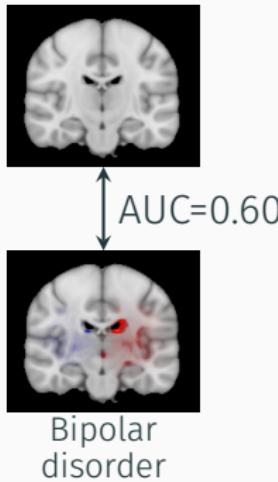


Bipolar
disorder

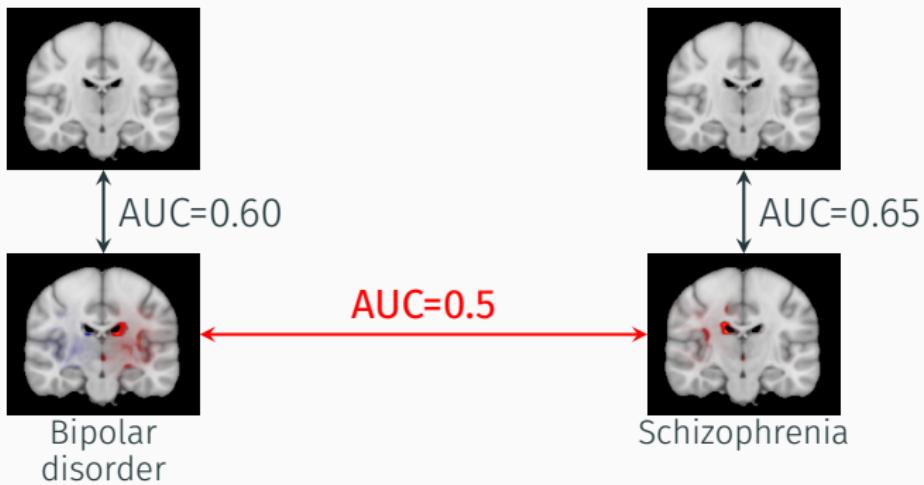


Schizophrenia

Explainable brain age: Results



Explainable brain age: Results



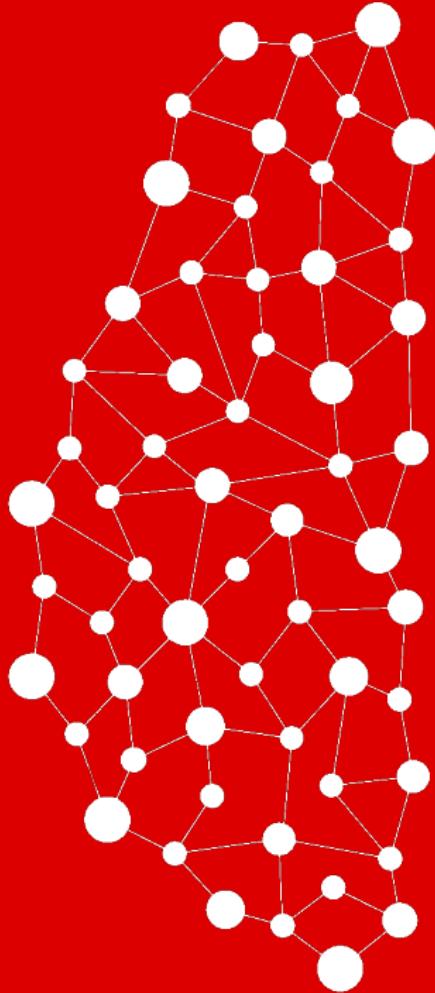
Summary

Explainable artificial intelligence represents a promising approach to procure precise characterizations of neuroimaging abnormalities in individual brains related to a phenotype of interest

- The spatial information from the heatmaps complement the predictions of the model they originate from
- The extent of their added value is still unclear
- Rigorous validations are **crucial**



Thank you for your attention!
estenhl@ui.no



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