

The role of neuroimaging beyond T1-weighted MRI in the diagnosis and prediction of neuropsychiatric disorders

Esten H. Leonardsen

26.10.23



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Overview

1. Background: Defining the scope of the lecture.
2. State-of-the-art: How is neuroimaging beyond T1-weighted MRI currently being used with respect to neuropsychiatric disorders.
3. The future: Challenges and opportunities in using neuroimaging for predicting neuropsychiatric disorders moving forward.



Background

- The role of neuroimaging beyond T1-weighted MRI in the diagnosis and prediction of neuropsychiatric disorders



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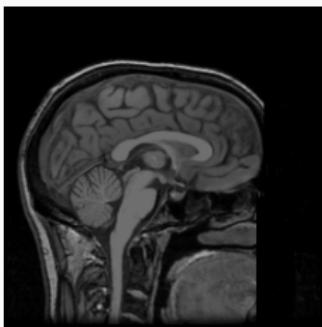


Bert from FreeSurfer 7.3

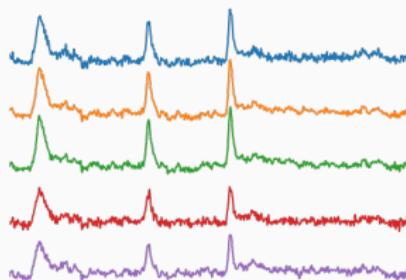


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Bert from FreeSurfer 7.3

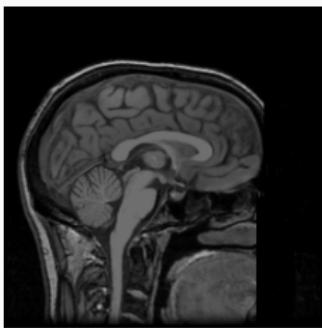


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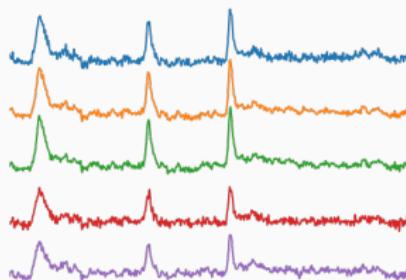


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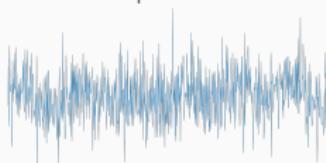
- The role of neuroimaging beyond T1-weighted MRI in the diagnosis and prediction of neuropsychiatric disorders



Bert from FreeSurfer 7.3



Sample from the MNE library



Sample from Tremlay et al., 2016

Tremblay, R., Lee, S., & Rudy, B. (2016). GABAergic interneurons in the neocortex: from cellular properties to circuits. *Neuron*, 91(2), 260-292

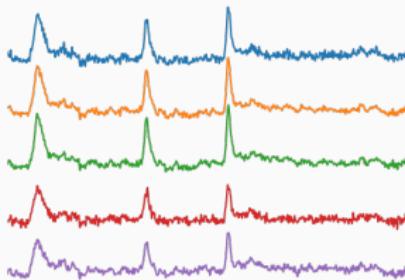


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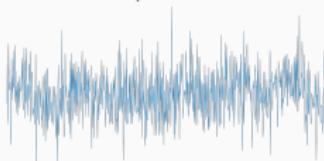
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Bert from FreeSurfer 7.3



Sample from the MNE library



Sample from Tremblay et al., 2016



Meta Quest Pro

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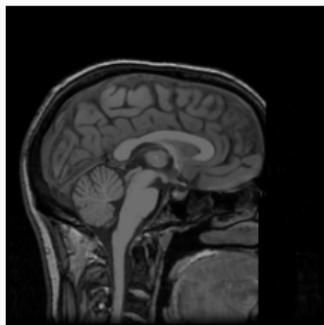


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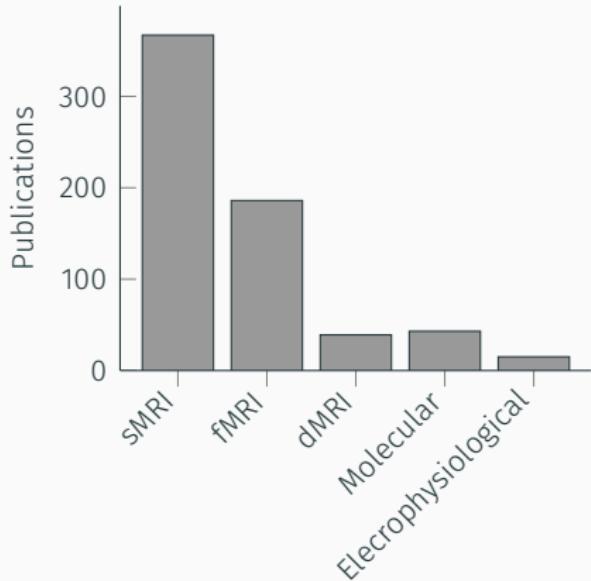


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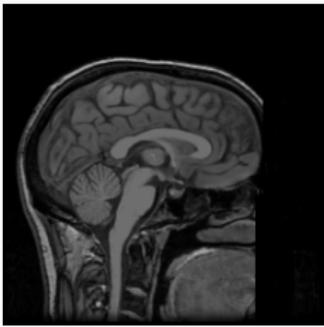


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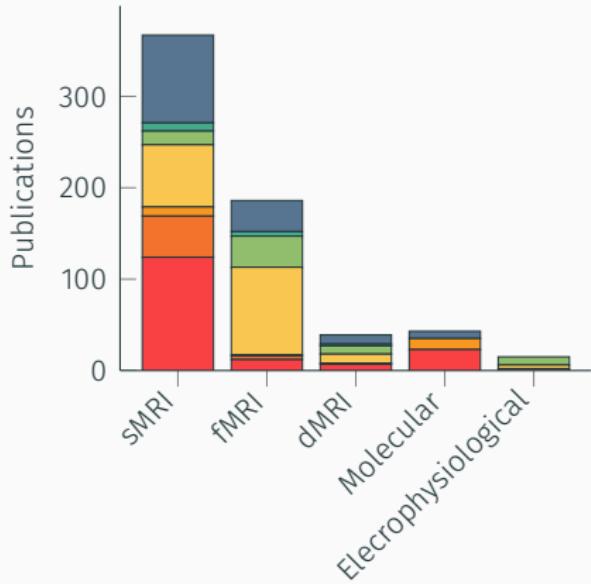


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Alzheimer's disease and other
causes of dementia

Multiple Sclerosis

Parkinson's Disease



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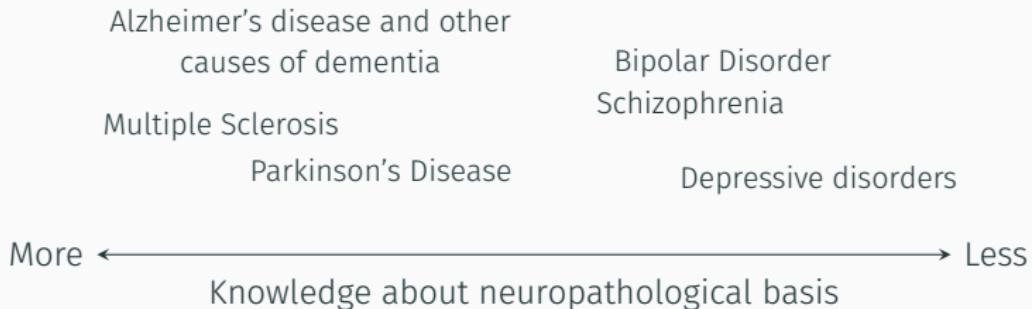
Bipolar Disorder
Schizophrenia

Depressive disorders



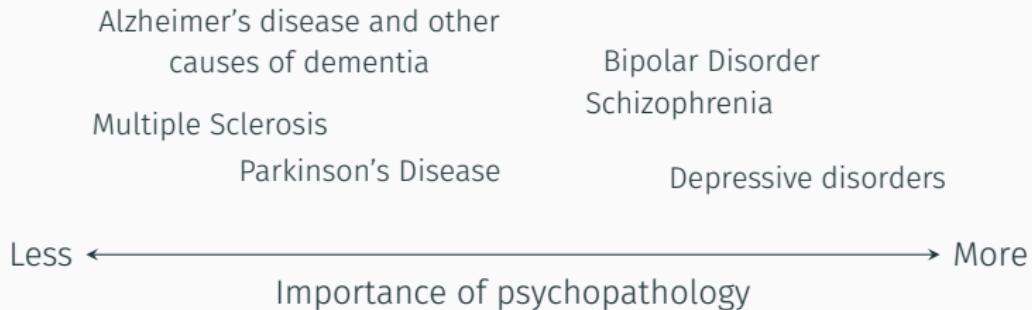
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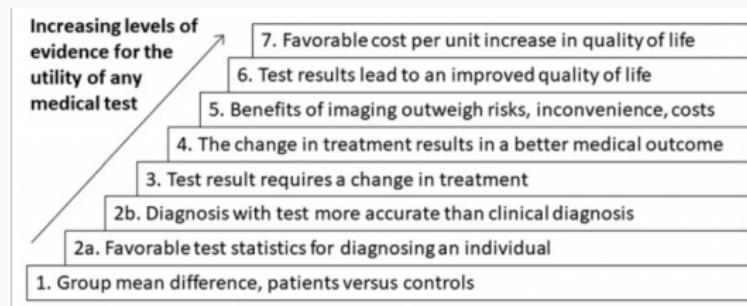


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Vogel & Black (2024)

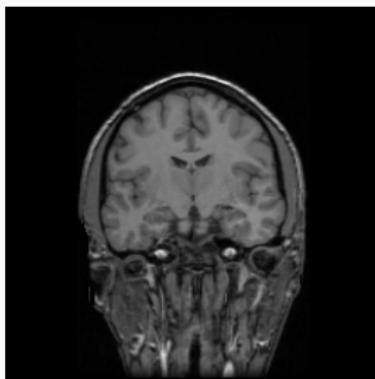


Vogel, A. C., & Black, K. J. (2024). Brain Imaging in Routine Psychiatric Practice. Missouri Medicine, 121(1), 37



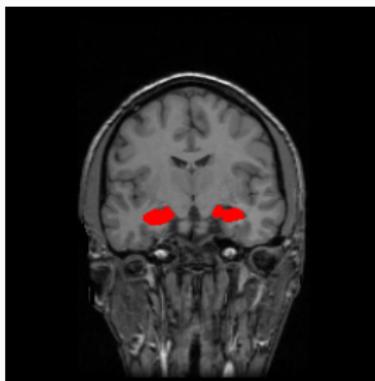
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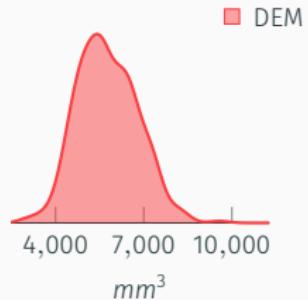
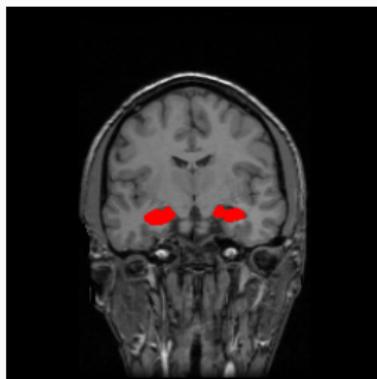
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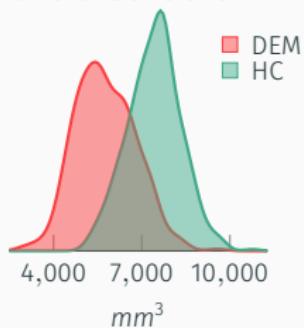
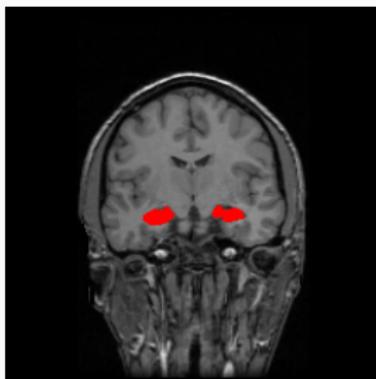
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Jack Jr, C. R., Bernstein, M. A., Fox, N. C., Thompson, P., Alexander, G., Harvey, D., ... & Weiner, M. W. (2008). The Alzheimer's disease neuroimaging initiative (ADNI): MRI methods. Journal of Magnetic Resonance Imaging: An Official Journal of the International Society for Magnetic Resonance in Medicine, 27(4), 685-691



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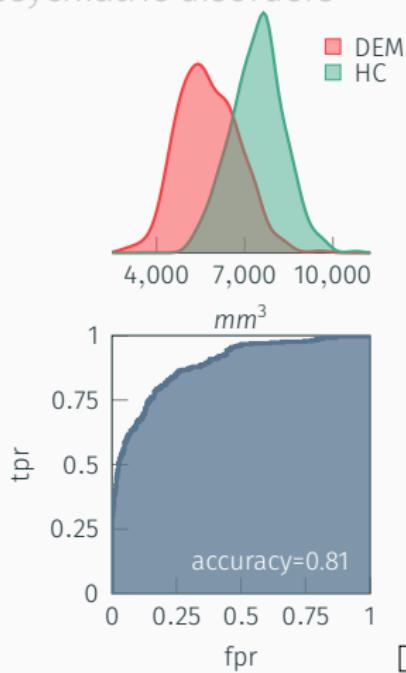
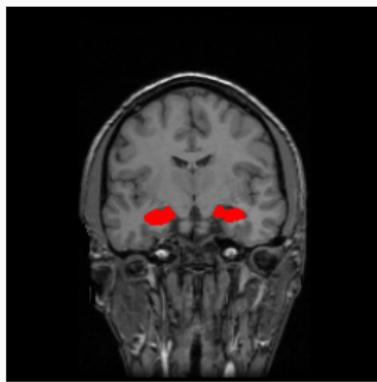
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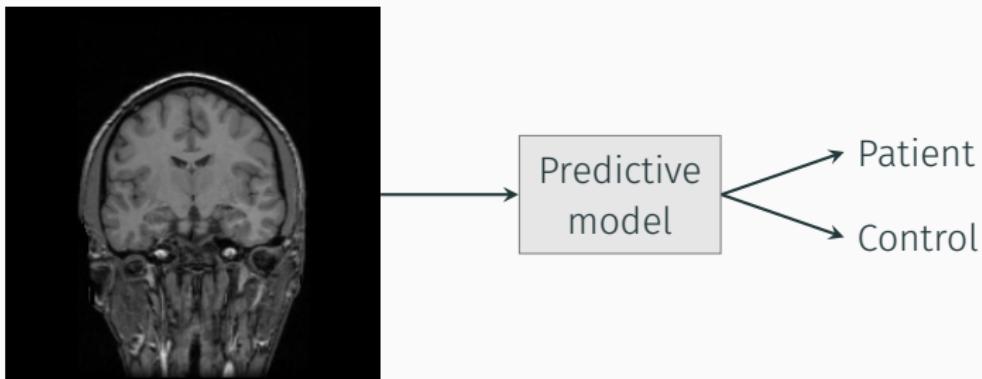
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Neuroimaging modalities for diagnostic predictions



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Approach

Non-T1 structural MRI

Diffusion MRI

Functional MRI

Molecular imaging



Approach

Non-T1 structural MRI

Diffusion MRI

Functional MRI

Molecular imaging

Dementia
Multiple sclerosis
Parkinson's disease
Schizophrenia
Major depressive disorder
Bipolar disorder



Approach

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Data



From estimating activation locality to predicting disorder: A review of pattern recognition for neuroimaging-based psychiatric diagnostics

Thomas Wolters^{a,b} , Jon K. Buitelaar^{c,d}, Christian F. Beckmann^{b,e,f}, Barbara Franke^{a,f}, Andre F. Marquand^{b,g}



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Single subject prediction of brain disorders in neuroimaging: Promises and pitfalls

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Towards a brain-based predictome of mental illness

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Towards a brain-based predictome of mental illness

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Deep learning applications for the classification of psychiatric disorders using neuroimaging data: Systematic review and meta-analysis

Mirjam Quak¹, Laurens van de Mortel³, Rajat Mani Thomas¹, Ouido van Wingen²



Data



Deep learning to detect Alzheimer's disease from neuroimaging: A systematic literature review

Mr Amir Ebrahimighahmavieh ³, Suhuai Luo ³, Raymond Chiong ²

Machine learning techniques for diagnosis of alzheimer disease, mild cognitive disorder, and other types of dementia

Golrokh Mirzaei ^a, R., Hajar Adeli ^b

Early diagnosis of Alzheimer's disease based on deep learning: A systematic review

Sina Fathi ¹, Maryam Ahmadi ², Afshaneh Dehrad ³





Applications of deep learning techniques for automated multiple sclerosis detection using magnetic resonance imaging: A review

Afshin Shoebi¹, Marjane Khodatani², Mahboobeh Jafari³, Parisa Moridian⁴, Mitra Rezaei⁵, Roohollah Alzadehsani⁶, Fahimeh Khozeirneh⁶, Juan Manuel Gomez⁷, Jonathan Heras⁸, Maryam Panahiazar⁹, Saeid Nahavandi¹⁰, U Rajendra Acharya¹⁰

Multiple Sclerosis Diagnosis Using Machine Learning and Deep Learning: Challenges and Opportunities

by Nida Aslam^{1,*} , Irfan Ulhan Khan¹ , Asma Bashirnakh¹, Fatima A. Alghool¹, Merina Absoulour¹ , Noorah M. Alsuwayyan¹, Rawa'a K. Alturaiif¹, Samiha Brahim², Sumayah S. Aljameel¹ and Kholoud Al Ghandi³



Data



Role of Artificial Intelligence Techniques and Neuroimaging Modalities
in Detection of Parkinson's Disease: A Systematic Review

Nikita Aggarwal¹ · B. S. Saini¹ · Savita Gupta²



Data



Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review

Bruno de Faria,^{4*} Elisa Anna Carbone,^{4*} Rafaella Gaetano,¹ Antonella Bruni,¹ Valentina Pugliese,¹ Cristina Segura-Garcia,² and Pasquale De Fazio¹

**Machine learning techniques for the Schizophrenia diagnosis:
a comprehensive review and future research directions**

Shradha Verma¹ · Tripti Goel¹ · M. Tanveer² · Weiping Ding³ · Rahul Sharma¹ · R. Murugan¹



Data



Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

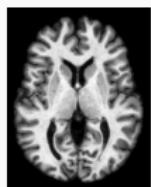
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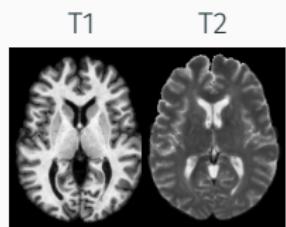
Other structural MRI modalities



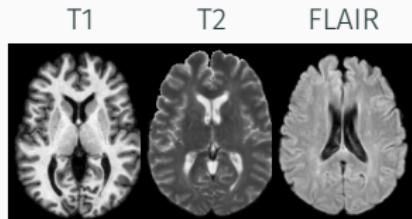
T1



Other structural MRI modalities



Other structural MRI modalities

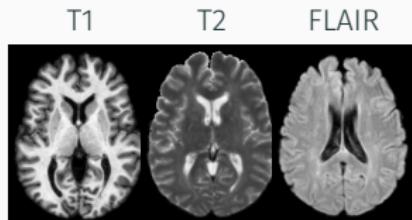


Adapted from Shoeibi et al., 2021

Shoeibi, A., Khodatars, M., Jafari, M., Moridian, P., Rezaei, M., Alizadehsani, R., ... & Acharya, U. R. (2021). Applications of deep learning techniques for automated multiple sclerosis detection using magnetic resonance imaging: A review. *Computers in Biology and Medicine*, 136, 104697.



Other structural MRI modalities

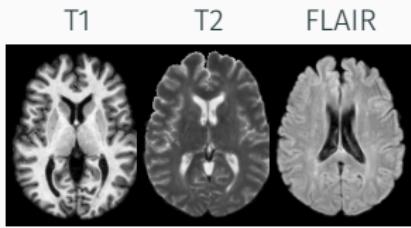


FLAIR lesion from MS patient

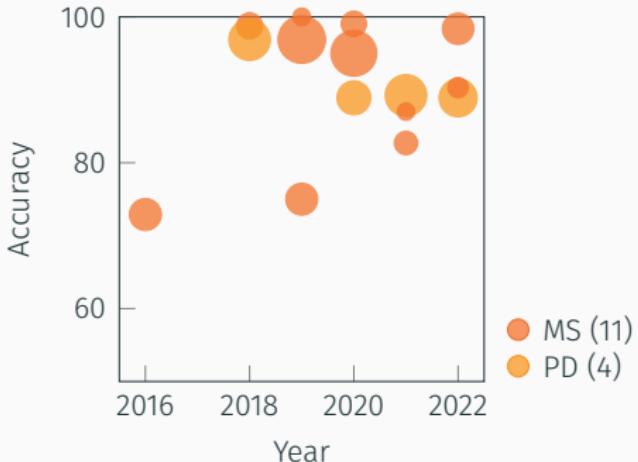
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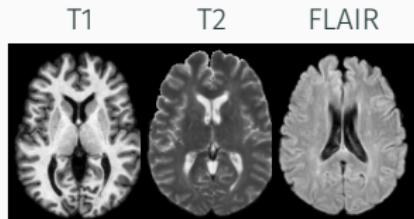
Other structural MRI modalities



Adapted from Shoeibi et al., 2021



Other structural MRI modalities

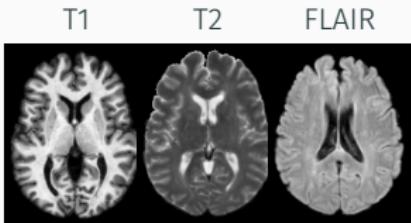


FLAIR lesion from MS patient++

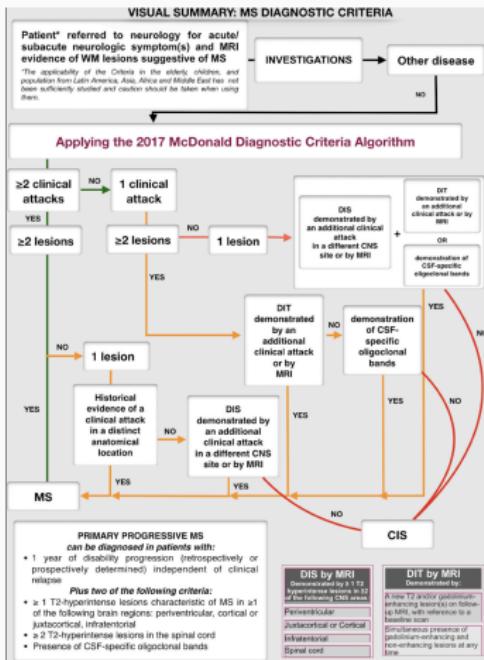
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Other structural MRI modalities



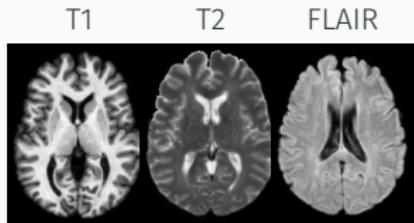
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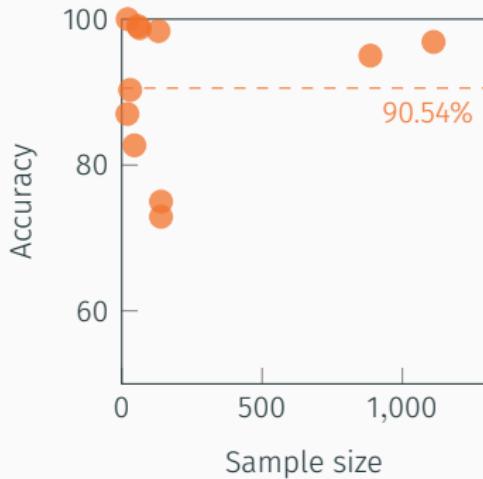
De Angelis et al., 2019

De Angelis, F., Brownlee, W. J., Chard, D. T., & Trip, S. A. (2019). New MS diagnostic criteria in practice. Practical Neurology, 19(1), 64-67

Other structural MRI modalities



Adapted from Shoeibi et al., 2021



Other structural MRI modalities



TABLE 3 - Accuracy, Sensitivity, and Specificity in the Prognosis of Disease Evolution for the Expert Raters and for the Proposed CNN Model on the Independent Test Set

		Prediction of Clinical Worsening (EDSS Model)	Prediction of Cognitive Worsening (SDMT Model)	Prediction of Clinical and Cognitive Worsening (EDSS + SDMT Model)	P*
CNN deep learning	Accuracy (%)	83.3	60.7	85.7	—
	Sensitivity (%)	57.3	60.0	75.0	—
	Specificity (%)	90.0	81.8	82.5	—
Expert raters consensus	Accuracy (%)	—	—	70.0	<0.001
	Sensitivity (%)	—	—	14.3	<0.0001
	Specificity (%)	—	—	80.0	<0.01

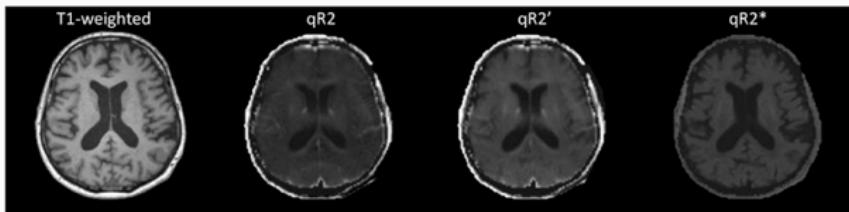
*P value for the comparisons between the expert raters consensus and the deep learning model.

Storelli et al., 2022

Storelli, L., Azzimonti, M., Gueye, M., Vizzino, C., Preziosa, P., Tedeschi, G., ... & Rocca, M. A. (2022). A deep learning approach to predicting disease progression in multiple sclerosis using magnetic resonance imaging. *Investigative Radiology*, 57(7), 423-432



Other structural MRI modalities



Talai, A. S., Sedlacik, J., Boelmans, K., & Forkert, N. D. (2021). Utility of multi-modal MRI for differentiating of Parkinson's disease and progressive supranuclear palsy using machine learning. *Frontiers in Neurology*, 12, 648548



Other structural MRI modalities



T2-weighted Image Features (based on quantitative R2, R2*, and R2* Features)

Class	TP Rate	FP Rate	Precision	Recall	F-Measure	MCC	ROC Area	Confusion Matrix			Accuracy
								HC	PD	PSP-RS	
HC	0.763	0.108	0.806	0.763	0.784	0.663	0.875	29	7	2	75.7%
PD	0.756	0.207	0.739	0.756	0.747	0.547	0.845	7	34	4	
PSP-RS	0.750	0.072	0.714	0.750	0.732	0.665	0.948	0	5	15	

TP, True Positive; FP, False Positive; MCC, Matthews Correlation Coefficient; ROC AUC, Area under the receiver operating characteristic curve; HC, Healthy Controls; PD, Parkinson's disease; PSP-RS, Progressive supranuclear palsy Richardson's syndrome.



Talai, A. S., Sedlacik, J., Boelmans, K., & Forkert, N. D. (2021). Utility of multi-modal MRI for differentiating of Parkinson's disease and progressive supranuclear palsy using machine learning. *Frontiers in Neurology*, 12, 648548



Other structural MRI modalities

- Non-T1 weighted structural MRI
 - High accuracies for classifying MS and PD (>90%).
 - T2-weighted images used by Storelli et al. for predicting MS prognosis.
 - T2-weighted images used by Talai et al. for differential diagnosis of PD and PSP-RS.



Diffusion MRI



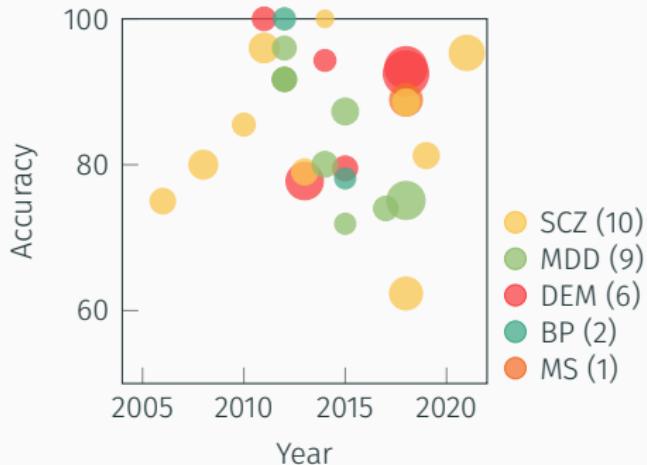
Explanation of DTI



Diffusion MRI



Explanation of DTI



Diffusion MRI

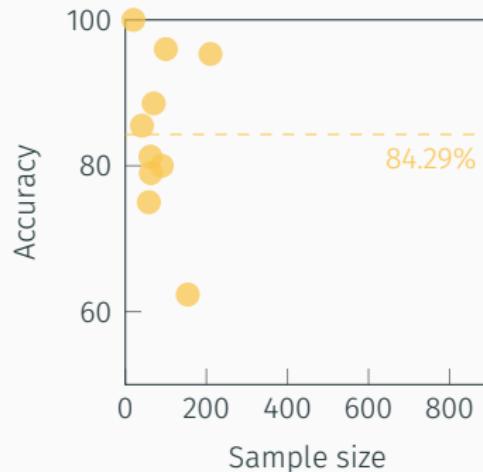


Explanation of DTI

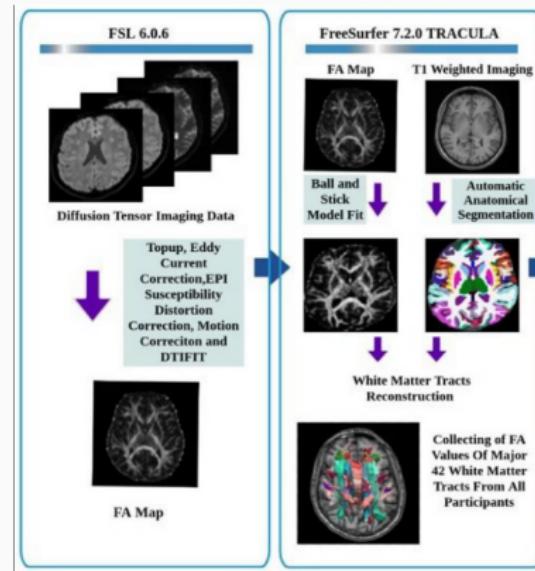
Lack of prediction studies



Diffusion MRI



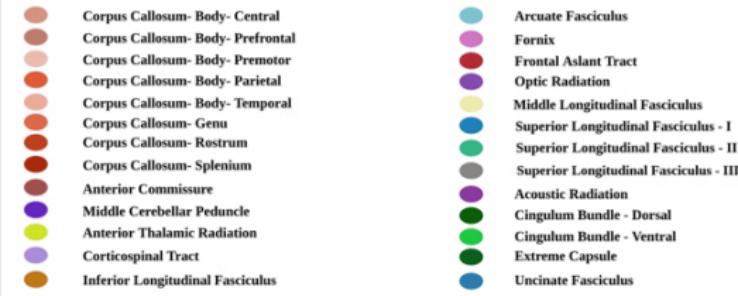
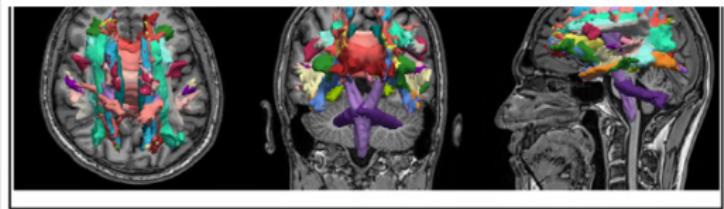
Diffusion MRI



Saglam, Y., Oz, A., Yildiz, G., Ermis, C., Kargin, O. A., Arslan, S., & Karacetin, G. (2023). Can diffusion tensor imaging have a diagnostic utility to differentiate early-onset forms of bipolar disorder and schizophrenia: A neuroimaging study with explainable machine learning algorithms. *Psychiatry Research: Neuroimaging*, 335, 111696.



Diffusion MRI



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Diffusion MRI

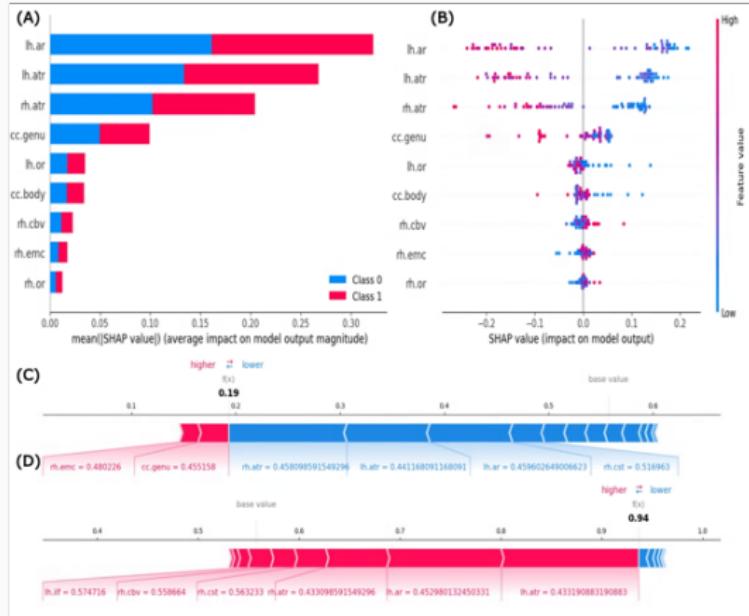


Classifier	AUC	Accuracy	Sensitivity	Specificity	Precision	F1 score	MCC
SVM-linear	0.85	0.80	0.75	0.86	0.79	0.77	0.74
Random forest	0.82	0.79	0.72	0.81	0.76	0.74	0.70
SVM-Gaussian	0.83	0.78	0.71	0.80	0.75	0.73	0.70
LR	0.78	0.76	0.70	0.79	0.73	0.71	0.68
Naive Bayes	0.75	0.72	0.65	0.74	0.68	0.66	0.62

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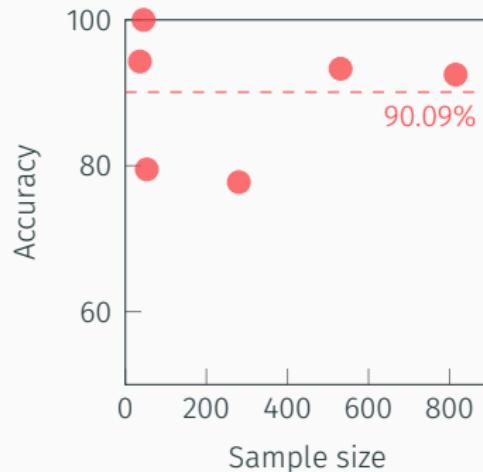
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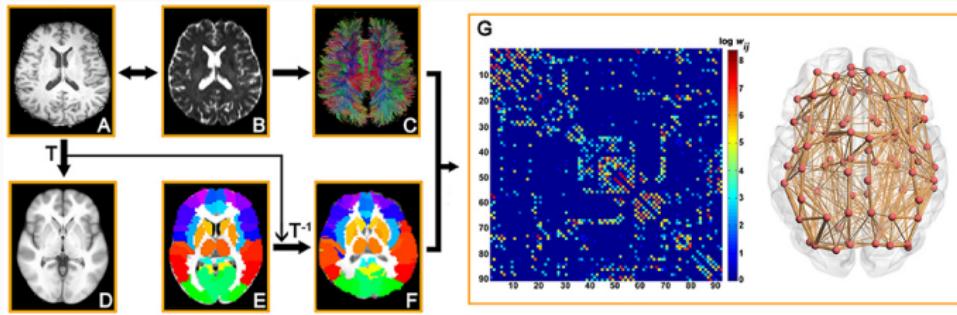
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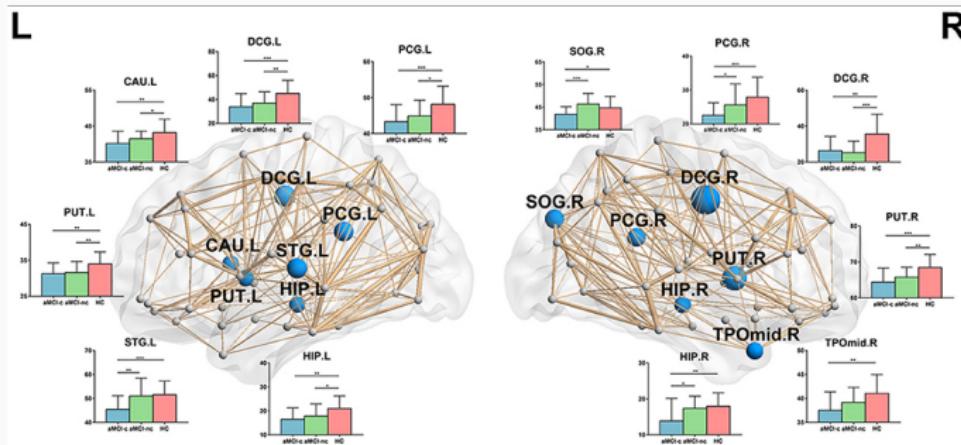
Diffusion MRI



Sun, Y., Bi, Q., Wang, X., Hu, X., Li, H., Li, X., ... & Han, Y. (2019). Prediction of conversion from amnestic mild cognitive impairment to Alzheimer's disease based on the brain structural connectome. *Frontiers in neurology*, 9, 1178



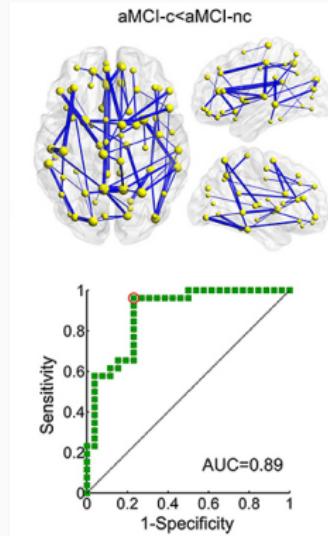
Diffusion MRI



Sun, Y., Bi, Q., Wang, X., Hu, X., Li, H., Li, X., ... & Han, Y. (2019). Prediction of conversion from amnestic mild cognitive impairment to Alzheimer's disease based on the brain structural connectome. *Frontiers in neurology*, 9, 1178



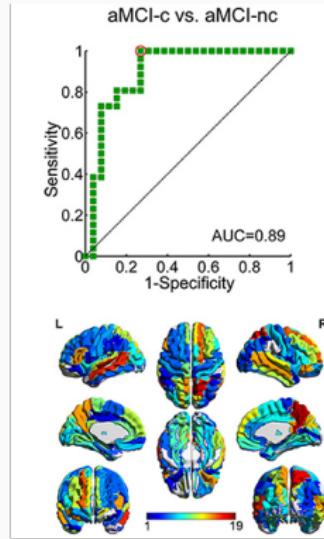
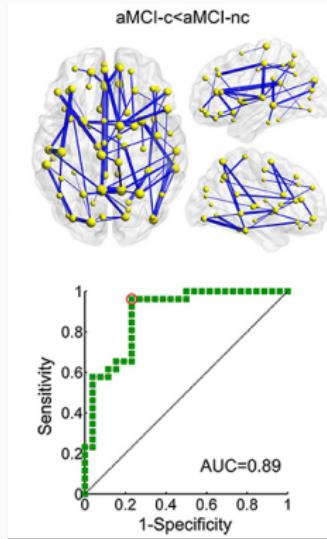
Diffusion MRI



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Diffusion MRI



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Diffusion MRI

- Non-T1 weighted structural MRI
 - High accuracies for classifying MS and PD (>90%).
 - T2-weighted images used by Storelli et al. for predicting MS prognosis.
 - T2-weighted images used by Talai et al. for differential diagnosis of PD and PSP-RS.
- Diffusion MRI
 - Few prediction studies, mostly for mental disorders with various accuracies (60-100%) and DEM (80-100%)
 - Used by Saglam et al. to differentially diagnose SCZ and BP with 80% accuracy.
 - Used by Sun et al. to predict conversion from MCI to AD with 81% accuracy



Functional Magnetic Resonance Imaging (fMRI)



Explanation of fMRI



Functional Magnetic Resonance Imaging (fMRI)



Explanation of fMRI

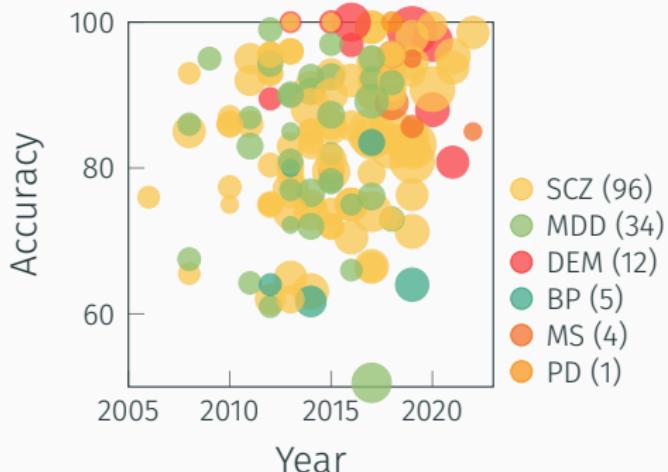
Task vs rest



Functional Magnetic Resonance Imaging (fMRI)



Explanation of fMRI



Functional Magnetic Resonance Imaging (fMRI)



fMRI use-case SCZ/treatment response



Functional Magnetic Resonance Imaging (fMRI)



fMRI use-case 2



Molecular imaging (PET/SPECT)



Explanation of molecular



Molecular imaging (PET/SPECT)



Explanation of molecular



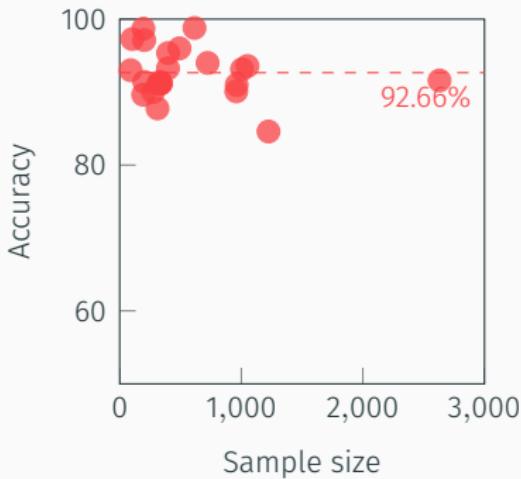
Molecular imaging (PET/SPECT)



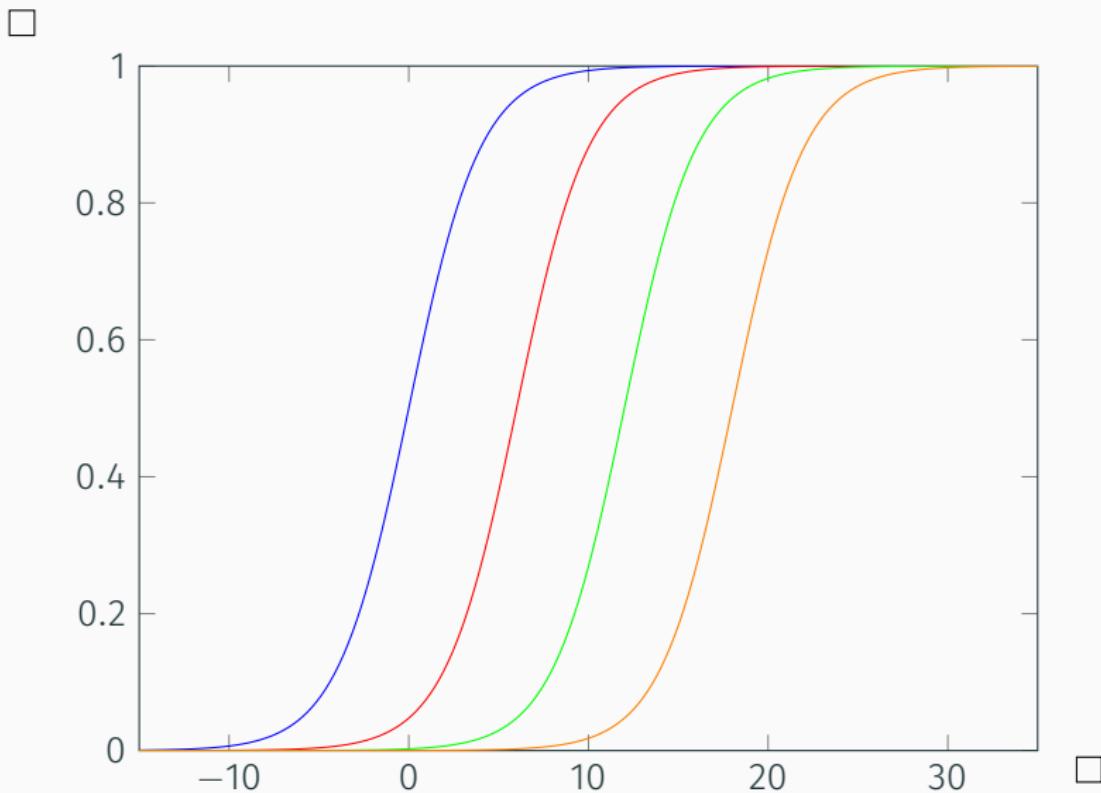
Explanation of PET



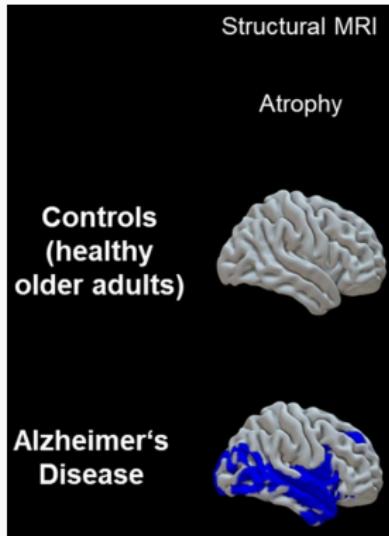
Molecular imaging (PET/SPECT)



Molecular imaging (PET/SPECT)



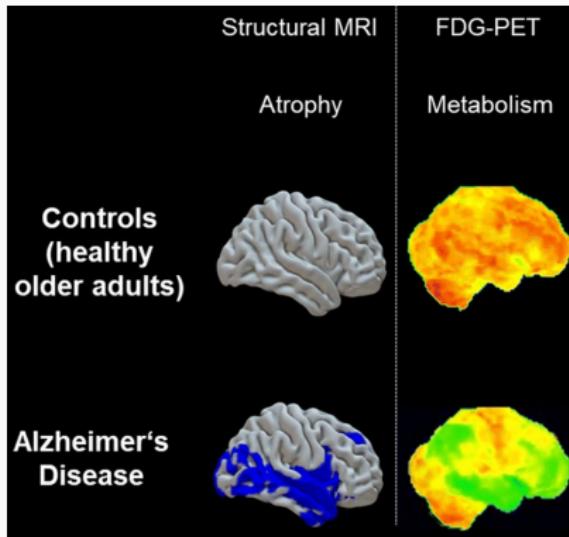
Molecular imaging (PET/SPECT)



Chételat, G., Arbizu, J., Barthel, H., Garibotto, V., Lammertsma, A. A., Law, I., ... & Drzezga, A. (2021). Finding our way through the labyrinth of dementia biomarkers. European journal of nuclear medicine and molecular imaging, 48, 2320-2324



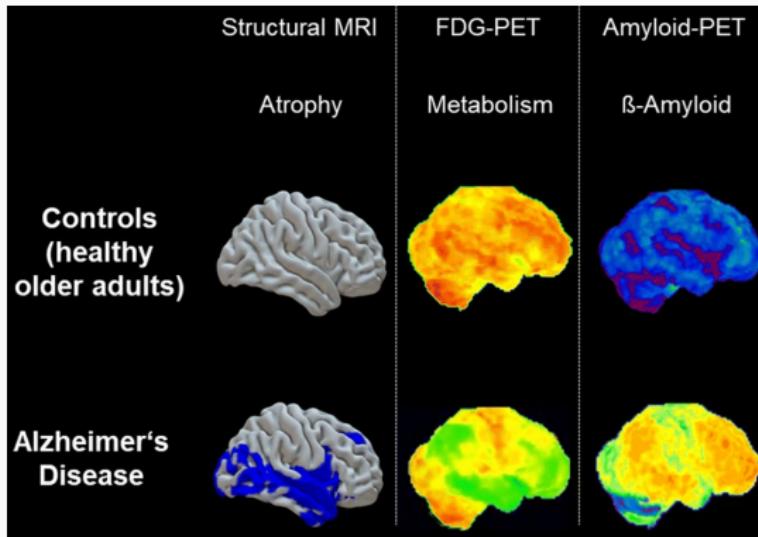
Molecular imaging (PET/SPECT)



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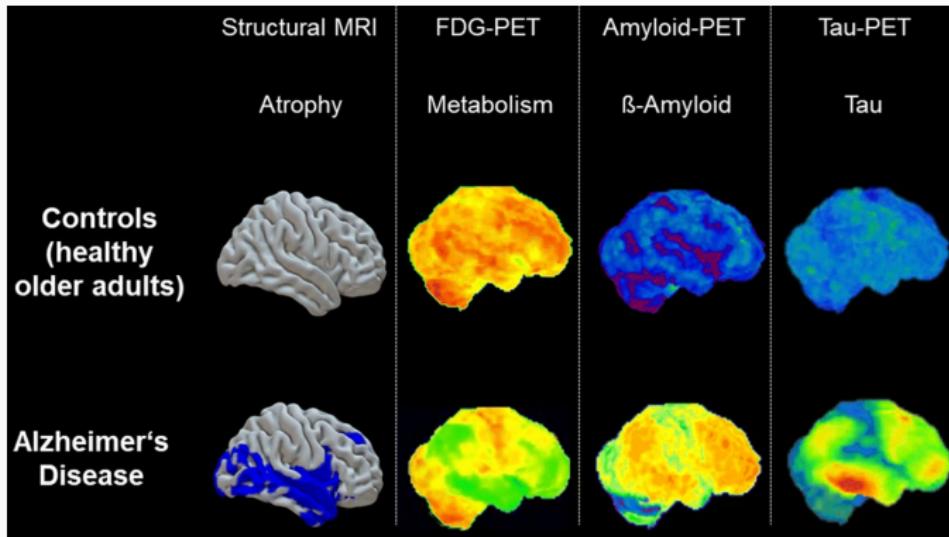
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Molecular imaging (PET/SPECT)



"It is necessary to separate syndrome (clinically identified impairment) from biology (etiology)

AD is defined by its biology with the following implications

The disease is first evident with the appearance of β -amyloid plaques, and later neocortical tau tangles, while people are asymptomatic. Pathophysiologic mechanisms involved with processing and clearance of protein fragments may be involved very early in the disease process, but these are not yet well understood.

In living people the disease is diagnosed by disease specific core biomarkers

Unimpaired individuals with abnormal biomarker testing are at risk for symptoms due to AD.

They are not at risk for a disease they already have.

Symptoms are a result of the disease process and are not necessary to diagnose AD

AD exists on a continuum not as discrete clinically defined entities

Clinical syndromes commonly seen with AD may also be caused by disorders other than AD and therefore clinical presentation alone is not diagnostic of AD

The same AD biology may result in different phenotypic presentations"



Revised Criteria for Diagnosis and Staging of Alzheimer's Disease: Alzheimer's Association Workgroup, <http://alz.org/diagnosticcriteria>



Summary

- Non-T1 weighted structural MRI
 - High accuracies for classifying MS and PD (>90%).
 - T2-weighted images used by Storelli et al. for predicting MS prognosis.
 - XXX used by YYY for ZZZ in PD.
- Diffusion MRI
 - Mostly used in mental disorders with various results (accuracies XX-YY), but also DEM (XX)
 - Used by Saglam et al. to differentially diagnose SCZ and BP with 80% accuracy.
 - XXX used by YYY for ZZZ in DEM.
- Functional MRI
 - Widely used for all disorders, with varying results
 - Task-based fMRI used by YYY for ZZZ in SCZ.
 - Resting state fMRI used by Segal et al. to make diagnostic predictions at various biological levels.
- Molecular imaging
 - Mostly used in DEM and PD with high accuracies (92%).
 - PET used clinically to diagnose Alzheimer's disease.
 - SPECT used clinically to XXX Parkinson's disease.

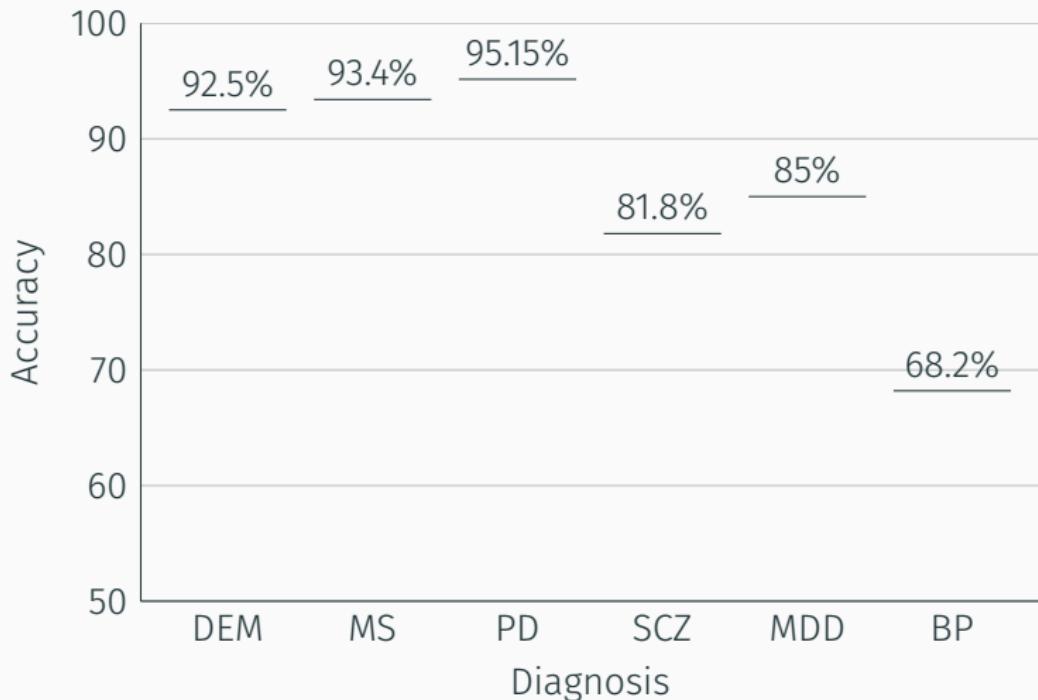


The future of neuroimaging-based prediction

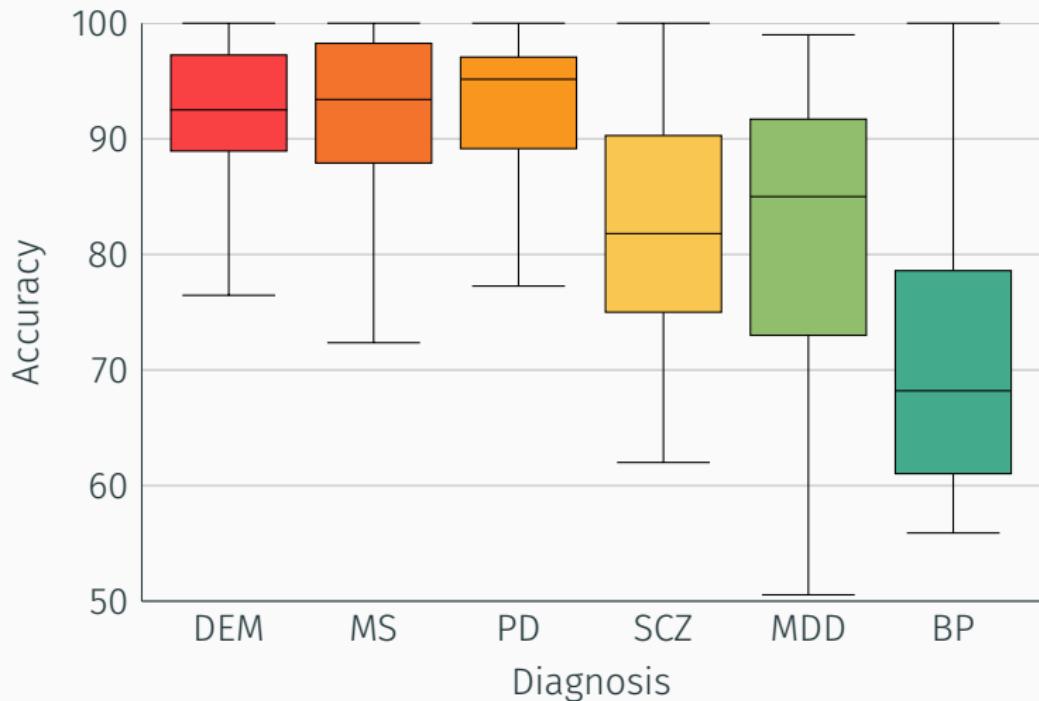


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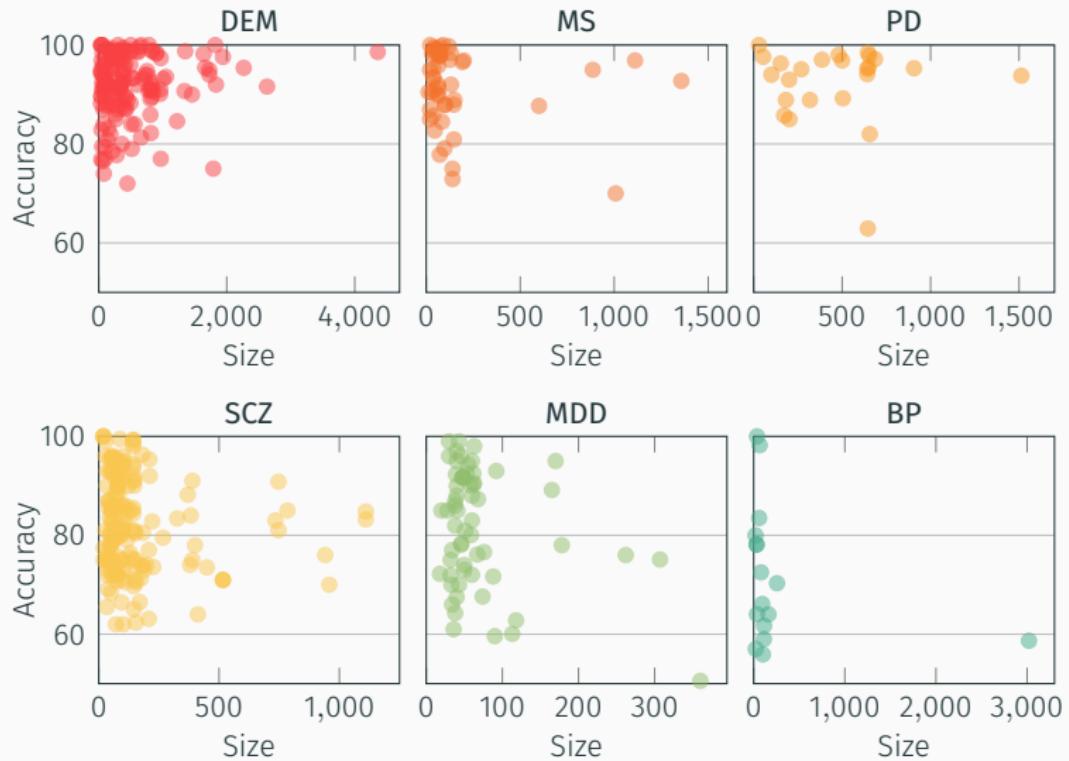
Challenges: Predictiveness



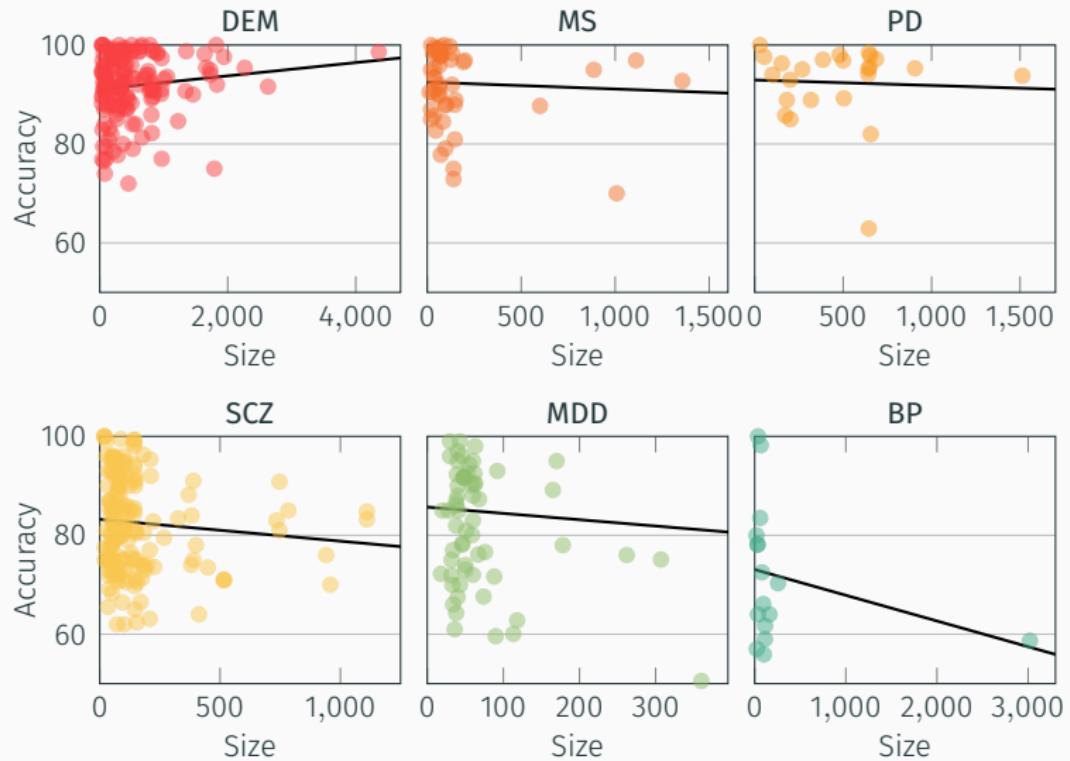
Challenges: Predictiveness



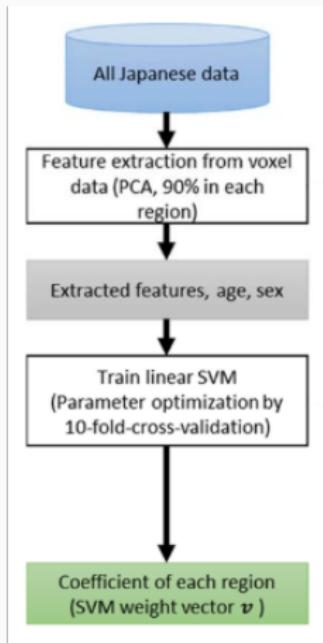
Challenges: Predictiveness



Challenges: Predictiveness



Challenges: Predictiveness

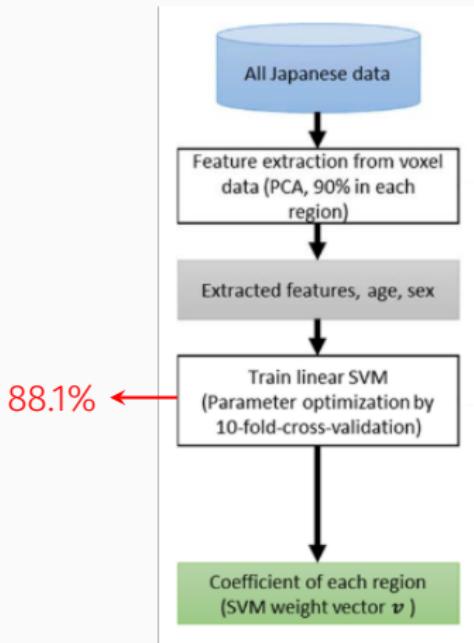


Matsuo et al., 2019

Matsuo, K., Harada, K., Fujita, Y., Okamoto, Y., Ota, M., Narita, H., ... & Watanabe, Y. (2019). Distinctive neuroanatomical substrates for depression in bipolar disorder versus major depressive disorder. *Cerebral Cortex*, 29(1), 202-214



Challenges: Predictiveness

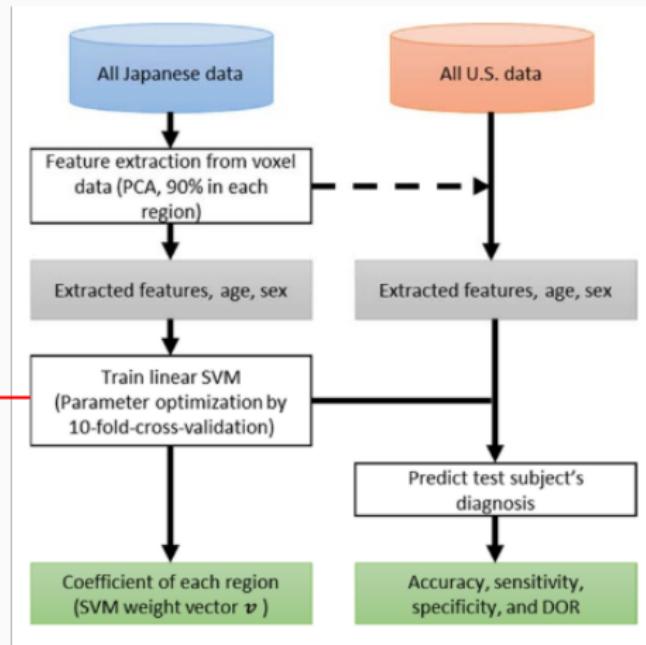


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Challenges: Predictiveness

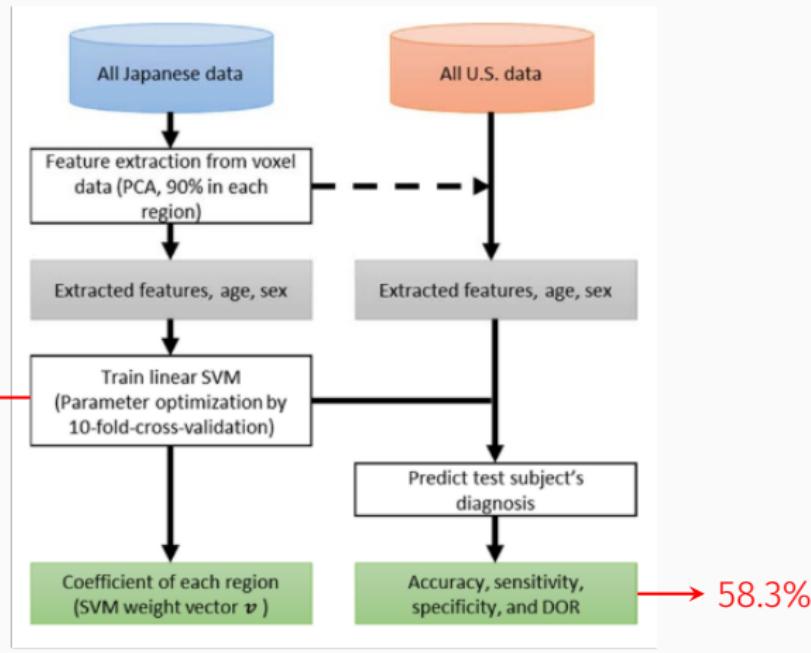


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Challenges: Predictiveness

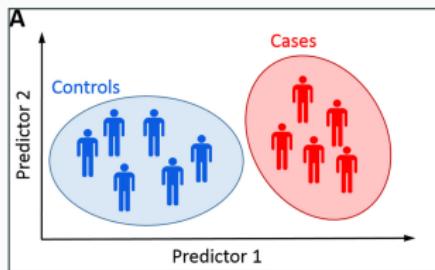


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Challenges: Predictive targets

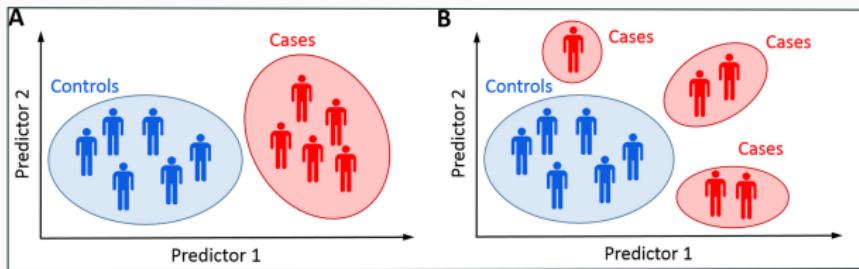


Marquand et al., 2016

Marquand, A. F., Rezek, I., Buitelaar, J., & Beckmann, C. F. (2016). Understanding heterogeneity in clinical cohorts using normative models: beyond case-control studies. *Biological psychiatry*, 80(7), 552-561



Challenges: Predictive targets

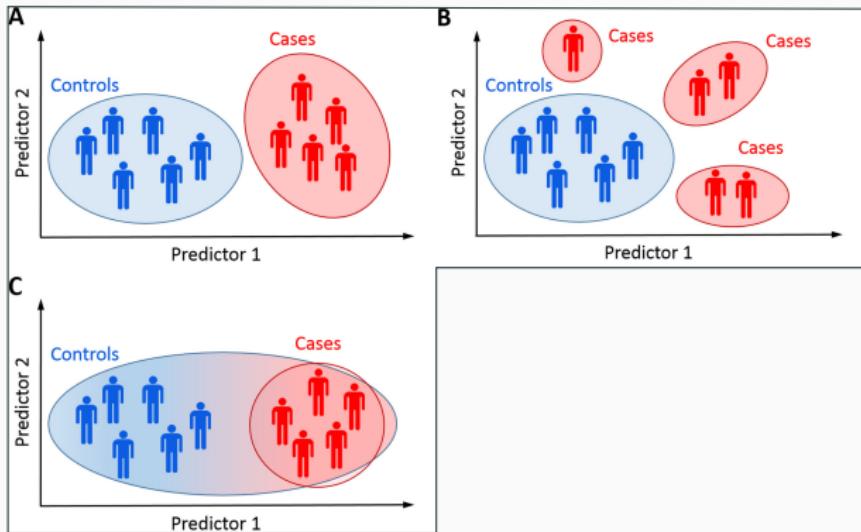


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Challenges: Predictive targets

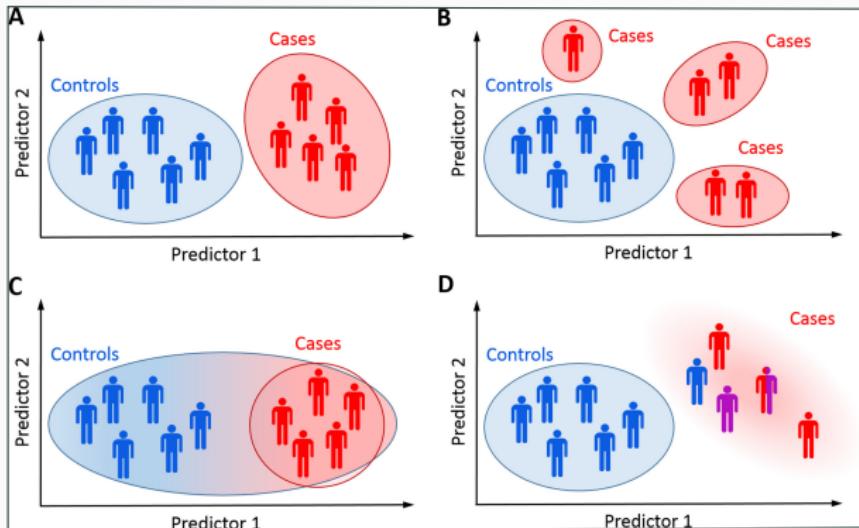


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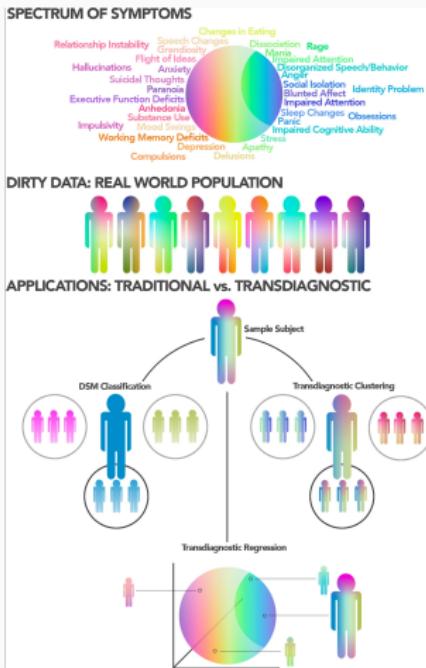


Challenges: Predictive targets

Diagnostic labels vs prognosis, treatment, differential

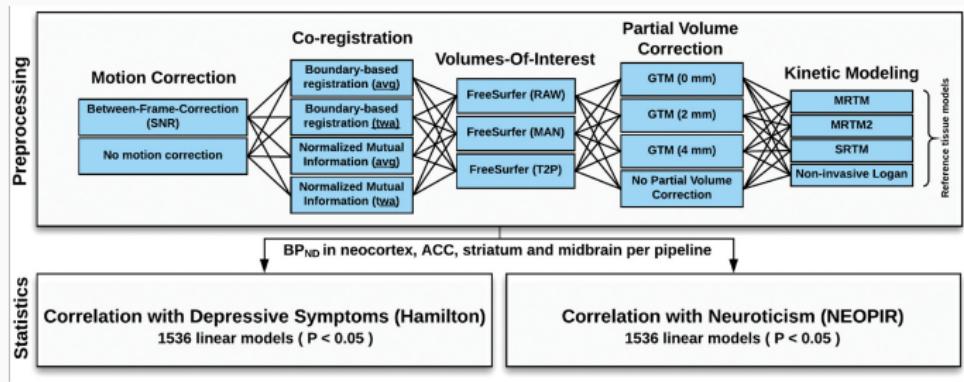


Challenges: Predictive targets



Vogel & Black (2024)

Challenges: Preprocessing and degrees of freedom

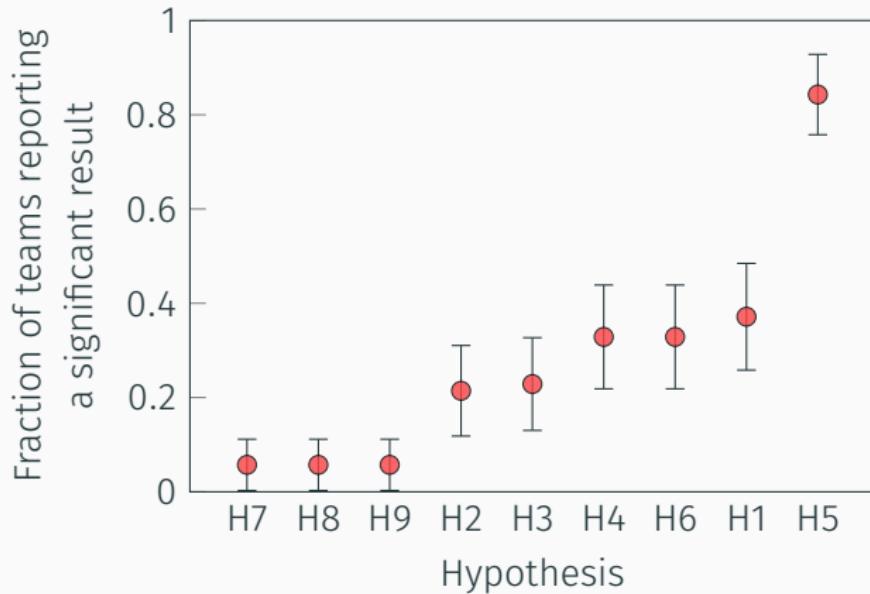


Nørgaard et al., 2020

Nørgaard, M., Ganz, M., Svarer, C., Frokjaer, V. G., Greve, D. N., Strother, S. C., & Knudsen, G. M. (2020). Different preprocessing strategies lead to different conclusions: a [11C] DASB-PET reproducibility study. *Journal of Cerebral Blood Flow & Metabolism*, 40(9), 1902-1911.



Challenges: Preprocessing and degrees of freedom

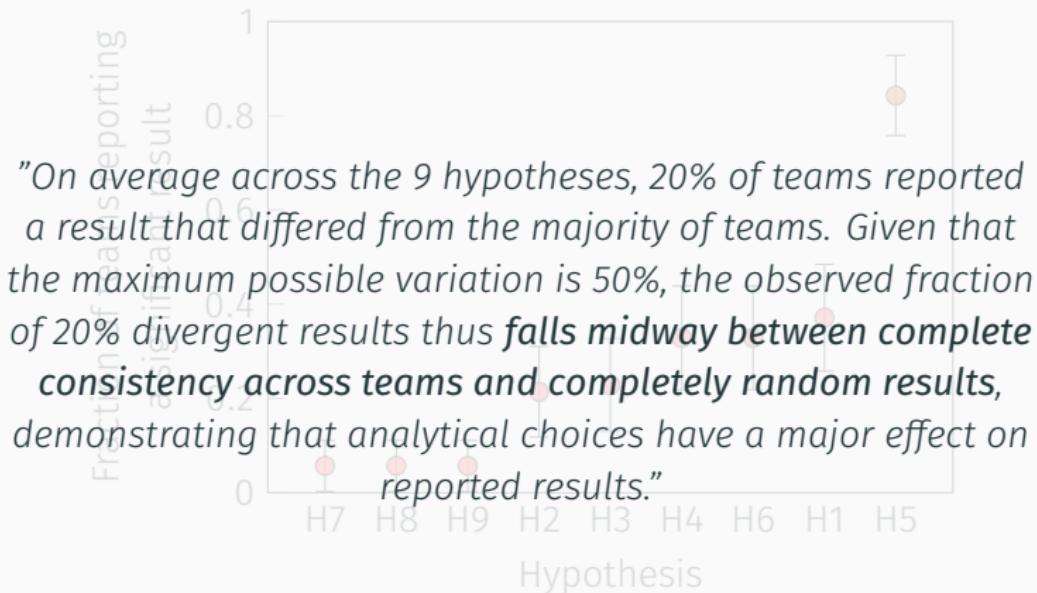


Adapted from Botvinik-Nezer et al., 2020

Botvinik-Nezer, R., Holzmeister, F., Camerer, C. F., Dreber, A., Huber, J., Johannesson, M., ... & Rieck, J. R. (2020). Variability in the analysis of a single neuroimaging dataset by many teams. *Nature*, 582(7810), 84-88



Challenges: Preprocessing and degrees of freedom

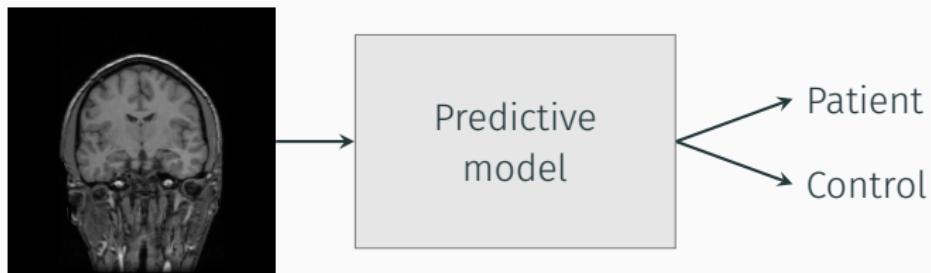


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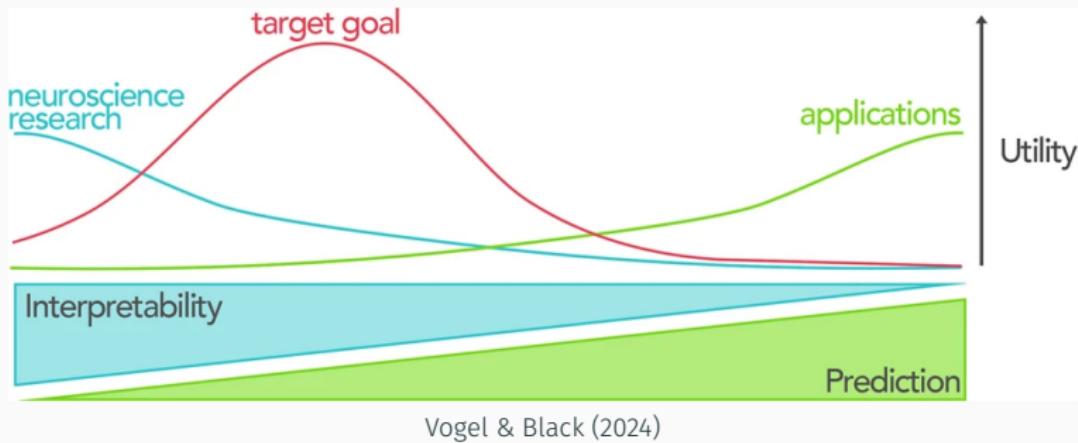
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Challenges: Interpretability



Challenges: Interpretability



Vogel, A. C., & Black, K. J. (2024). Brain Imaging in Routine Psychiatric Practice. Missouri Medicine, 121(1), 37

The role of neuroimaging beyond T1-weighted MRI in the diagnosis and prediction of neuropsychiatric disorders

Challenges: Interpretability

Predictive
model

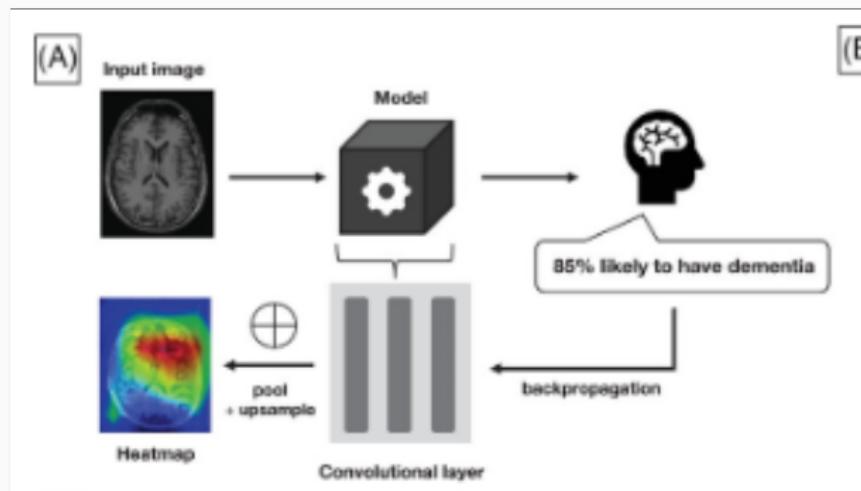


Challenges: Interpretability

a+b+c+d



Challenges: Interpretability



Opportunities: New modalities

DEBBIE

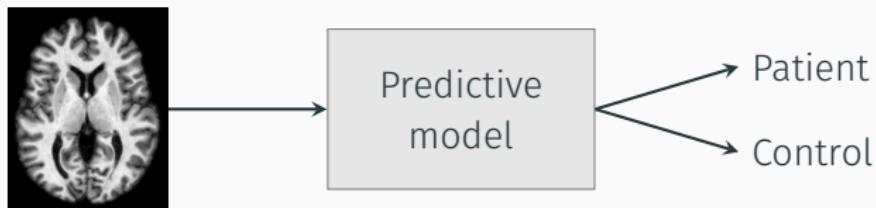


Opportunities: New modalities

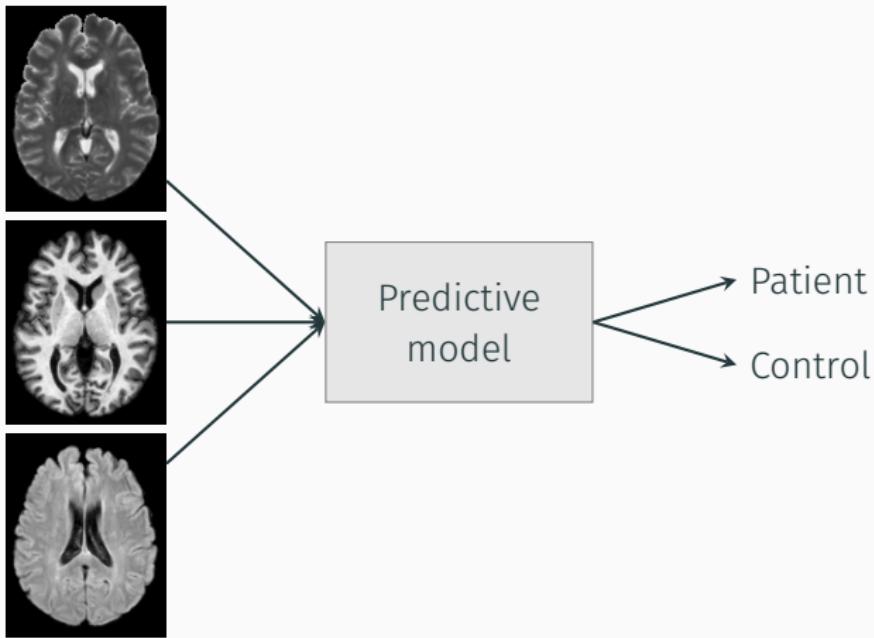
QSM



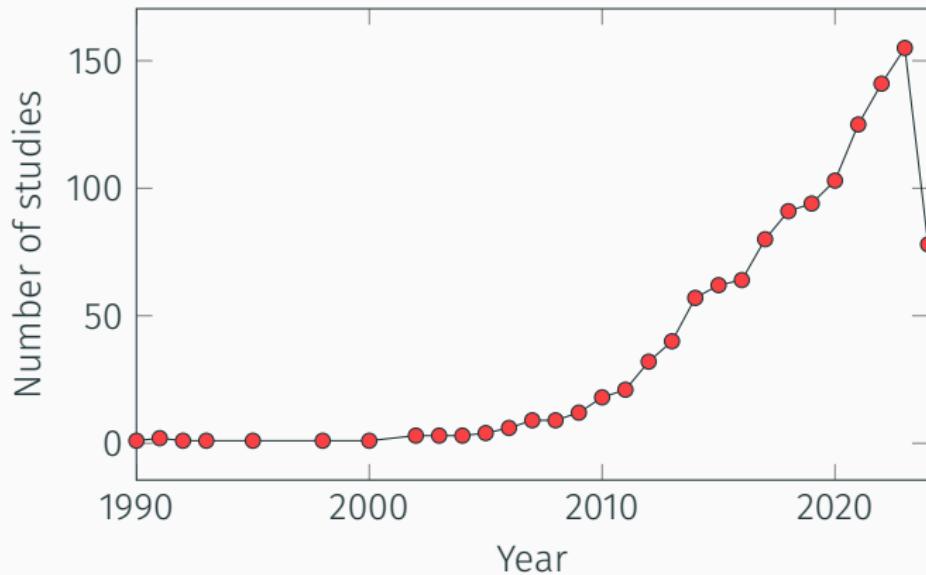
Opportunities: Multimodality



Opportunities: Multimodality



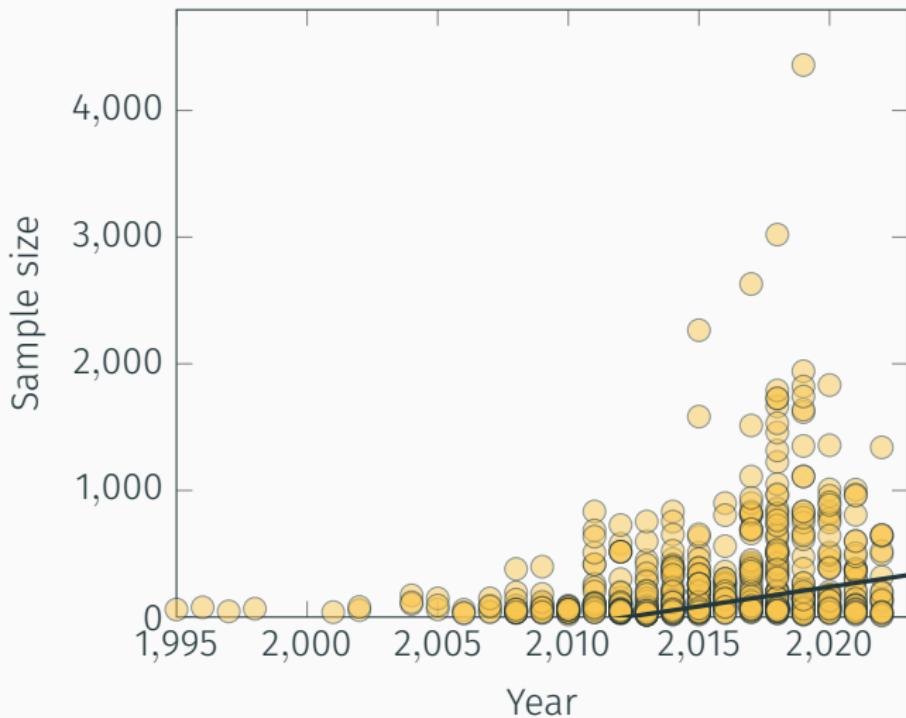
Opportunities: Multimodality



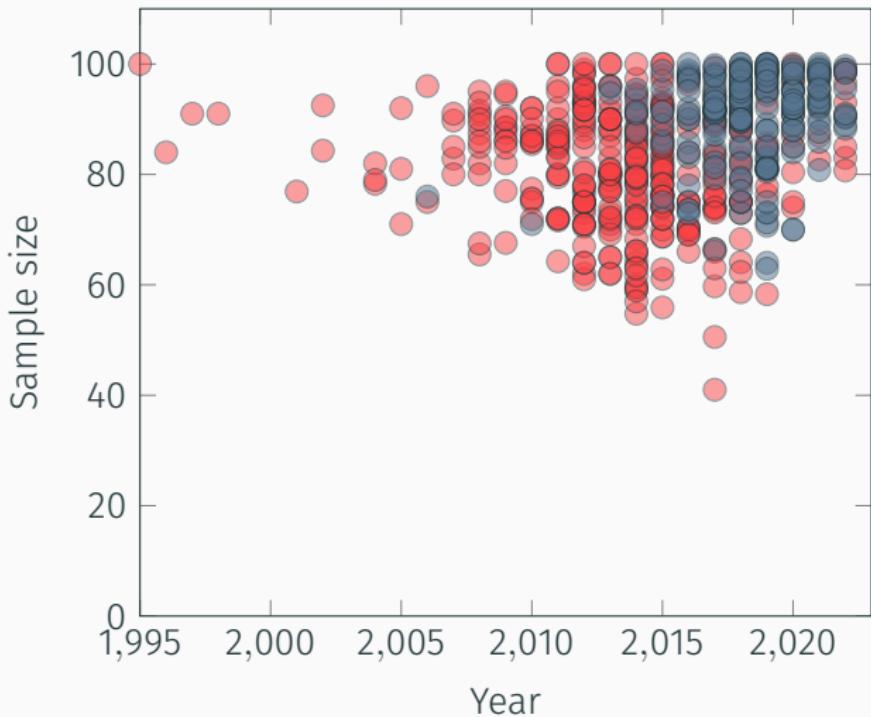
Pubmed search: multimodal[Title] AND (neuroimaging[Title] or MRI[Title])



Opportunities: Larger datasets



Opportunities: Better methods



Opportunities: Better methods

