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

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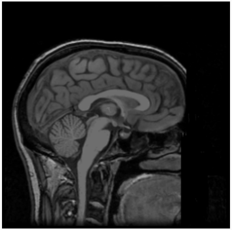

Bert from FreeSurfer 7.3

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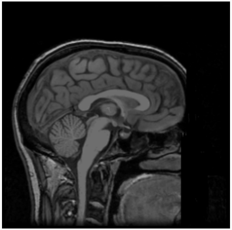

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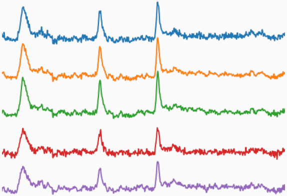

Sample from the MNE library

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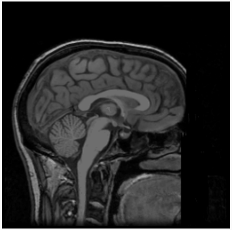

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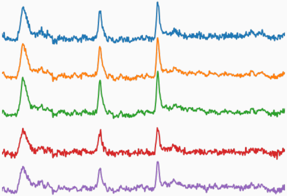

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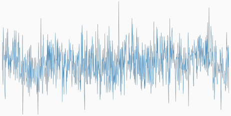

Sample from Tremlay et al., 2016

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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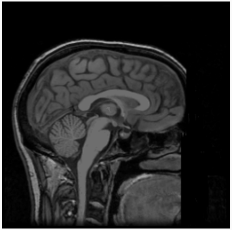

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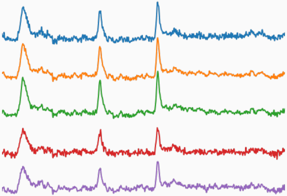

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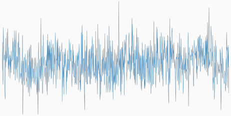

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Meta Quest Pro

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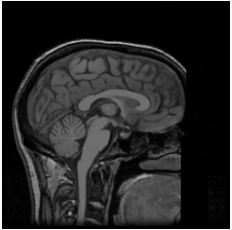

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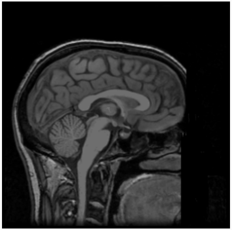

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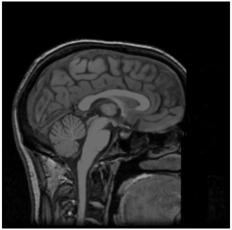

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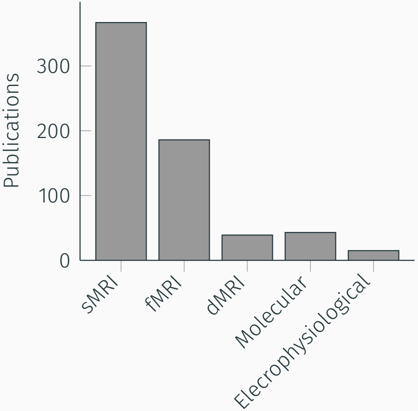

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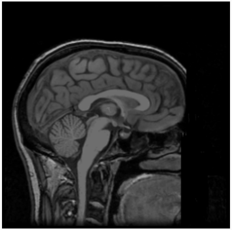

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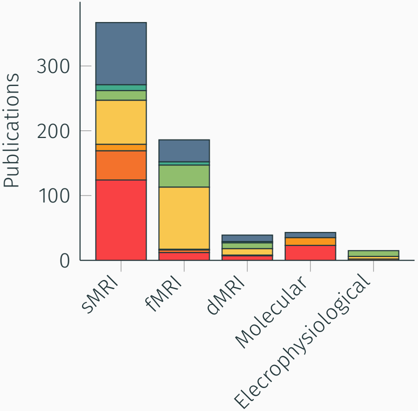

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Alzheimer's disease and other causes of dementia

Multiple Sclerosis

Parkinson's Disease

Background

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Alzheimer's disease and other causes of dementia

Multiple Sclerosis

Parkinson's Disease

Bipolar Disorder

Schizophrenia

Depressive disorders

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Alzheimer's disease and other causes of dementia

Multiple Sclerosis

Parkinson's Disease

Bipolar Disorder

Schizophrenia

Depressive disorders

More ⟷ Less

Knowledge about neuropathological basis

Background

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

Alzheimer's disease and other causes of dementia

Multiple Sclerosis

Parkinson's Disease

Bipolar Disorder

Schizophrenia

Depressive disorders

Less ⟷ More

Importance of psychopathology

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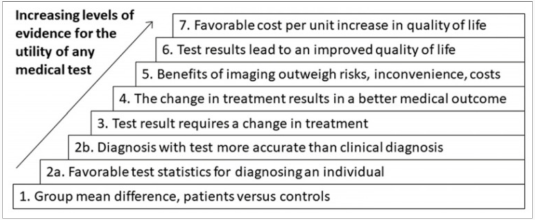

Vogel & Black (2024)

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

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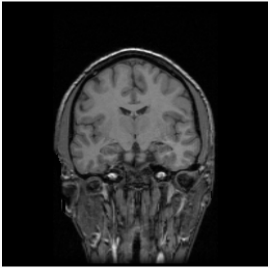

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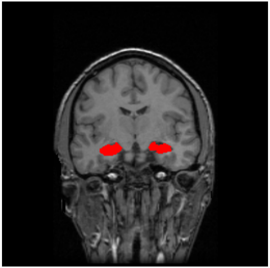

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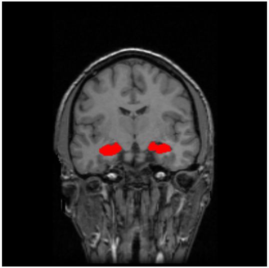

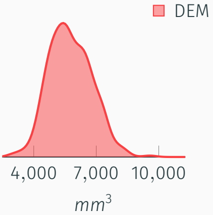

Data from ADNI

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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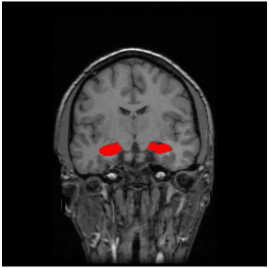

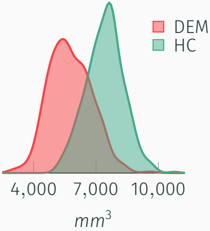

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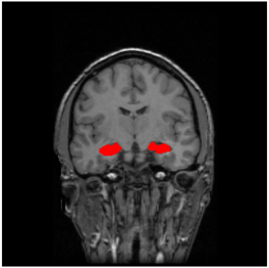

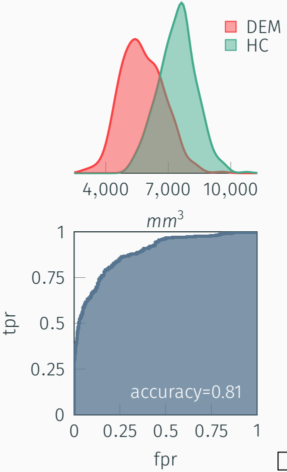

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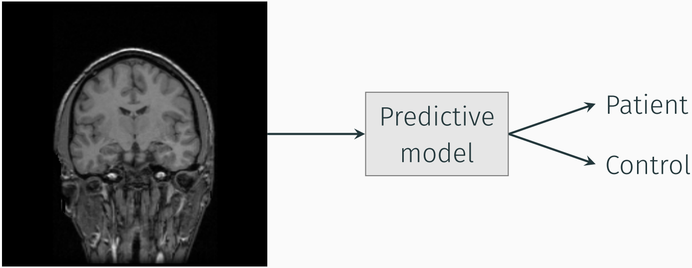

Neuroimaging modalities for diagnostic predictions

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

	Dementia	Multiple sclerosis	Parkinson's disease	Schizophrenia	Major depressive disorder	Bipolar disorder
Non-T1 structural MRI						
Diffusion MRI						
Functional MRI						
Molecular imaging						

Data

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

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Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun

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

Mirjam Quaak[1], Laurens van de Mortel[1], Rajat Mani Thomas[1], Guido van Wingen[2]

Data

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

Mr Amir Ebrahimighahnavieh [1], Suhuai Luo [1], Raymond Chiong [2]

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

Golrokh Mirzaei [a], Hojjat Adeli [b]

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

Sina Fathi [1], Maryam Ahmadi [2], Afsaneh Dehnad [3]

Data

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

Afshin Shoeibi [1], Marjane Khodatars [2], Mahboobeh Jafari [3], Parisa Moridian [4], Mitra Rezaei [5], Roohallah Alizadehsani [6], Fahime Khozeimeh [6], Juan Manuel Gorriz [7], Jónathan Heras [8], Maryam Panahiazar [9], Saeid Nahavandi [6], U Rajendra Acharya [10]

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

by Nida Aslam [1,*], Irfan Ullah Khan [1], Asma Bashamakh [1], Fatima A. Alghool [1], Menna Aboulnour [1], Noorah M. Alsuwayan [1], Rawa'a K. Alturaif [1], Samiha Brahimi [2], Sumayh S. Aljameel [1] and Kholoud Al Ghamdi [3]

Data

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

Nikita Aggarwal[1] · B. S. Saini[1] · Savita Gupta[2]

Data

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

Renato de Filippis,[#1] Elvira Anna Carbone,[#1] Raffaele Gaetano,[1] Antonella Bruni,[1] Valentina Pugliese,[1] Cristina Segura-Garcia,[2] and Pasquale De Fazio[1]

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

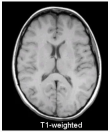
Shradha Verma[1] · Tripti Goel[1] · M. Tanveer[2] · Weiping Ding[3] · Rahul Sharma[1] · R. Murugan[1]

Data

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

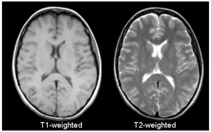
Laurie-Anne Claude, Josselin Houenou, Edouard Duchesnay, Pauline Favre

Other structural MRI modalities



Preson D. C., (2006), MRI Basics, https://case.edu/med/neurology/NR/MRI%20Basics

Other structural MRI modalities



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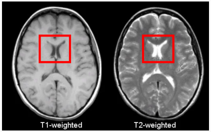

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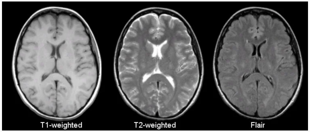

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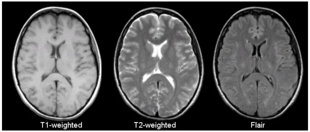

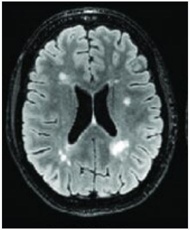

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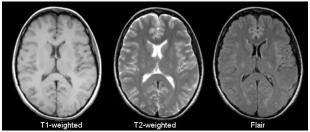

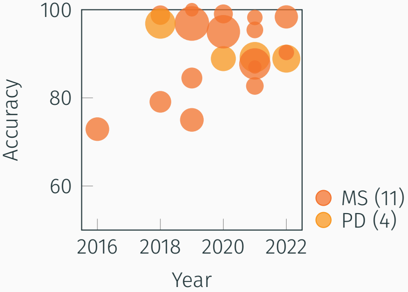

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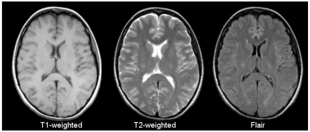
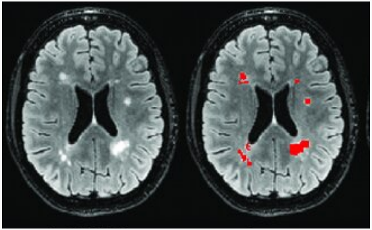
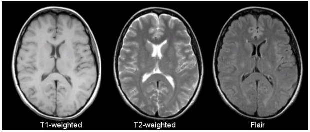
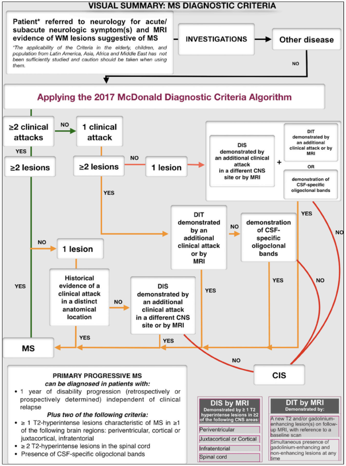




Weeda, M. M., Brouwer, I., de Vos, M. L., de Vries, M. S., Barkhof, F., Pouwels, P. J. W., & Vrenken, H. (2019). Comparing lesion segmentation methods in multiple sclerosis: Input from one manually delineated subject is sufficient for accurate lesion segmentation. NeuroImage: Clinical, 24, 102074

Other structural MRI modalities





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

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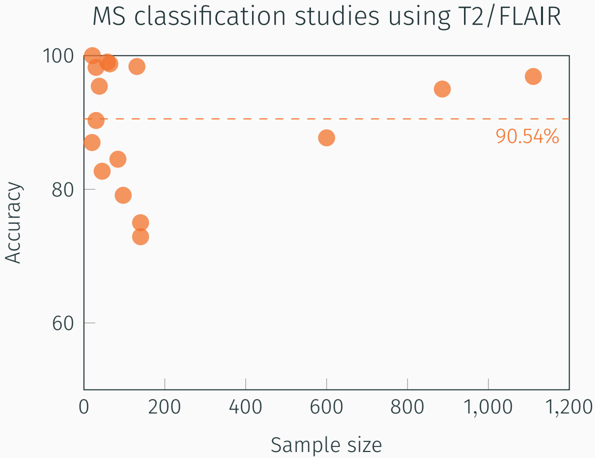


Other structural MRI modalities

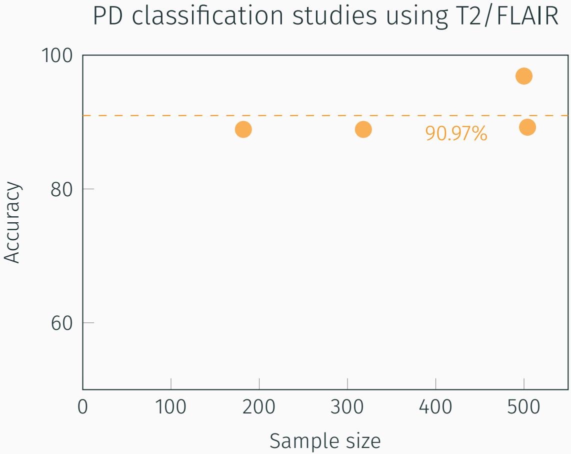
TABLE 3 - Accuracy, Sensitivity, and Specificity in the Prognosis of Disease Evolution for the Expert Raters and for the Proposed CNN Model on the Independent Test Set

		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	67.7	85.7	—
	Sensitivity (%)	57.1	60.0	75.0	—
	Specificity (%)	90.0	81.8	87.5	—
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, 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



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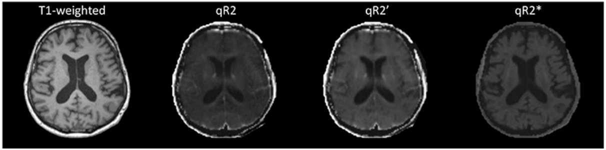

Talai, A. S., Sedlacik, J., Boelmans, K., & Forkert, N. D. (2021). Utility of multi-modal MRI for differentiating of Parkinson's disease and progressive supranuclear palsy using machine learning. Frontiers in Neurology, 12, 648548

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.

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Other structural MRI modalities

Non-T1 weighted structural MRI

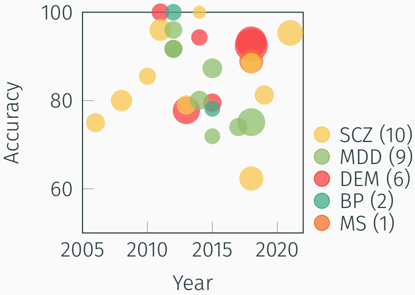
- High accuracies for classifying MS and PD (>90%).
- T2-weighted images used by Storelli et al. for predicting MS prognosis.
- T2-weighted images used by Talai et al. for differential diagnosis of PD and PSP-RS.

Diffusion MRI

Explanation of DTI

Diffusion MRI

Explanation of DTI

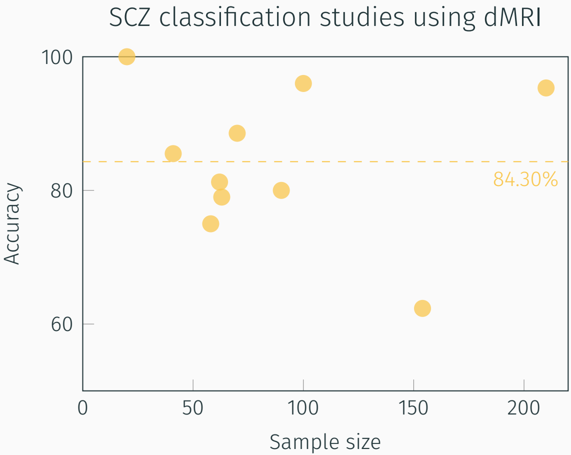


Diffusion MRI

Explanation of DTI

Lack of prediction studies

Diffusion MRI



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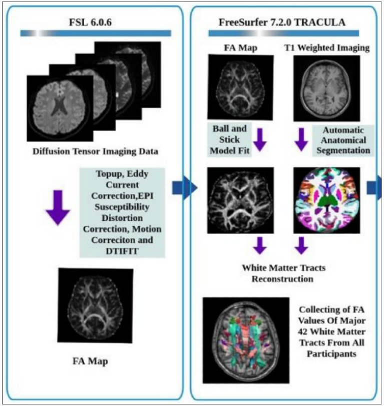

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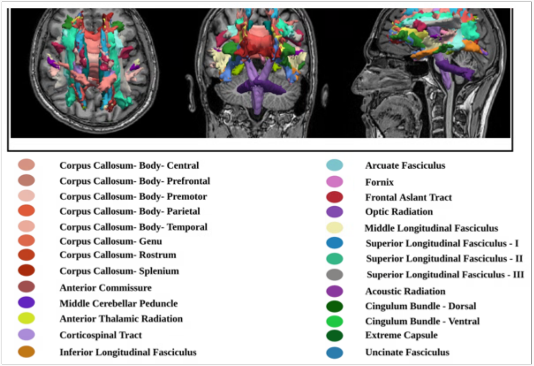

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Diffusion MRI

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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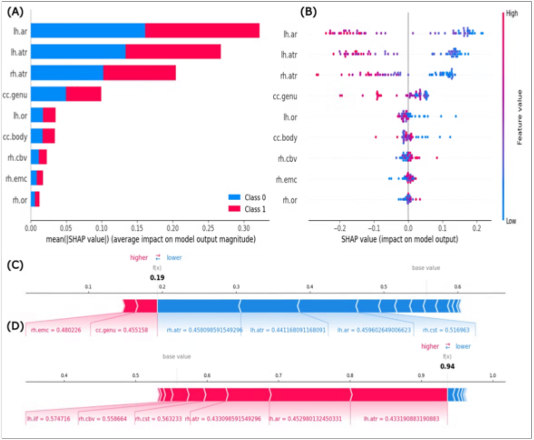

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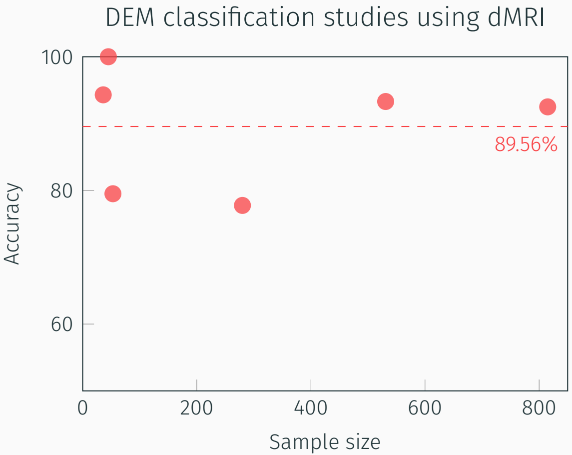

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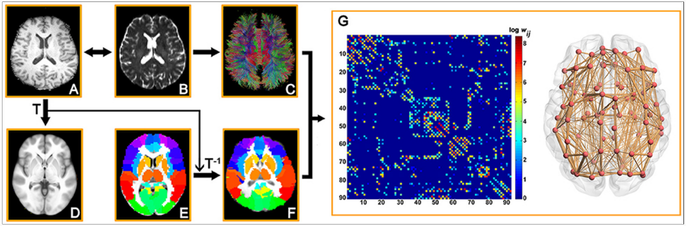

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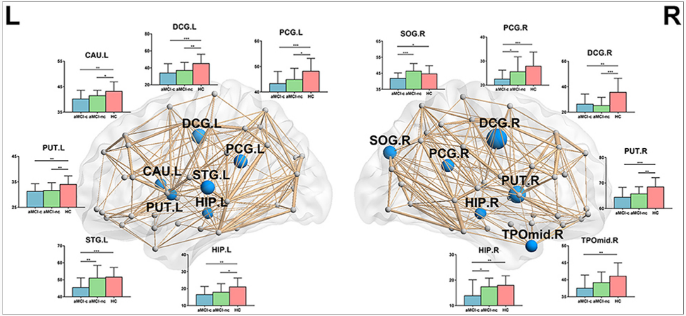

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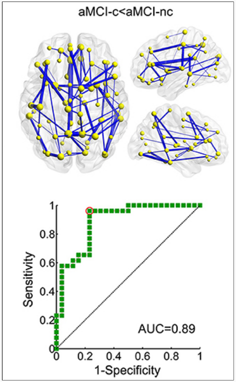

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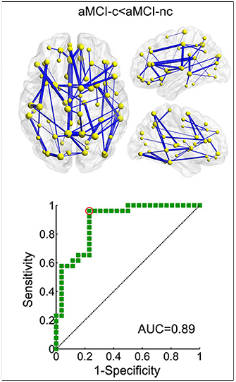

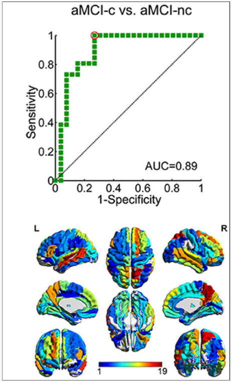

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Functional Magnetic Resonance Imaging (fMRI)

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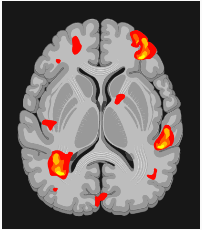

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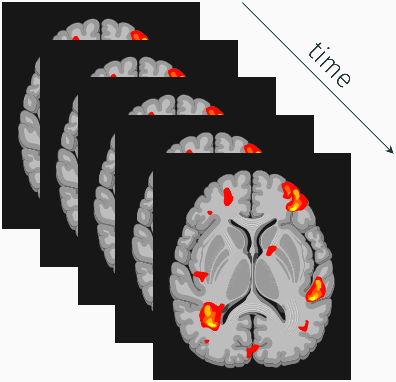

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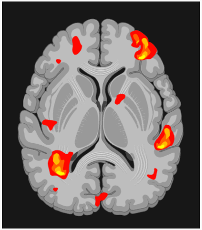

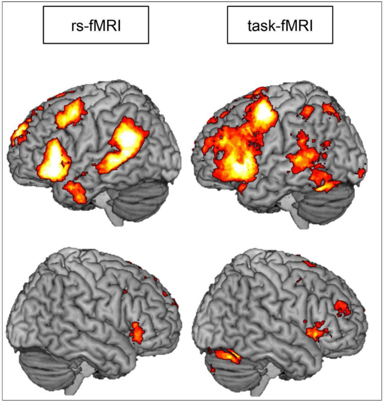

Branco, P., Seixas, D., Deprez, S., Kovacs, S., Peeters, R., Castro, S. L., & Sunaert, S. (2016). Resting-state functional magnetic resonance imaging for language preoperative planning. Frontiers in human neuroscience, 10, 11

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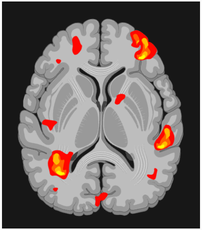

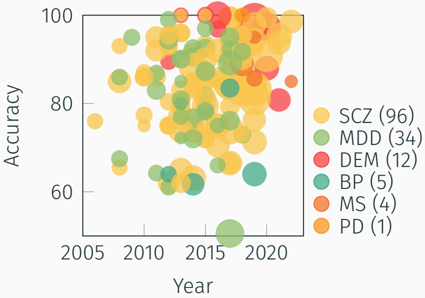

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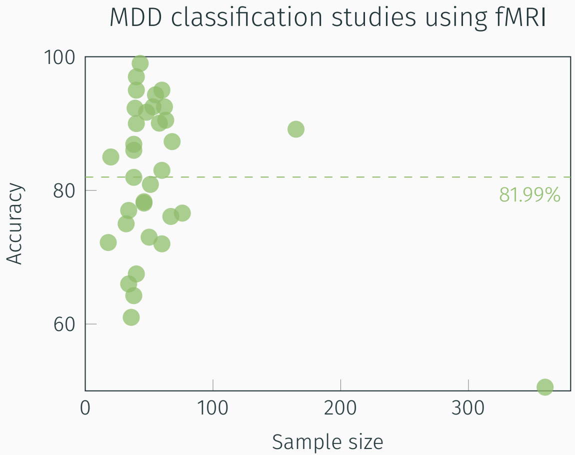

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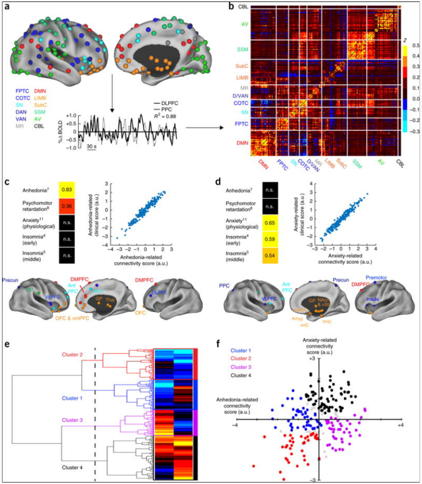

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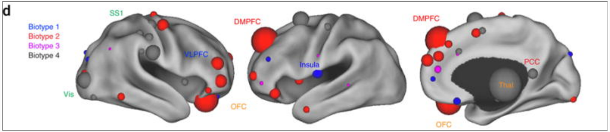

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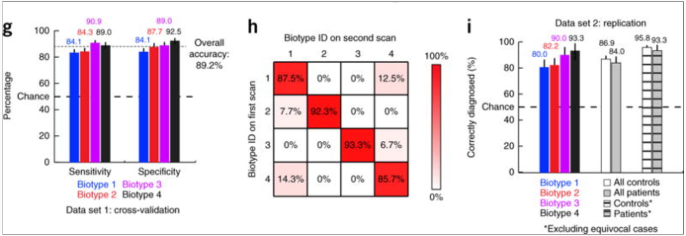

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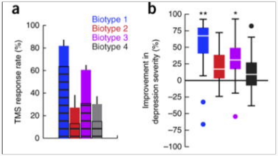

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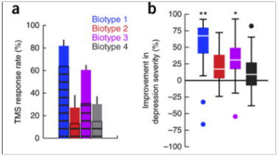

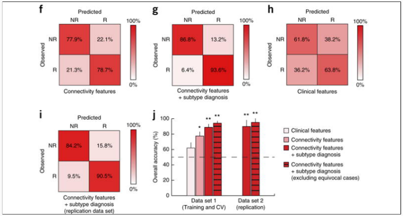

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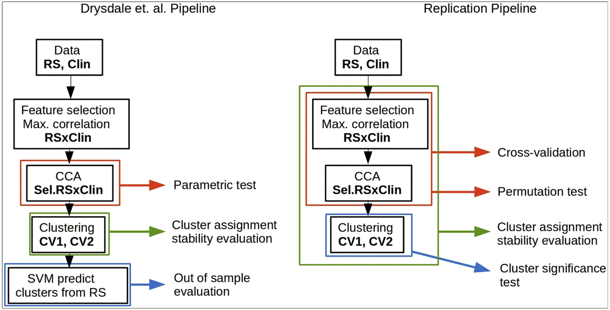

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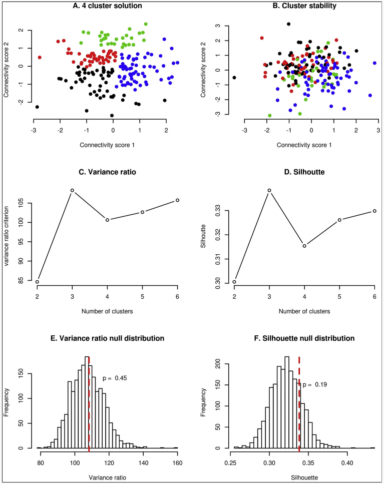

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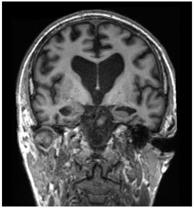
  - Used by Sun et al. to predict conversion from MCI to AD with 81% accuracy.
- Functional MRI
  - Widely used for all conditions, most prominently SCZ and MDD with varying accuracies (60-100%) and DEM (80-100%).
  - Used by Drysdale et al. to detect biotypes of MDD that reacted differently to treatment by transcranial magnetic stimulation.
  - However, Dinga et al. failed to replicate their results WHY.

Molecular imaging (PET/SPECT)



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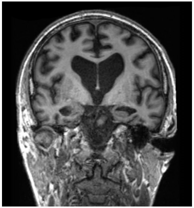

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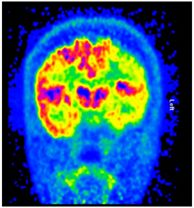

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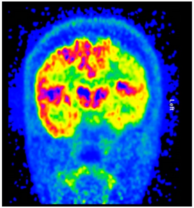
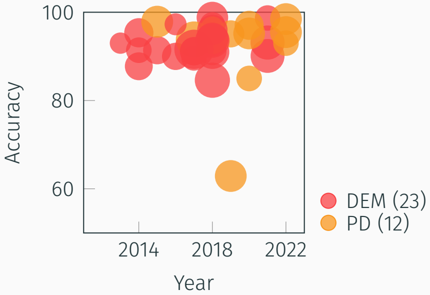
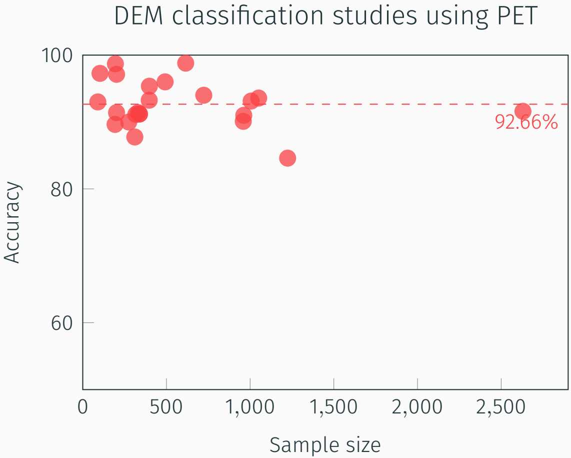




Molecular imaging (PET/SPECT)

Explanation of PET

Molecular imaging (PET/SPECT)



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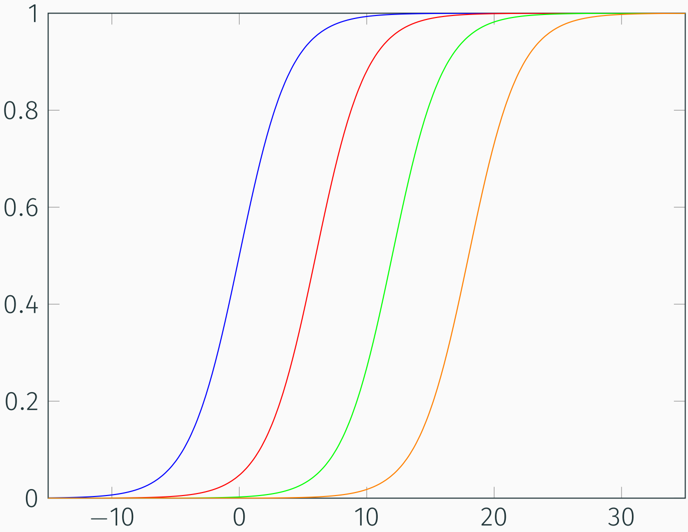

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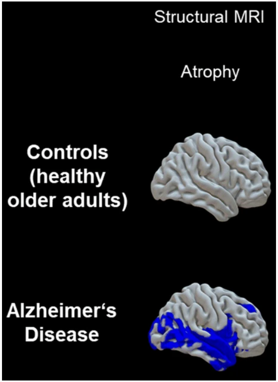

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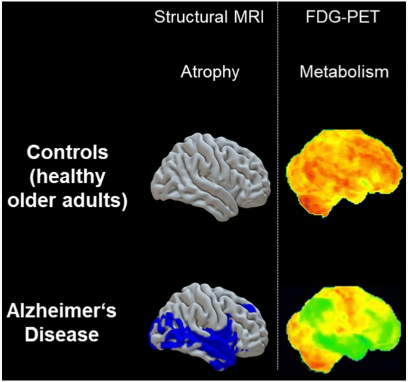

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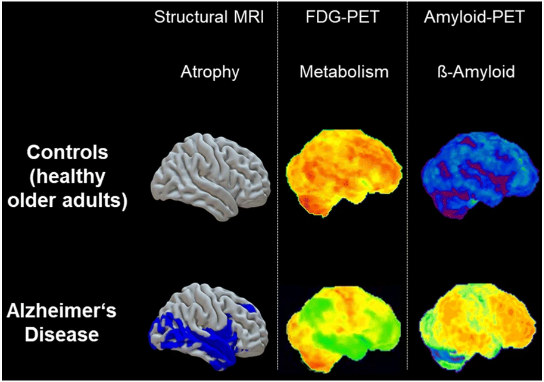

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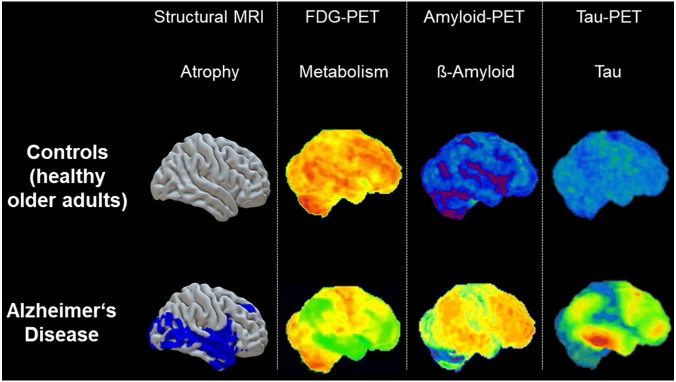


Molecular imaging (PET/SPECT)

”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.

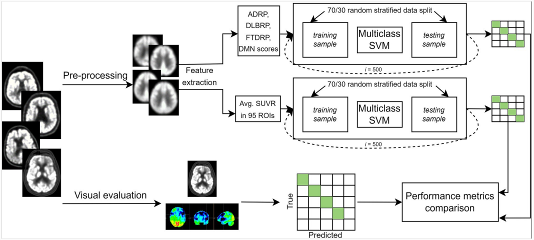
Symptoms are a result of the disease process and are not necessary to diagnose AD

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”

Molecular imaging (PET/SPECT)



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Molecular imaging (PET/SPECT)

	AD	DLB	FTD	NC
AD	53	7		3
DLB	9	65	1	4
FTD		1	21	1
NC	2			39

Model predicted diagnosis (86%)

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NC	2			39

Model predicted diagnosis (86%)

	AD	DLB	FTD	Other	NC
AD	50	4		8	1
DLB	5	54		19	1
FTD	3		16	24	
Other					
NC					41

Human predicted diagnosis (78%)

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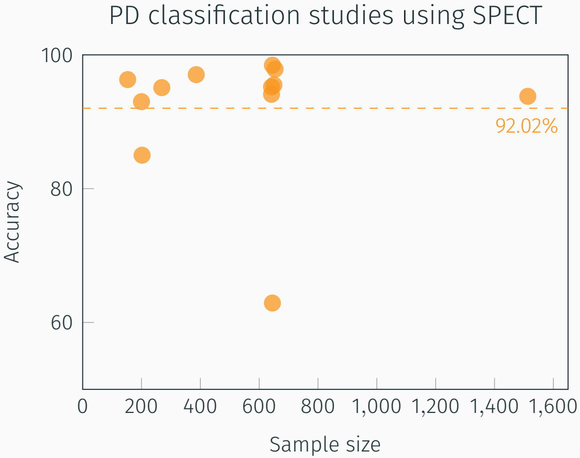

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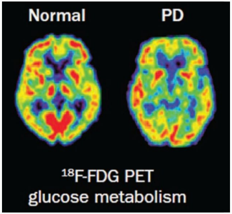

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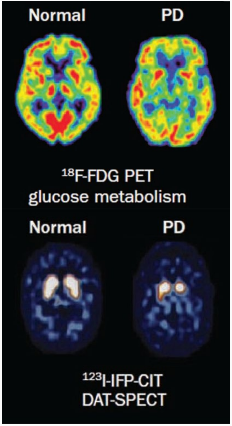

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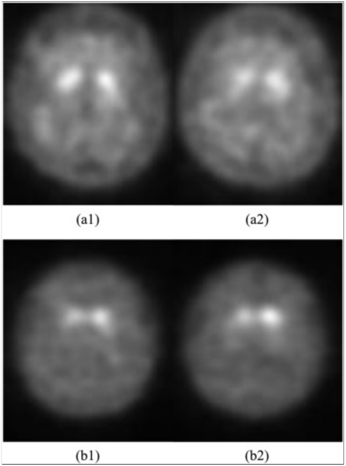
Molecular imaging (PET/SPECT)

Explanation of SPECT

Molecular imaging (PET/SPECT)



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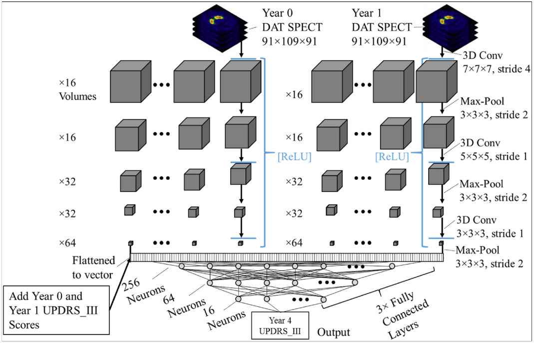

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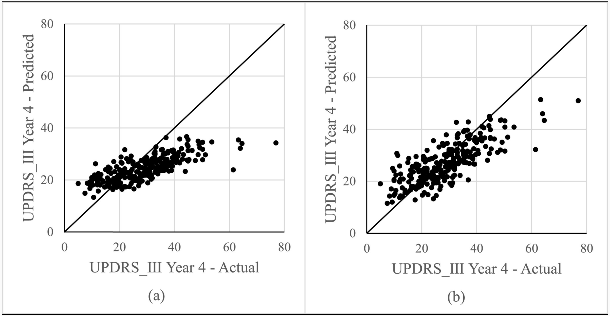

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  - However, Dinga et al. failed to replicate their results.
- Molecular imaging
  - Used in a moderate amount of studies predicting PD and DEM with good results (mean accuracy=92%).

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

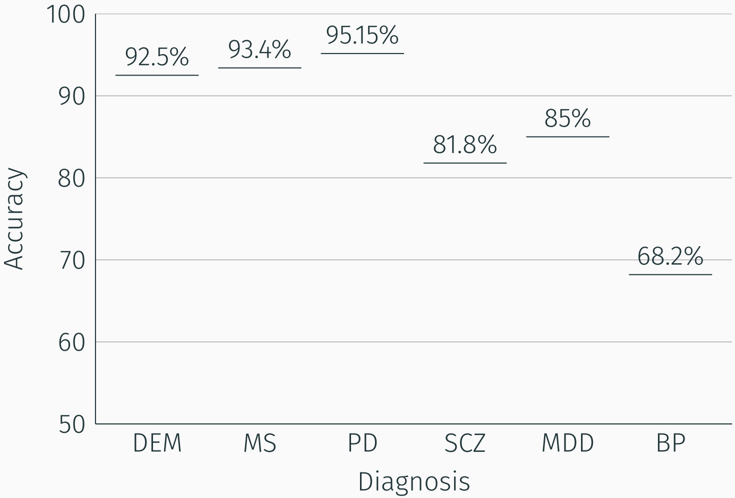
- Widely used for all disorders, with varying results
- Task-based fMRI used by YYY for ZZZ in SCZ.
- Resting state fMRI used by Segal et al. to make diagnostic predictions at various biological levels.

Molecular imaging

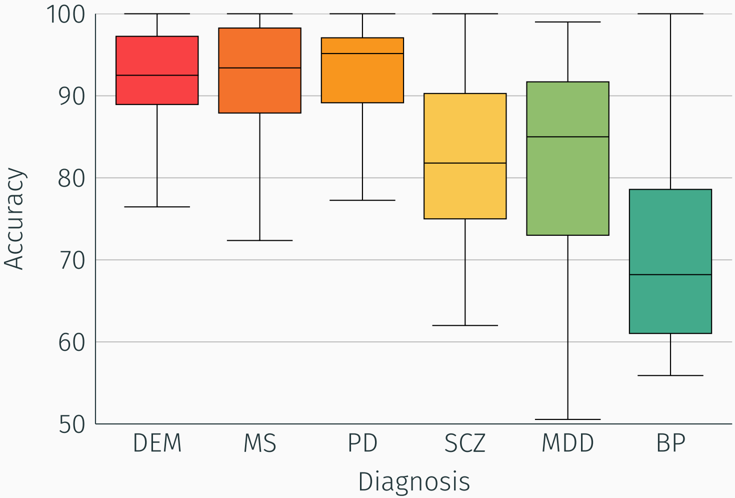
- Mostly used in DEM and PD with high accuracies (92%).
- PET used clinically to diagnose Alzheimer's disease.
- SPECT used clinically to XXX Parkinson's disease.

The future of neuroimaging-based prediction

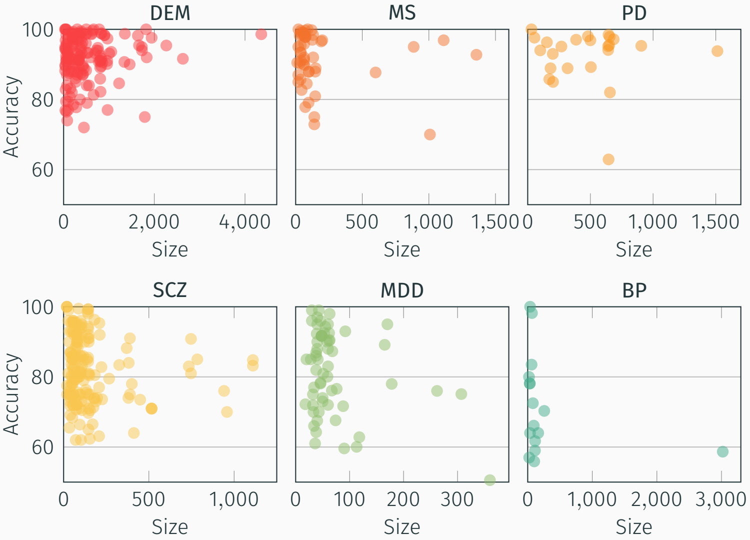
Challenges: Predictiveness



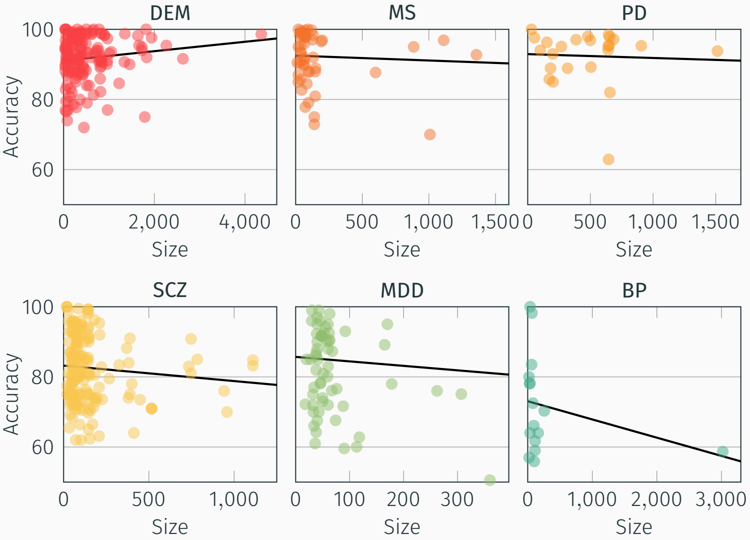
Challenges: Predictiveness



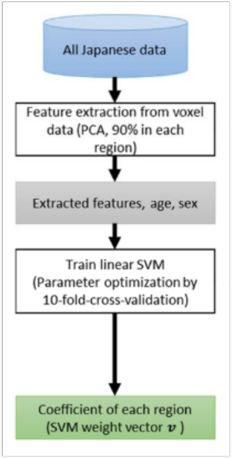
Challenges: Predictiveness



Challenges: Predictiveness



Challenges: Predictiveness

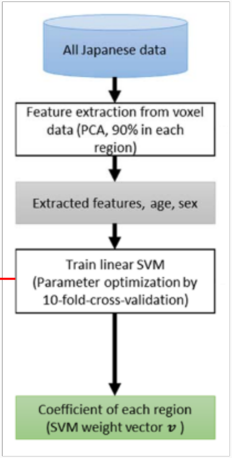


Matsuo et al., 2019

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

88.1%



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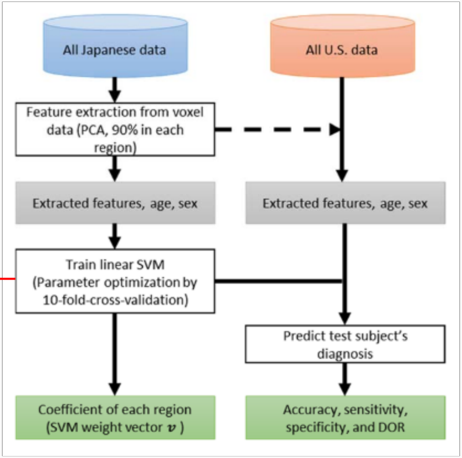

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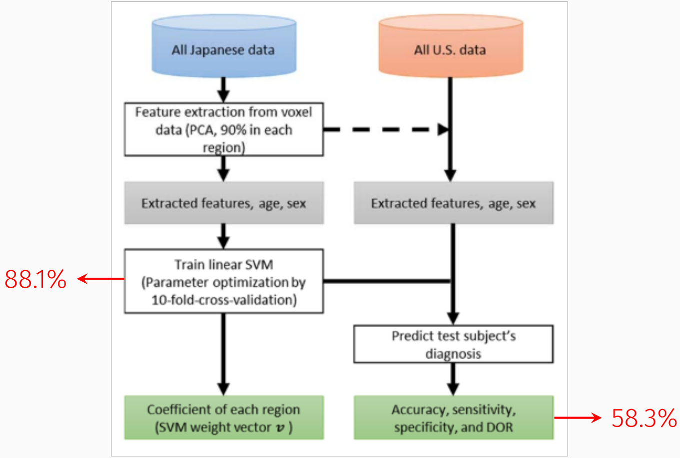

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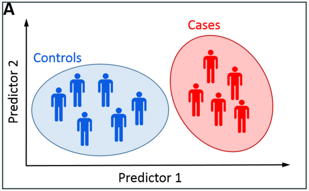
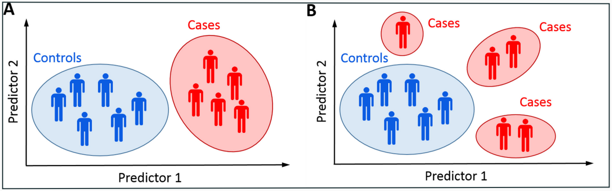
Challenges: Predictive targets



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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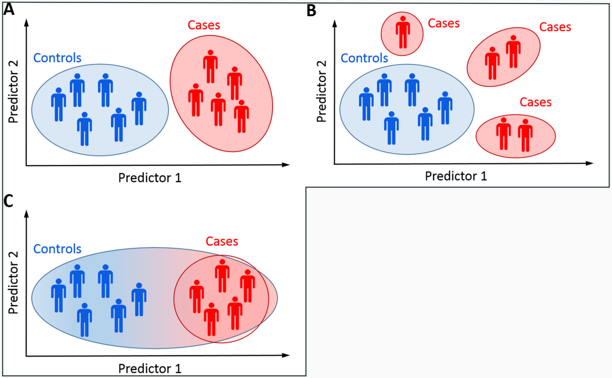

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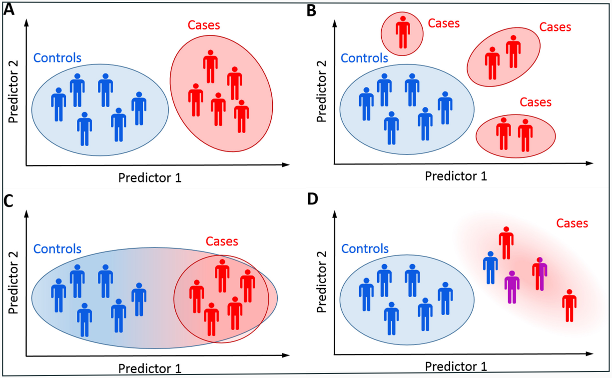

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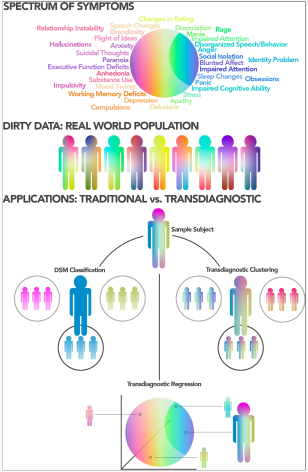
Challenges: Predictive targets

Diagnostic labels vs prognosis, treatment, differential

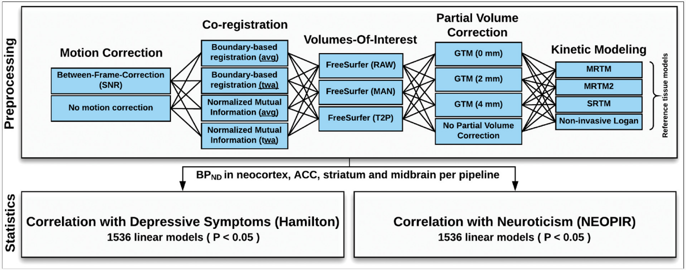
Challenges: Predictive targets



Vogel & Black (2024)

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

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

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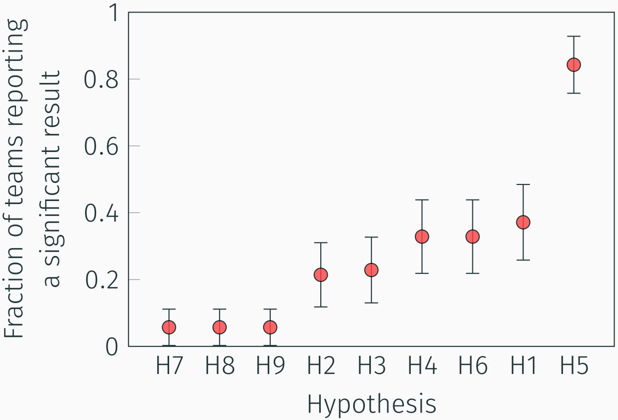

Adapted from Botvinik-Nezer et al., 2020

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

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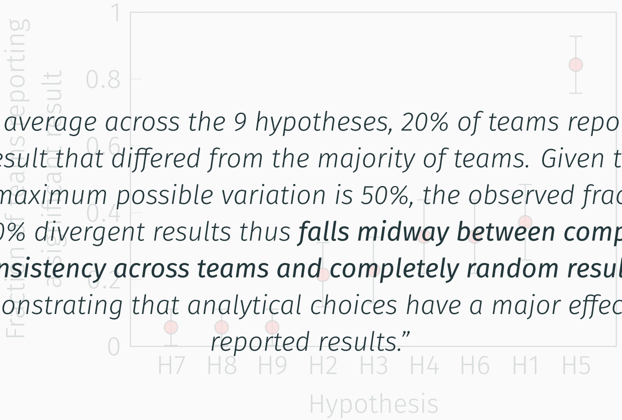
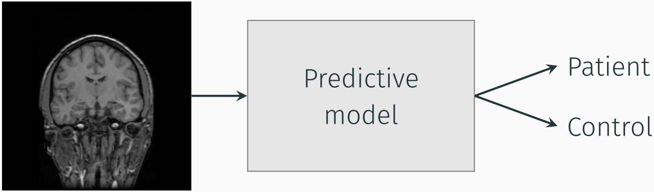


"On average across the 9 hypotheses, 20% of teams reported a result that differed from the majority of teams. Given that the maximum possible variation is 50%, the observed fraction of 20% divergent results thus ***falls midway between complete consistency across teams and completely random results****, demonstrating that analytical choices have a major effect on reported results."*

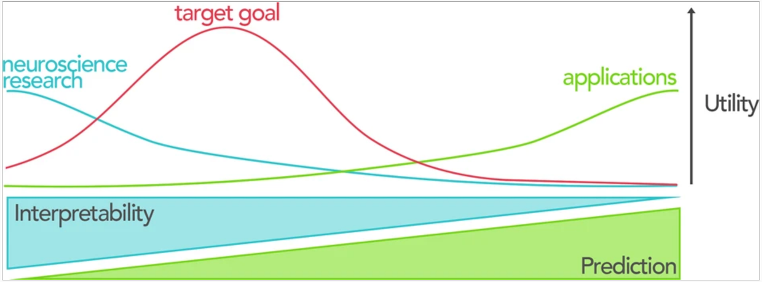
Adapted from Botvinik-Nezer et al., 2020

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: Interpretability



Challenges: Interpretability



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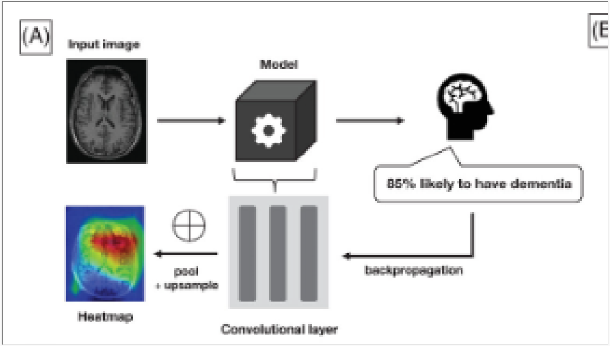
Challenges: Interpretability

Predictive
model

Challenges: Interpretability

a+b+c+d

Challenges: Interpretability



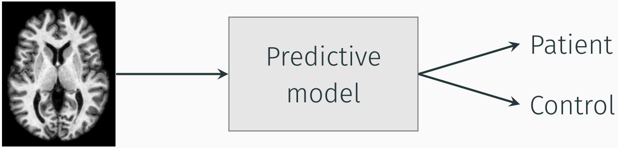
Opportunities: New modalities

DEBBIE

Opportunities: New modalities

QSM

Opportunities: Multimodality



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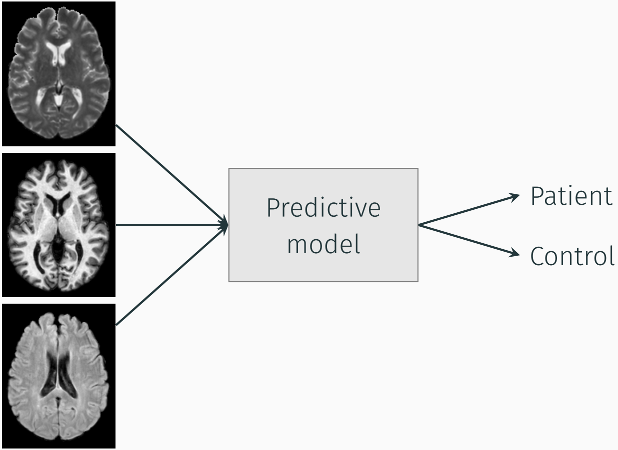
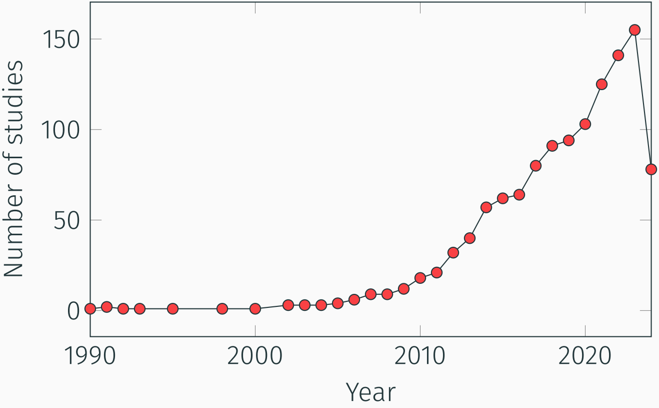
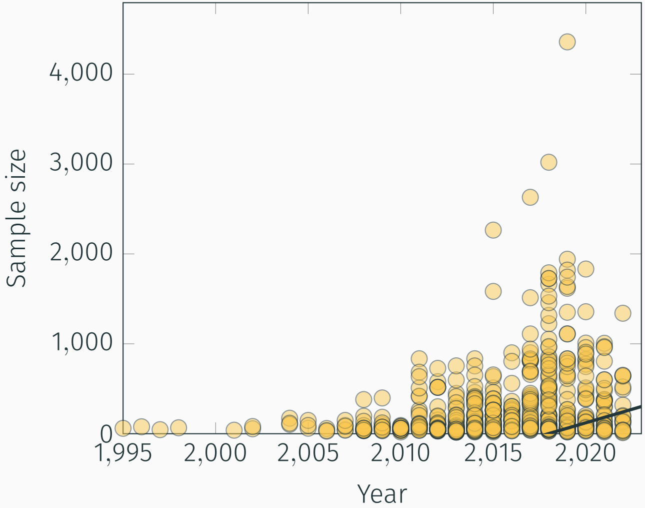


Opportunities: Multimodality

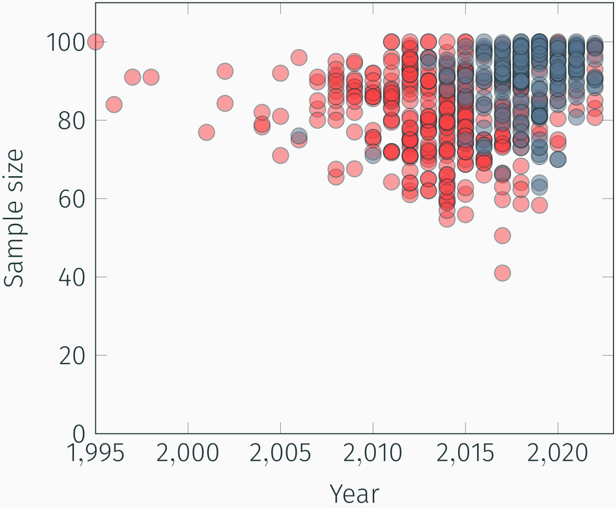


Pubmed search: multimodal[Title] AND (neuroimaging[Title] or MRI[Title])

Opportunities: Larger datasets



Opportunities: Better methods



Opportunities: Better methods