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

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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.

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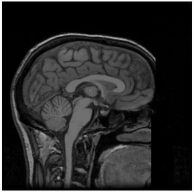

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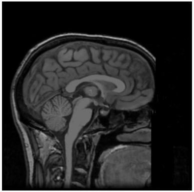

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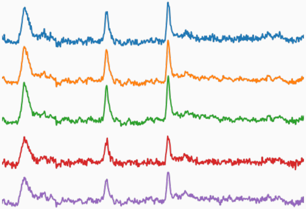

Sample from the MNE library

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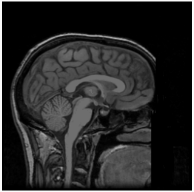

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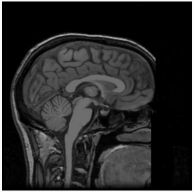

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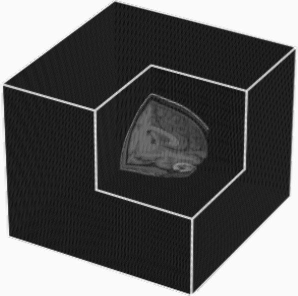

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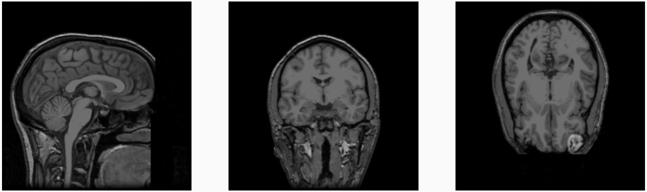

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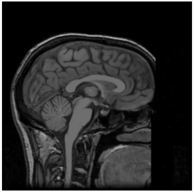

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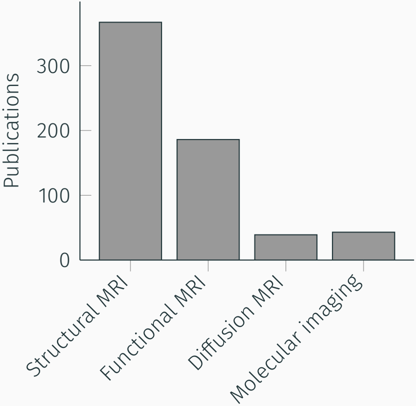

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Alzheimer's disease (AD) and other causes of dementia (DEM)

Multiple Sclerosis (MS)

Parkinson's Disease (PD)

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Alzheimer's disease (AD) and other causes of dementia (DEM)

Multiple Sclerosis (MS)

Parkinson's Disease (PD)

Bipolar Disorder (BP)

Schizophrenia (SCZ)

Depressive disorders, including major depressive disorder (MDD)

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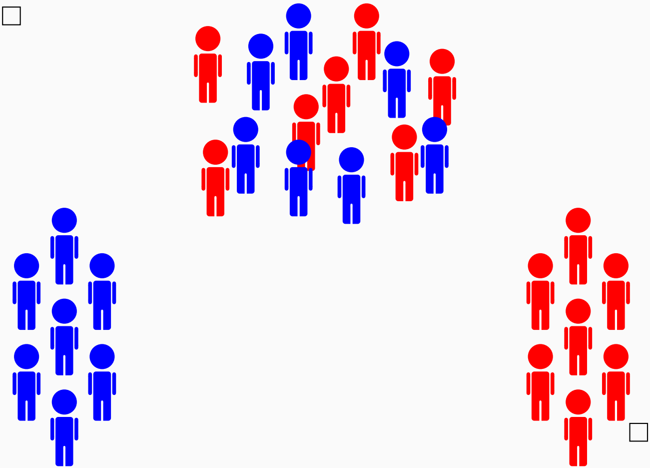


Neuroimaging modalities for diagnostic predictions

Approach

DEM MS PD SCZ MDD BP

Diagnosis

Approach

DEM MS PD SCZ MDD BP

Diagnosis

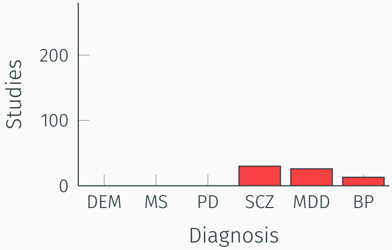
sMRI dMRI fMRI MOL

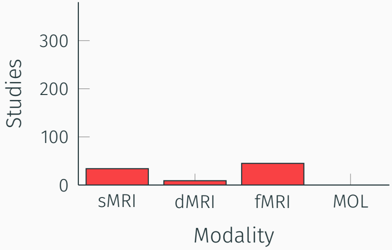
Modality

Approach

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

Thomas Wolfers [a b], Jan K. Buitelaar [c d], Christian F. Beckmann [b c e], Barbara Franke [a f], Andre F. Marquand [b g]





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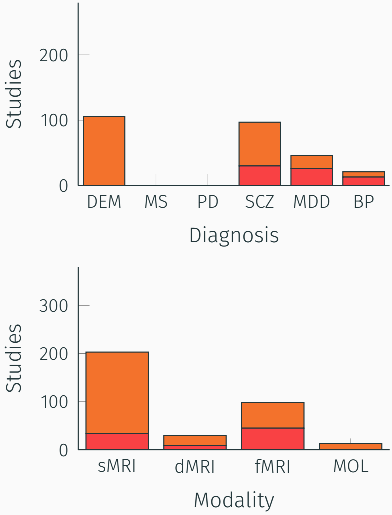
Single subject prediction of brain disorders in neuroimaging: Promises and pitfalls

Mohammad R. Arbabshirani [a b], Sergey Plis [a], Jing Sui [a c], Vince D. Calhoun [a d]



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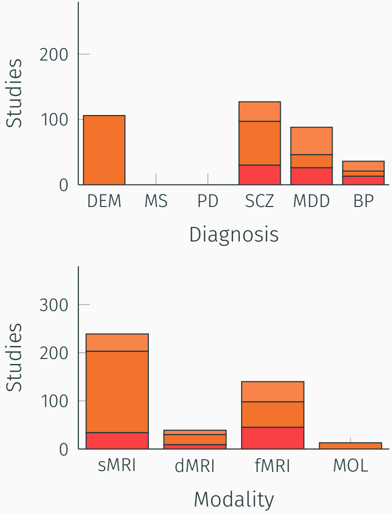
Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun



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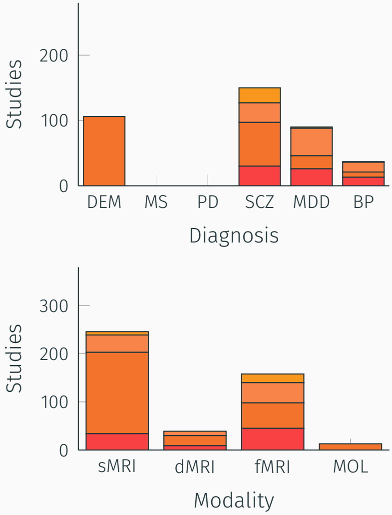
Towards a brain-based predictome of mental illness

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]



Approach

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

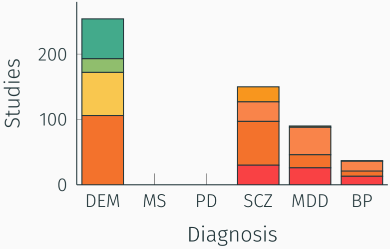
Mr Amir Ebrahimighahnavieh [1], Suhuai Luo [1], Raymond Chiong [2]

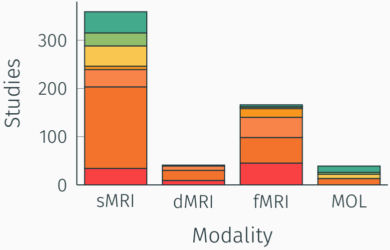
Machine learning techniques for diagnosis of alzheimer disease, mild cognitive disorder, and other types of dementia

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]





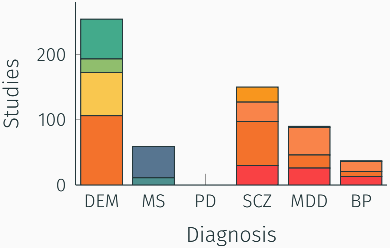
Approach

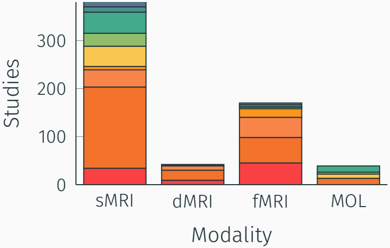

Applications of deep learning techniques for automated multiple sclerosis detection using magnetic resonance imaging: A review

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

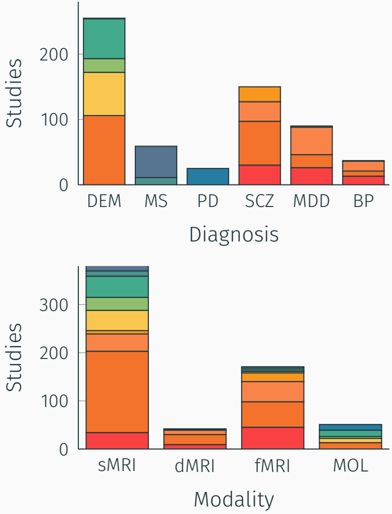
by Nida Aslam [1,*], Irfan Ullah Khan [1], Asma Bashamakh [1], Fatima A. Alghool [1], Menna Aboulnour [1], Noorah M. Alsuwayan [1], Rawa'a K. Alturaif [1], Samiha Brahimi [2], Sumayh S. Aljameel [1] and Kholoud Al Ghamdi [3]





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]



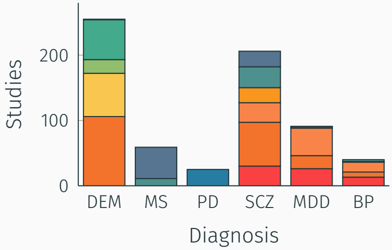
Approach

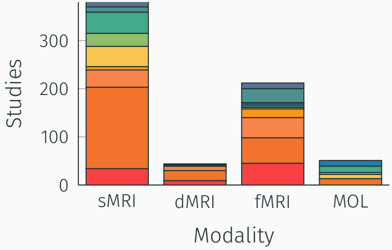
Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review

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]





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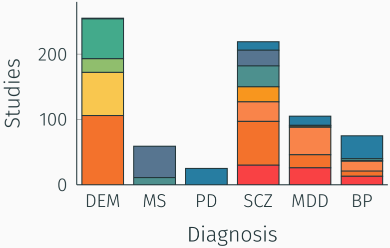
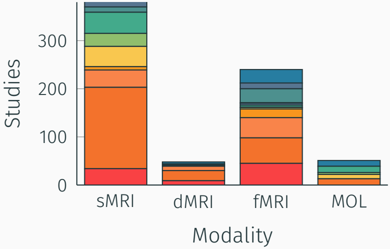
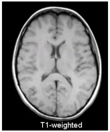


Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

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

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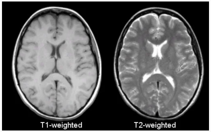

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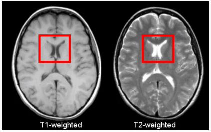

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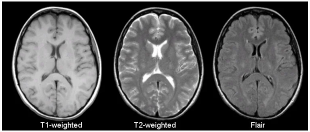

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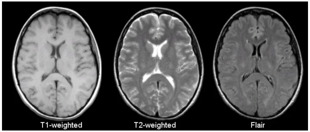

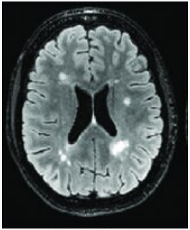

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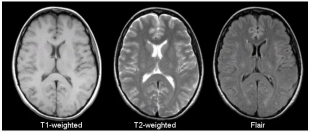

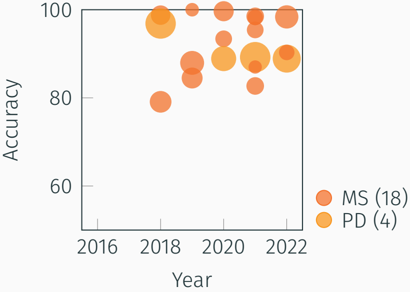

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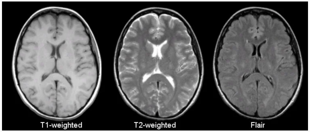
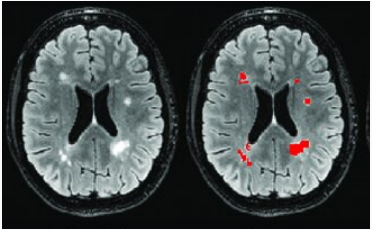
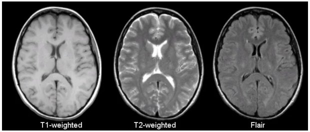
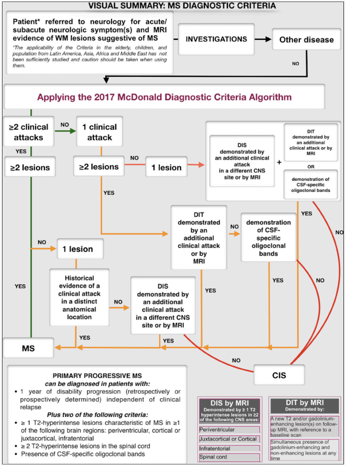




Weeda, M. M., Brouwer, I., de Vos, M. L., de Vries, M. S., Barkhof, F., Pouwels, P. J. W., & Vrenken, H. (2019). Comparing lesion segmentation methods in multiple sclerosis: Input from one manually delineated subject is sufficient for accurate lesion segmentation. NeuroImage: Clinical, 24, 102074

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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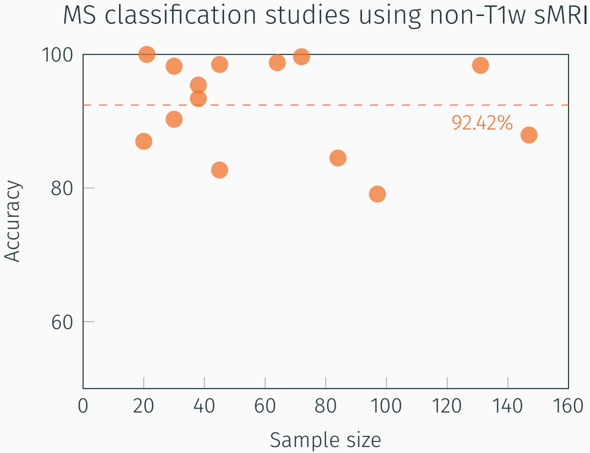

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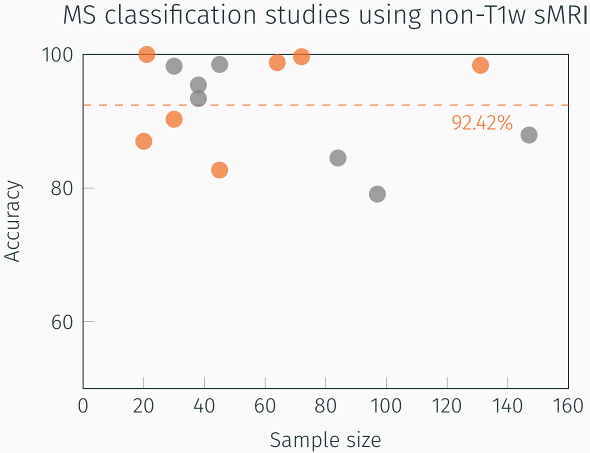

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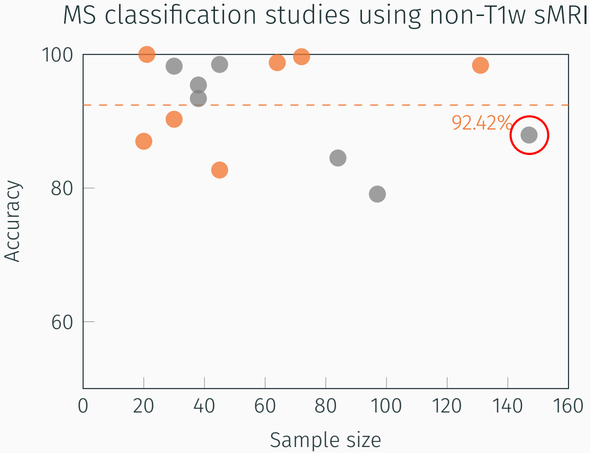

Eitel, F., Soehler, E., Bellmann-Strobl, J., Brandt, A. U., Ruprecht, K., Giess, R. M., ... & Ritter, K. (2019). Uncovering convolutional neural network decisions for diagnosing multiple sclerosis on conventional MRI using layer-wise relevance propagation. NeuroImage: Clinical, 24, 102003

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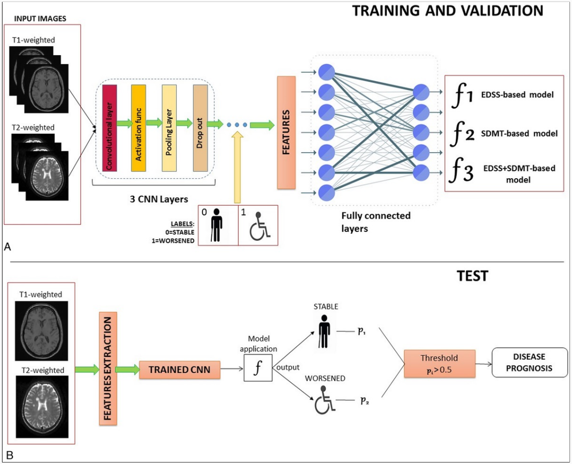

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Other structural MRI modalities

		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.

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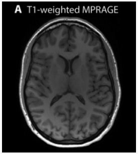
Other structural MRI modalities

- (Non T1-weighted) structural MRI
  - Most prevalent in studies classifying MS and PD, yielding high accuracies ($\sim$90%).
  - T2 intimately linked with MS due to its efficacy at exposing characteristic lesions.
  - Machine learning models trained on T1 and T2-weighted scans shown by Storelli et al. to predict prognosis better than expert humans.

Diffusion MRI



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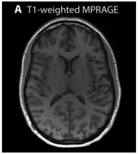

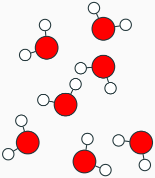

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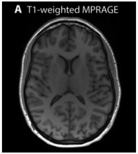

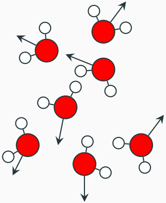

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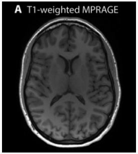

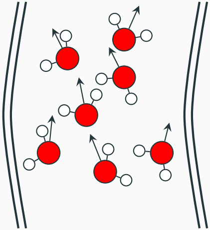

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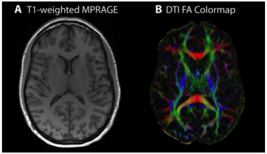

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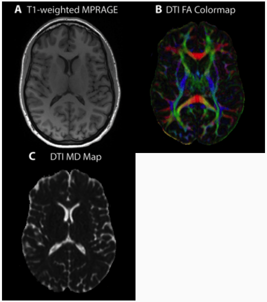

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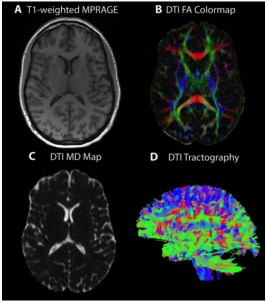
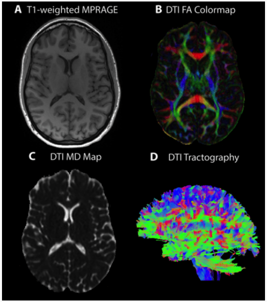
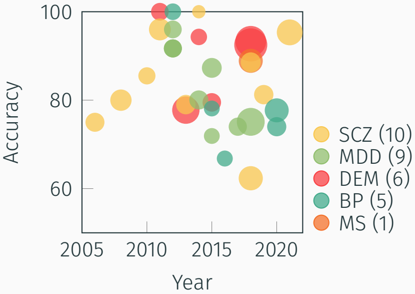


Diffusion MRI





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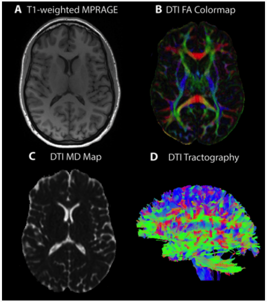

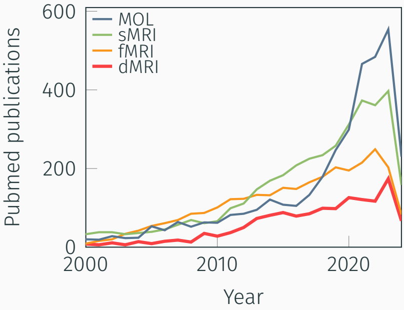

MOL:	((molecular[Title] AND imaging[Title]) OR PET[Title] OR SPECT[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)”
sMRI:	((structural[Title] AND MRI[Title]) OR sMRI[Title] OR T1[Title] OR T2[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)
fMRI:	((functional[Title] AND MRI[Title]) OR fMRI[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)
dMRI:	((diffusion[Title] AND MRI[Title]) OR dMRI[Title] OR DTI[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)

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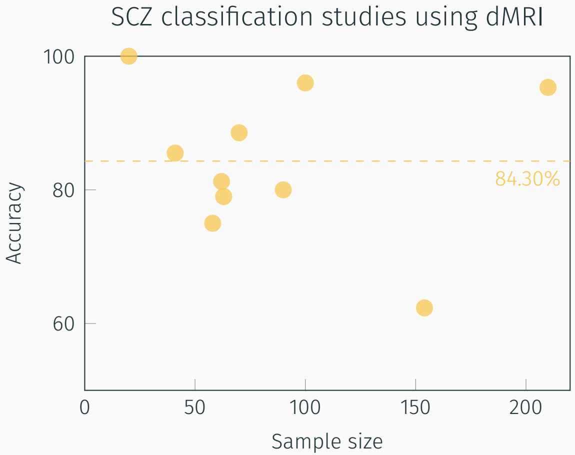

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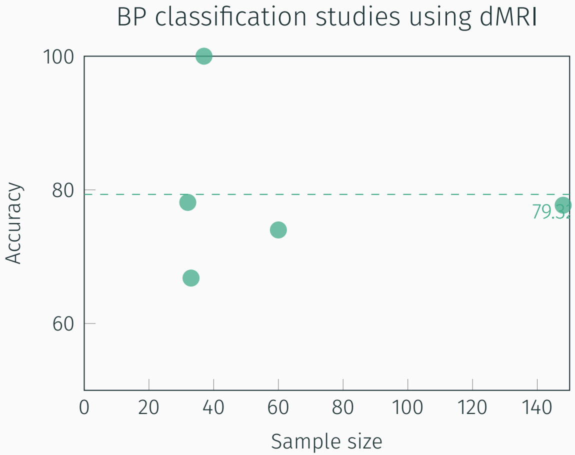

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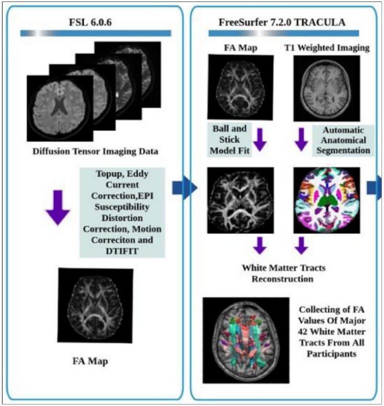

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Diffusion MRI

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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  - Used by Saglam et al. to differentially diagnose SCZ and BP with 80% accuracy.

Functional Magnetic Resonance Imaging (fMRI)

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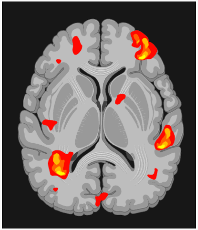

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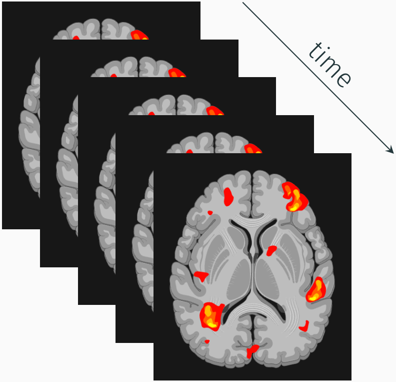

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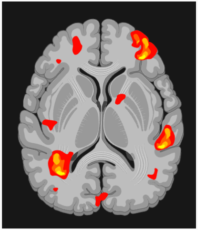

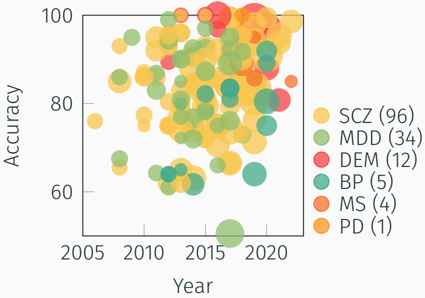

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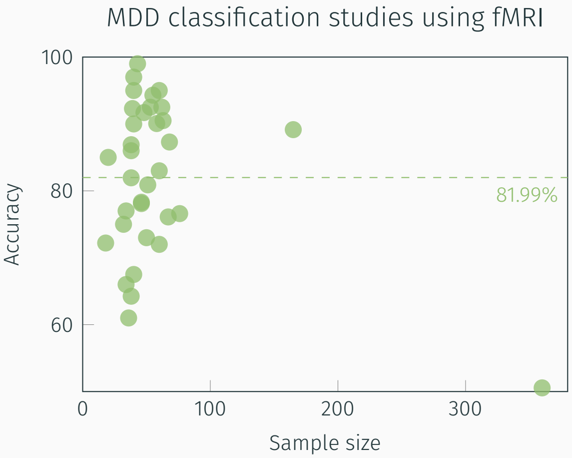

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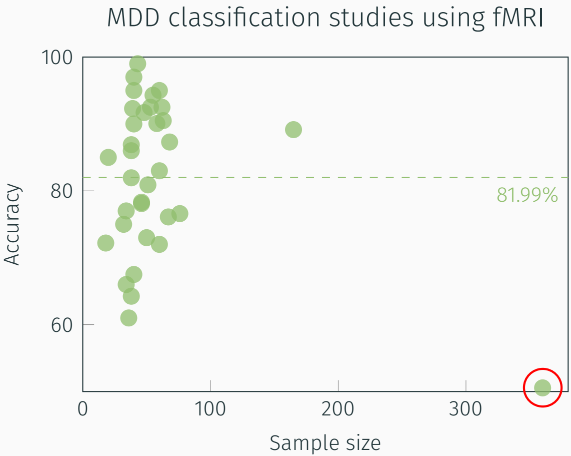

Sundermann, B., Feder, S., Wersching, H., Teuber, A., Schwindt, W., Kugel, H., ... & Pfleiderer, B. (2017). Diagnostic classification of unipolar depression based on resting-state functional connectivity MRI: effects of generalization to a diverse sample. Journal of Neural Transmission, 124, 589-605

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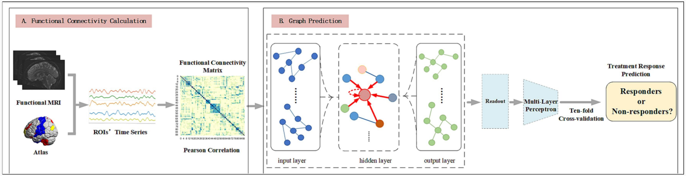

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Functional Magnetic Resonance Imaging (fMRI)

Methods	Accuracy(%)	Sensitivity(%)	Specificity(%)	F1-score(%)	Auc(%)
MLP	55.47	62.65	47.11	59.54	54.88
BrainGNN	54.88	74.22	56.20	69.34	65.21
FGDN	65.68	76.18	52.36	70.17	64.27
GIN	74.24	79.82	67.42	77.06	73.50

MLP, Multi-layer Perceptron; GNN, Graph Neural Networks; FDGN, Functional Graph Discriminative Network;GIN, Graph Isomorphism Network.

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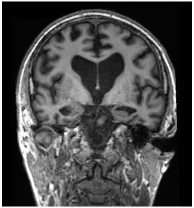
Molecular imaging



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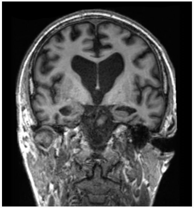

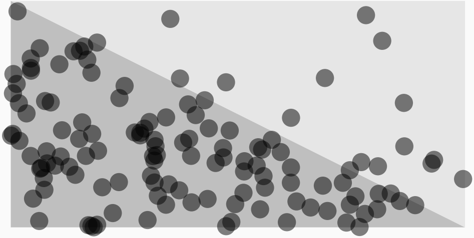

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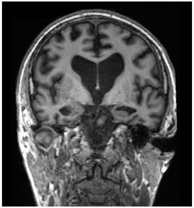

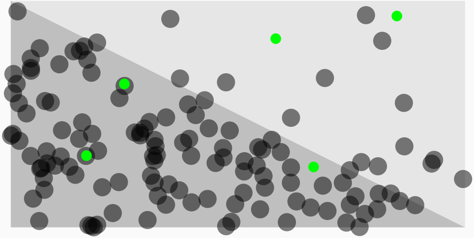

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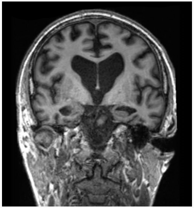

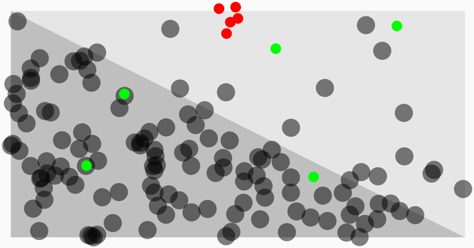

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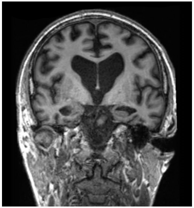

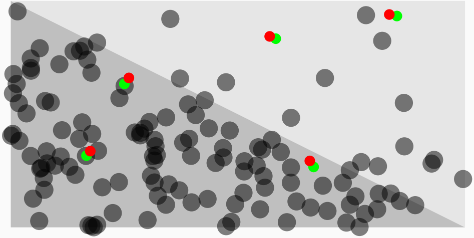

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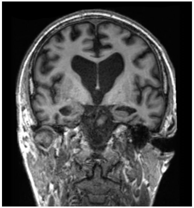

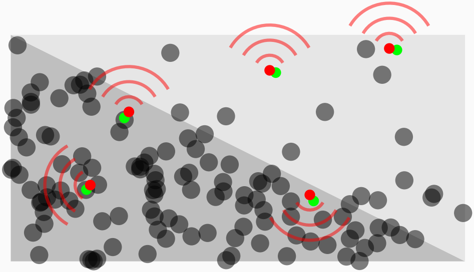

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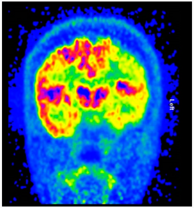

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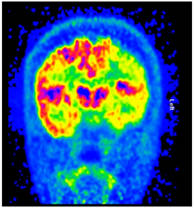

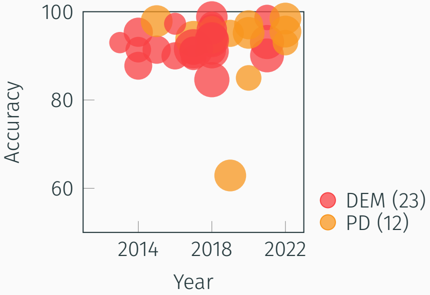

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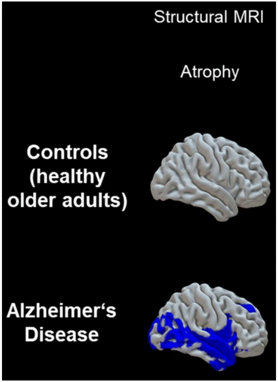

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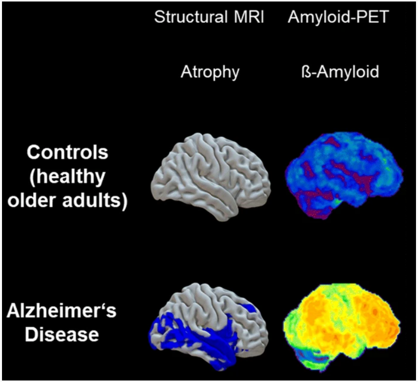

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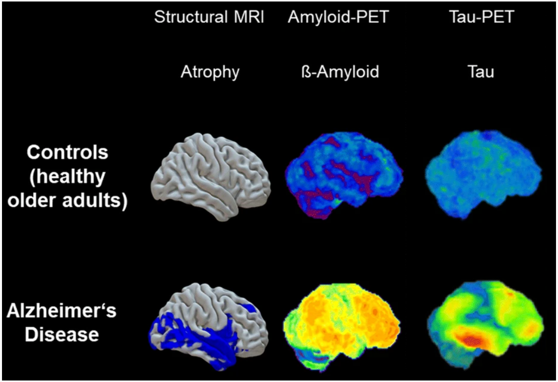

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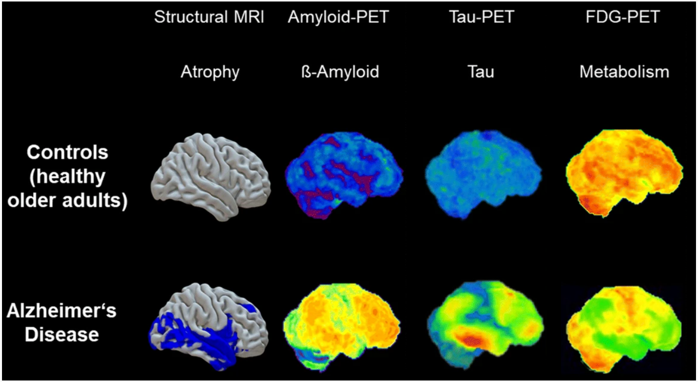

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Molecular imaging

”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

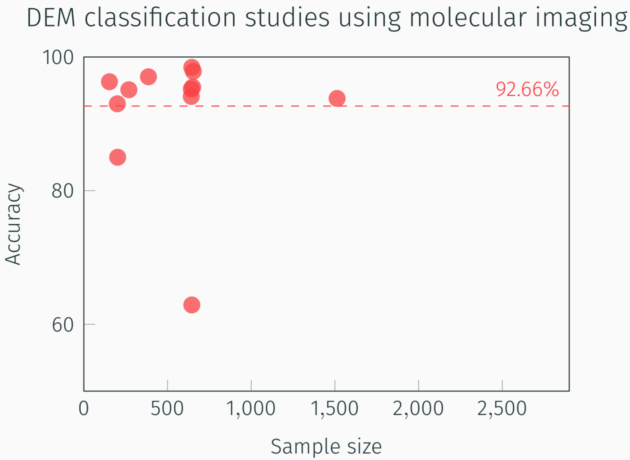
AD exists on a continuum not as discrete clinically defined entities

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, alz.org/diagnosticcriteria

Molecular imaging



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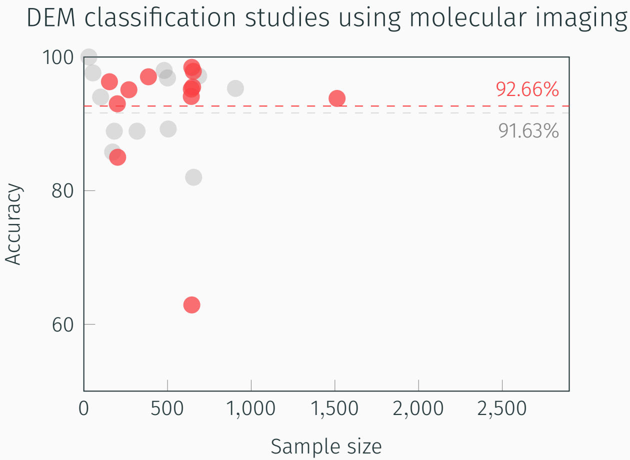

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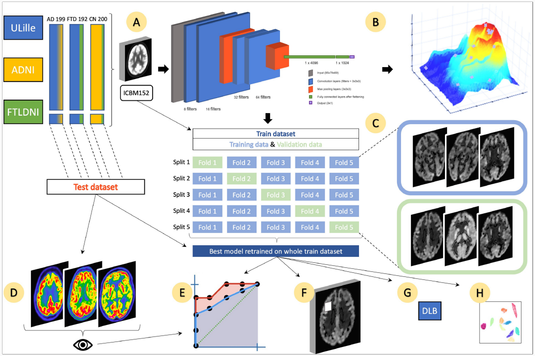

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Molecular imaging

		Metrics				
		Se	**Sp**	**Precision**	**F1-score**	**Support**
Model	AD	75 % (15/20)	97 % (38/39)	94 % (15/16)	83 %	20
	FTD	95 % (18/19)	90 % (36/40)	82 % (18/22)	88 %	19
	CN	100 % (20/20)	97 % (38/39)	95 % (20/21)	98 %	20
		Se	**Sp**	**Precision**	**F1-score**	**Support**
Physician	AD	70 % (14/20)	87 % (34/39)	74 % (14/19)	72 %	20
	FTD	47 % (9/19)	92 % (37/40)	75 % (9/12)	58 %	19
	CN	90 % (18/20)	74 % (29/39)	64 % (18/28)	75 %	20

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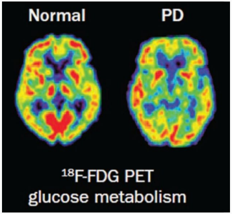

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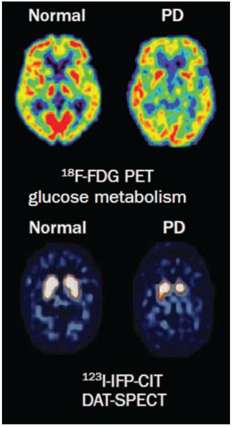

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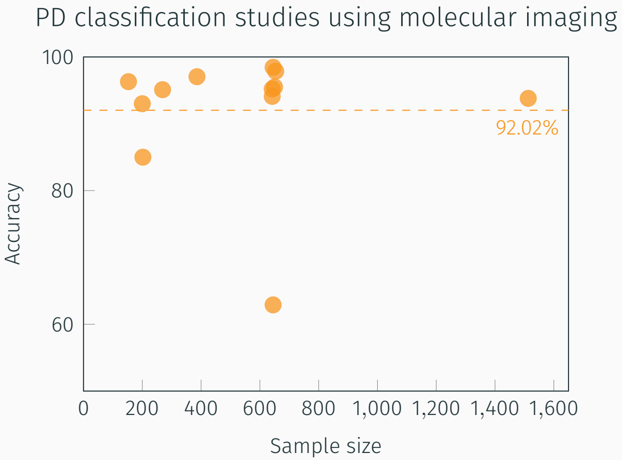

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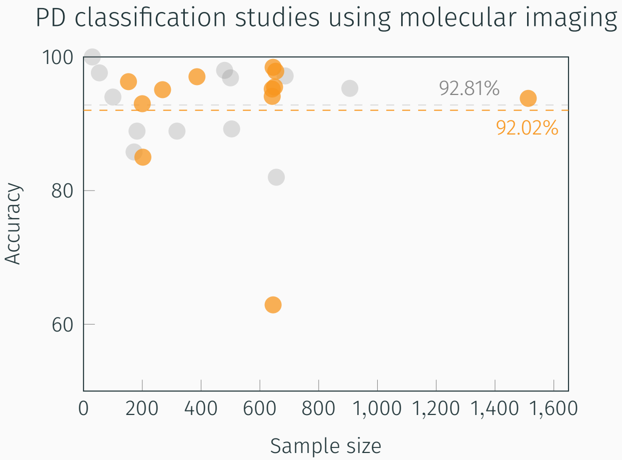

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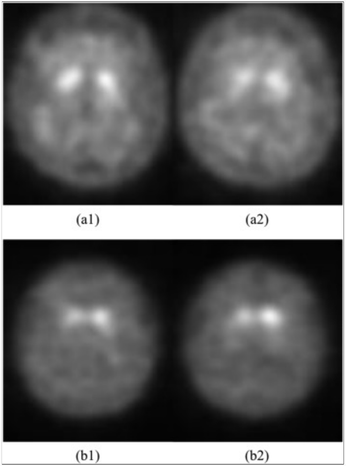

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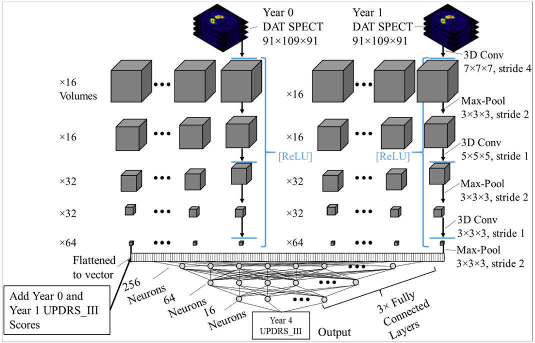

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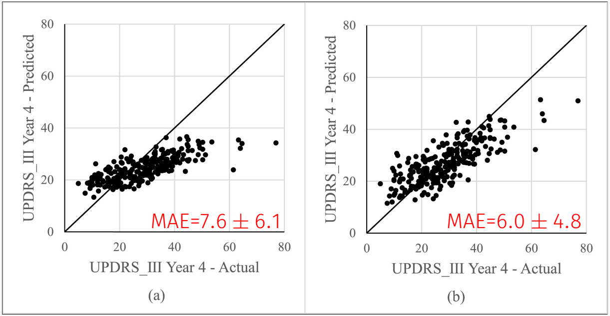

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  - Used by Sun et al. to predict conversion from MCI to DEM with 81% accuracy.
- Functional MRI
  - Widely used for all conditions, most prominently SCZ and MDD with varying accuracies (60-100%) and DEM (80-100%).
  - Used by Drysdale et al. to characterize MDD biotypes responding differently to MTS.
  - However, Dinga et al. failed to replicate their results.
- Molecular imaging (PET/SPECT)
  - Used in studies classifying PD and DEM with good results (accuracies >90%).
  - PET is excellent for detecting AD-related pathology, both Aβ plaues and TAU tangles.
  - SPECT useful to characterize degeneration of dopamine-producing cells in PD, and, as shown by Adams et al., is plausibly useful to predict prognosis.

The future of neuroimaging-based prediction

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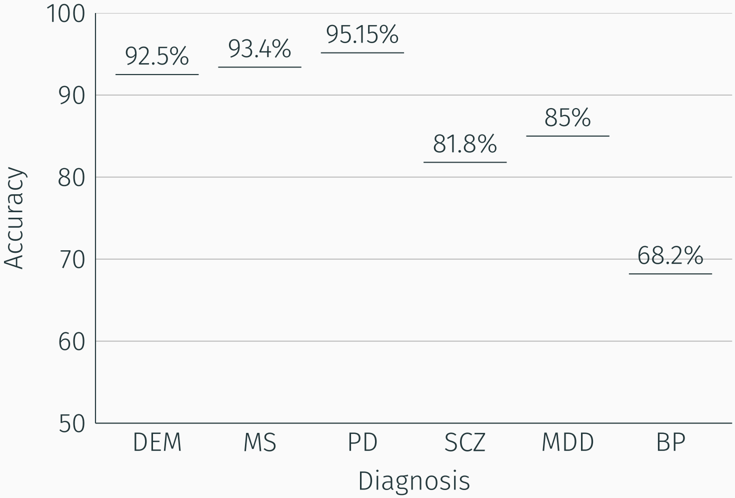
Challenges: Predictiveness



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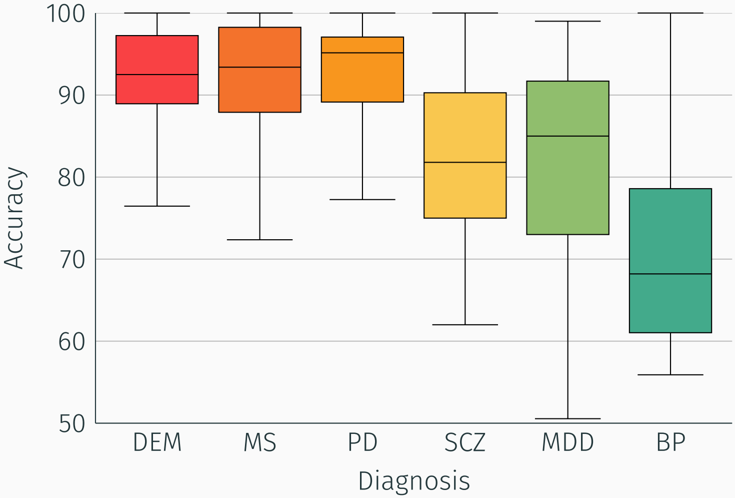

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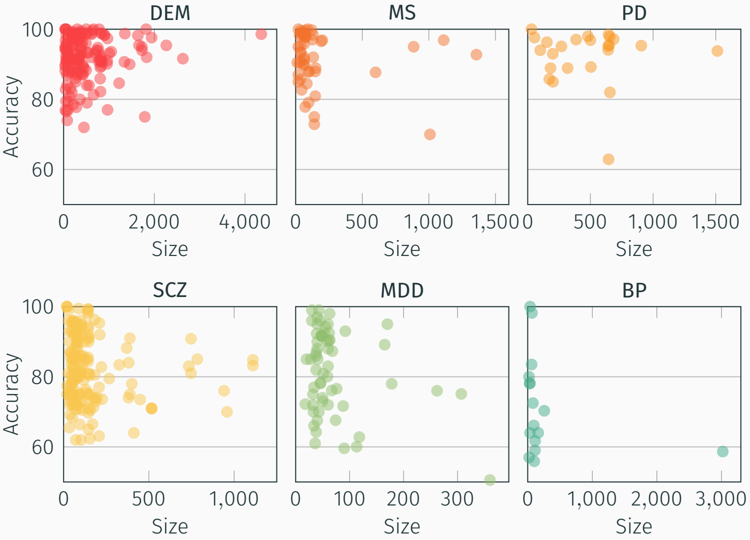

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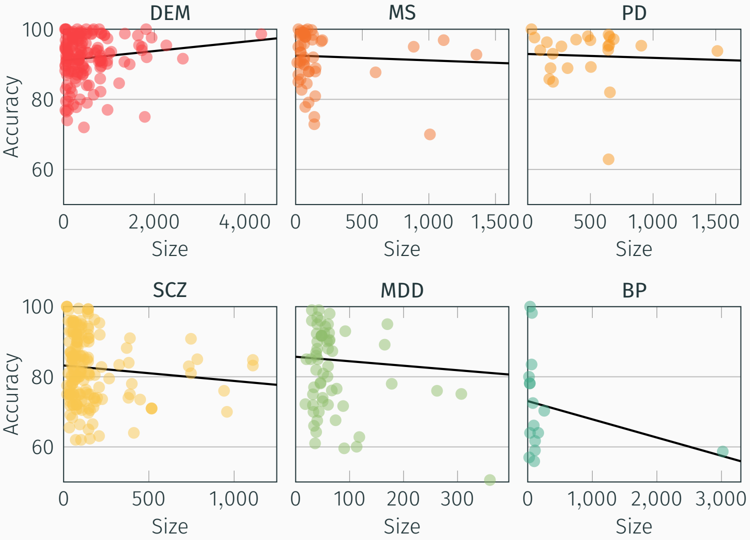
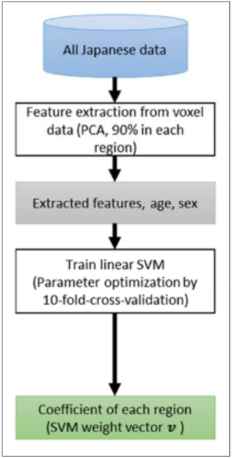
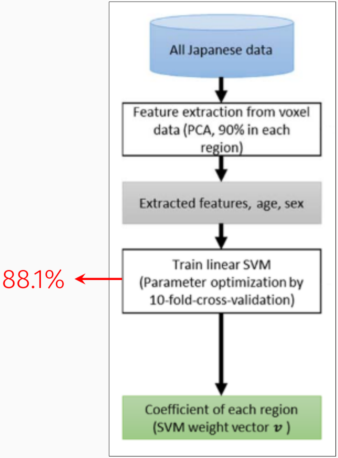


Challenges: Generalization



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: Generalization



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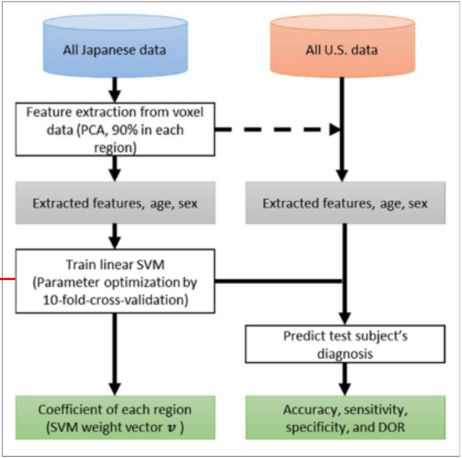
Challenges: Generalization

88.1%



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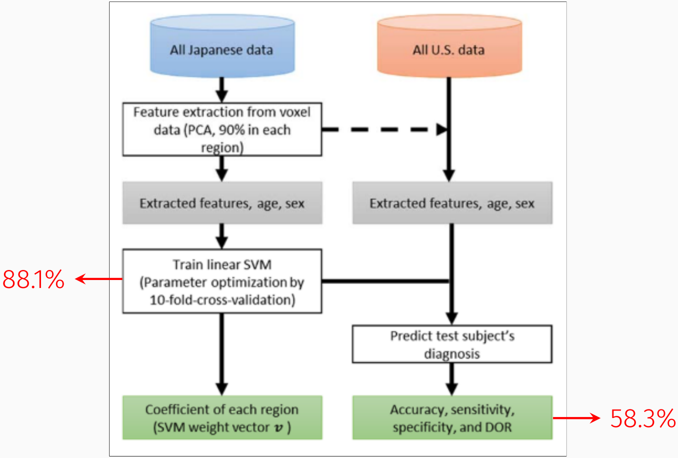
Challenges: Generalization



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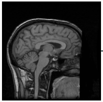
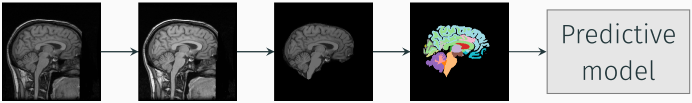
Challenges: Researcher degrees of freedom

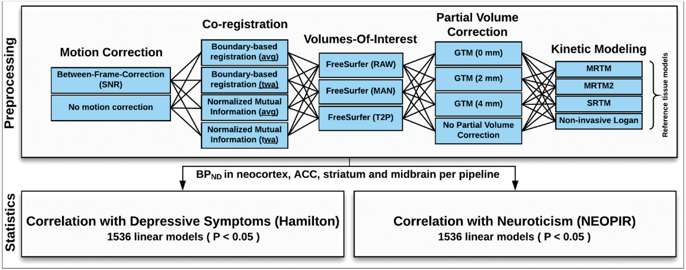


Predictive model

Challenges: Researcher degrees of freedom



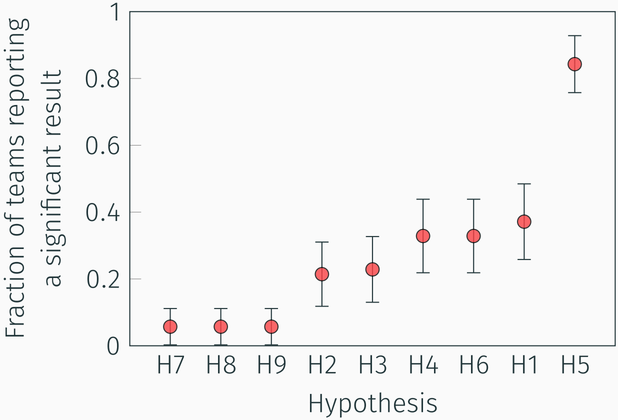
Challenges: Researcher degrees of freedom



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

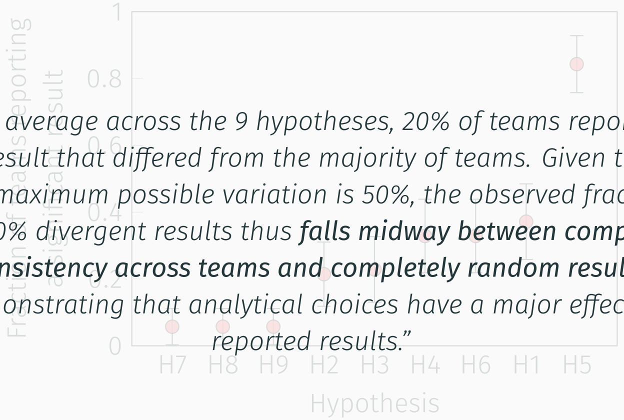
Challenges: Researcher degrees of freedom



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: Researcher degrees of freedom

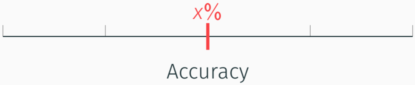


*"On average across the 9 hypotheses, 20% of teams reported a result that differed from the majority of teams. Given that the maximum possible variation is 50%, the observed fraction of 20% divergent results thus **falls midway between complete consistency across teams and completely random results**,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

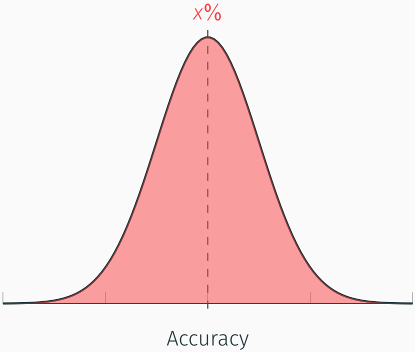
Adapted from Botvinik-Nezer et al., 2020

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

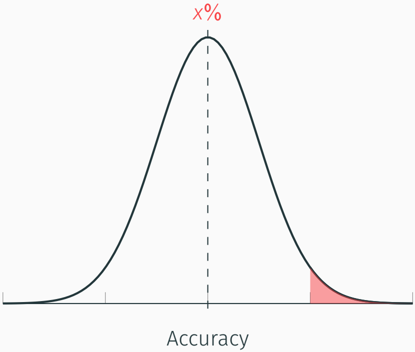
Challenges: Researcher degrees of freedom



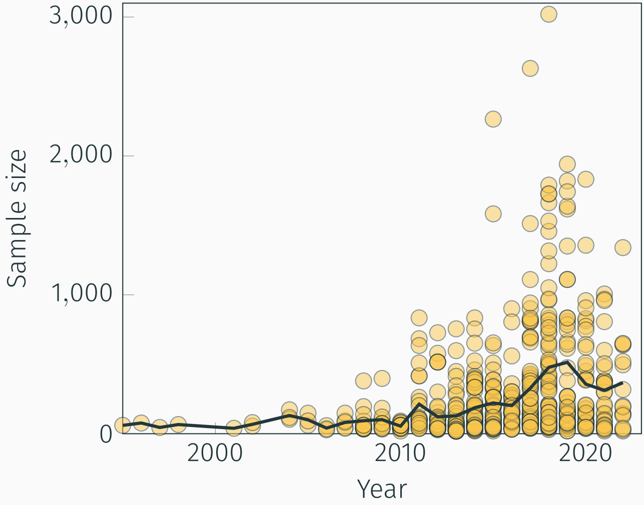
Challenges: Researcher degrees of freedom



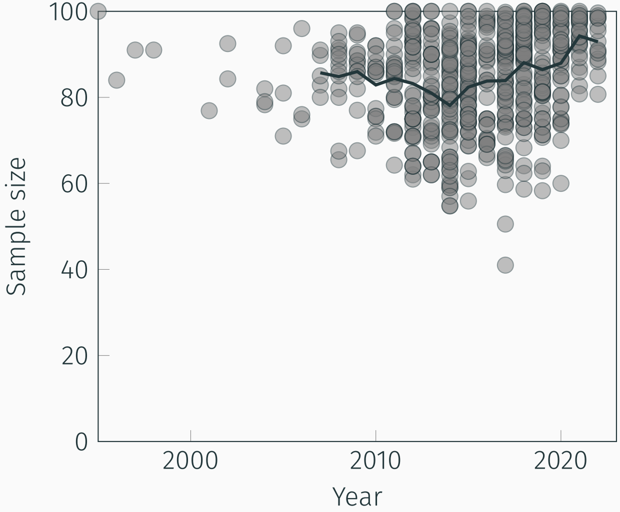
Challenges: Researcher degrees of freedom



Opportunities: Larger datasets



Opportunities: Better methods



Opportunities: Better methods