

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



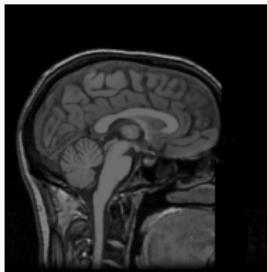
Background

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

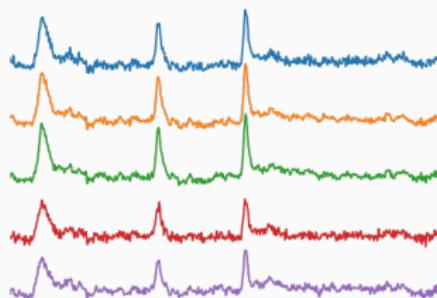


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Bert from FreeSurfer 7.3



Sample from the MNE library



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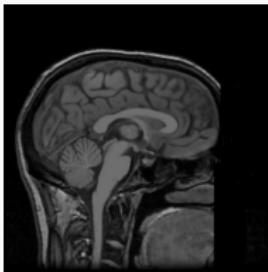


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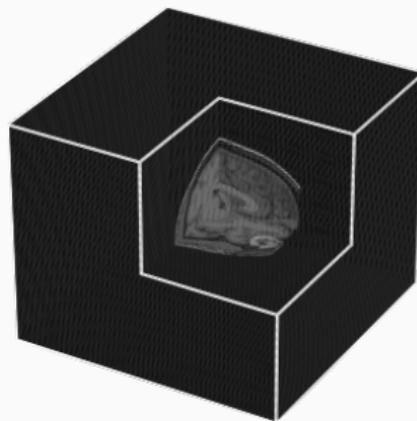


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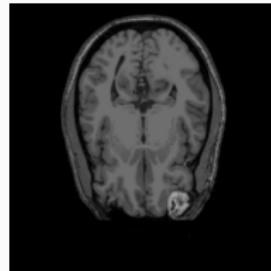
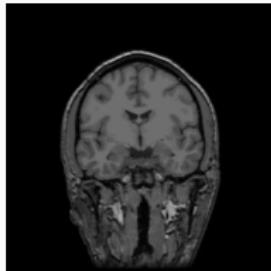
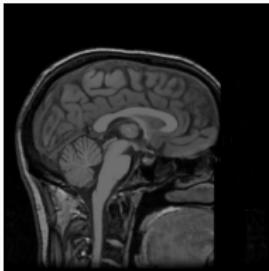


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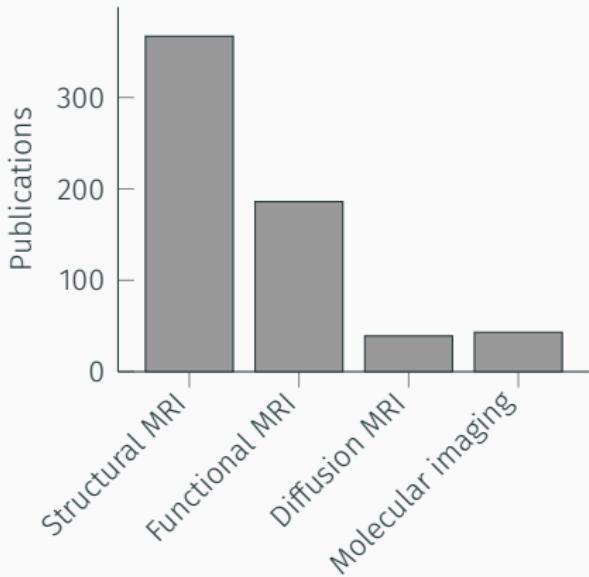


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Alzheimer's disease (AD) and other causes of dementia (DEM)

Multiple Sclerosis (MS)
Parkinson's Disease (PD)



Background

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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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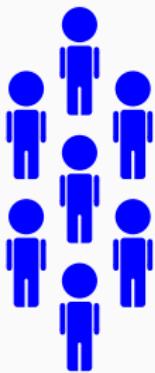
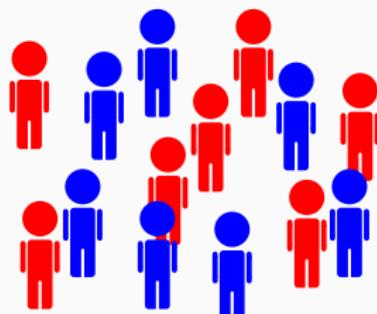


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Background

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



Neuroimaging modalities for diagnostic predictions



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Approach



DEM MS PD SCZ MDD BP
Diagnosis



Approach



DEM MS PD SCZ MDD BP
Diagnosis

sMRI dMRI fMRI MOL
Modality

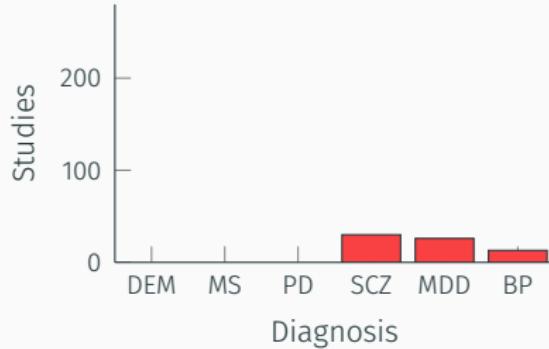


Approach



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

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



Approach

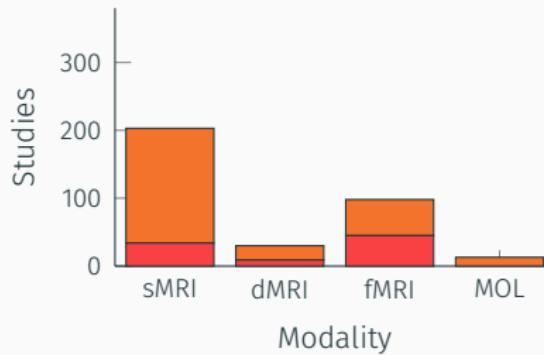
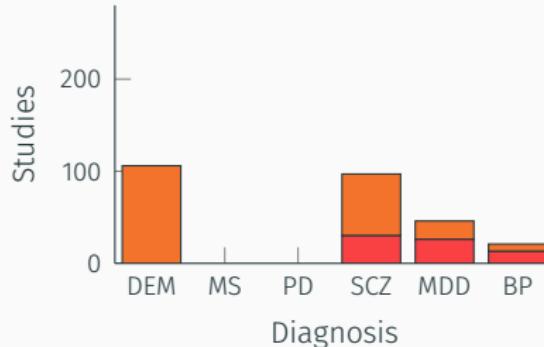


From estimating activation locality to predicting disorder: A review of pattern recognition for neuroimaging-based psychiatric diagnostics

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

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

Mohammad R. ArbabiShirani^{a b}, , Sergey Pliushch^b, Jing Sui^{a c}, Vince D. Calhoun^{a d}



Approach



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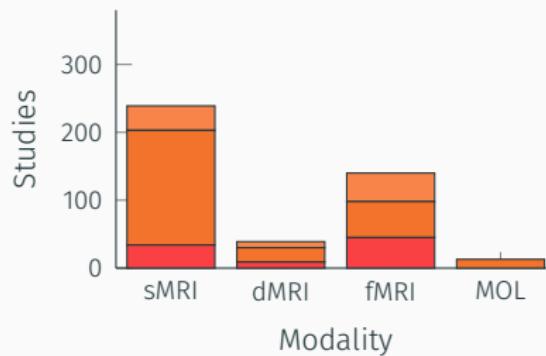
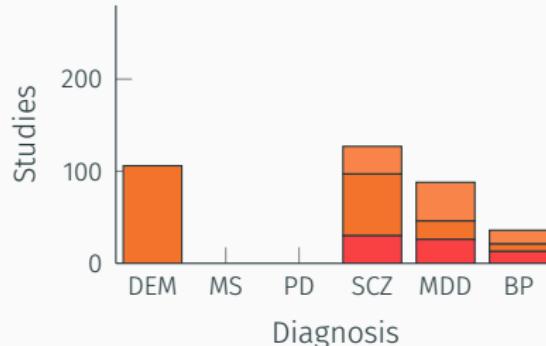
Thomas Wolters^{a b}, , Jon K. Buitelaar^{c d}, Christian F. Beckmann^{b c e}, Barbara Franke^{a f}, Andre F. Marquand^{b g}

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

Mohammad R. Arbabi Shirani^{a b}, , Sergey Pliushch^b, Jing Sui^{a c}, Vince D. Calhoun^{a d}

Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun



Approach



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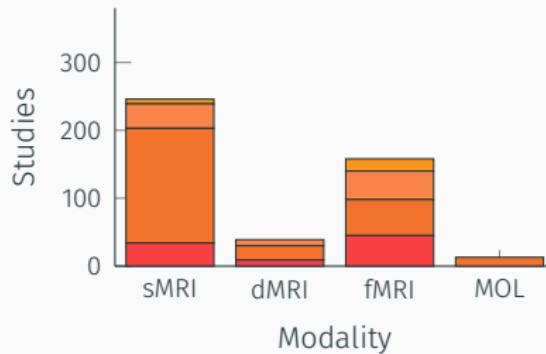
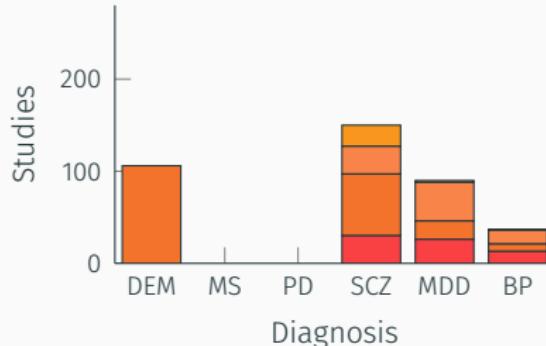
Mohammad R. Arbabi Shirani^{a,b}, , Sergey Pliushch^b, Jing Sui^{a,c}, Vince D. Calhoun^{a,d}

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 Quaak¹, Laurens van de Mortel³, Rajat Mani Thomas³, Guido van Wingen²



Approach



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

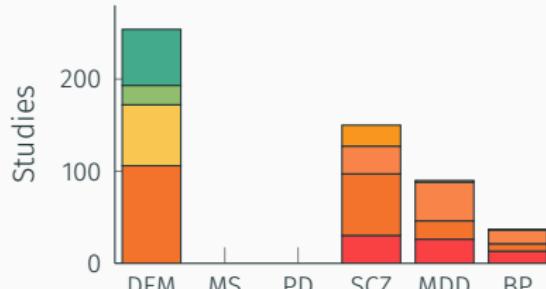
Mr Amir Ebrahimighavvaghieh ¹, Suhuai Luo ¹, Raymond Chiong ²

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

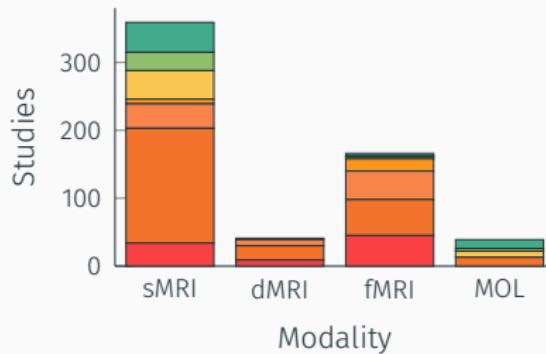
Golrokh Mirzaei ³, R. Hojjat Adeli ³

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

Sina Fathi ¹, Maryam Ahmadi ², Alsaneh Dehnad ³



Diagnosis

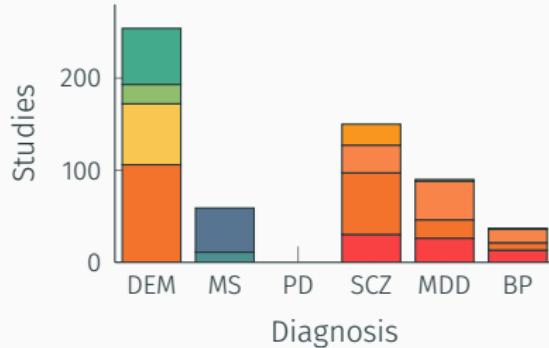


Approach



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

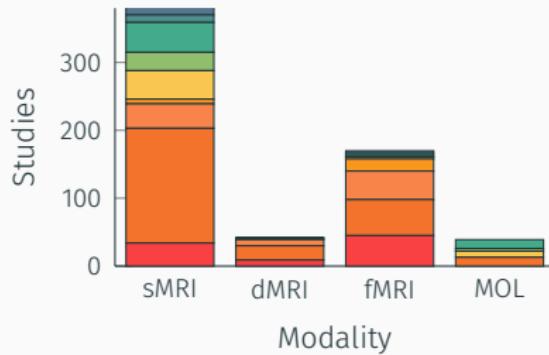
Afshin Shoibei¹, Marjane Khodatian², Mahboobeh Jafari³, Parisa Mordinian⁴, Mitra Rezaei⁵, Roohallah Alizadehsani⁶, Fahime Khozeinreh⁶, Juan Manuel Gorric⁷, Jonathan Heras⁸, Maryam Panahazar⁹, Saeid Nahavandi⁸, U Rajendra Acharya¹⁰



Diagnosis

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

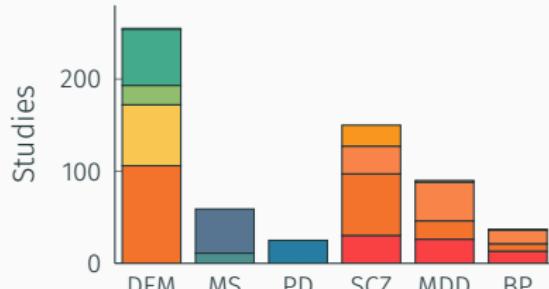
by Nida Aslam^{1,*} , Irfan Ulta Khan¹ , Asma Bashashati¹, Fatima A. Alghool¹, Menna Abouelrour¹ , Noorah M. Alsuwayyan¹, Rawaa K. Alturaiif¹, Samira Brahimi², Sumayyah S. Aljamees¹ and Khaloud Al Ghandi³



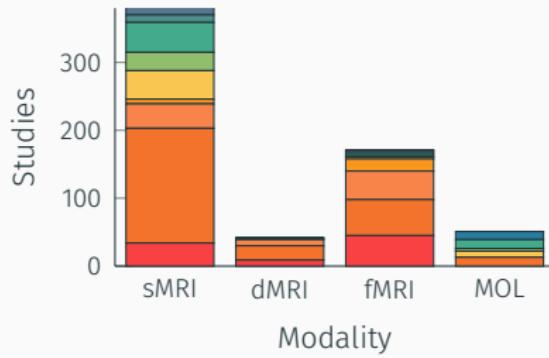
Modality



Approach



Diagnosis



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

Nikita Aggarwal¹ · B. S. Saini¹ · Savita Gupta²

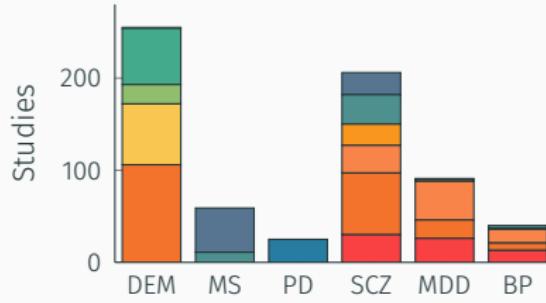


Approach

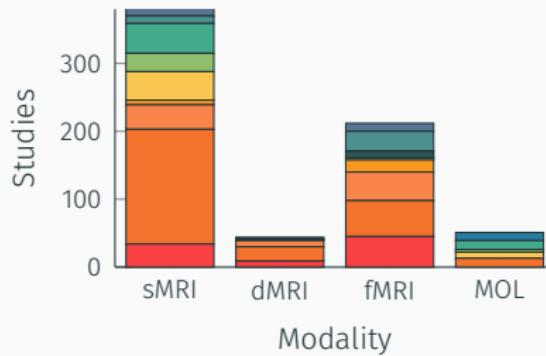


Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review
Renato de Filippi,^{1*} Elvira Anna Carboni,^{1†} Raffaele Gaetano,¹ Antonella Bruni,¹ Valentina Puglisi,¹ Cristina Sepura-Garcia,² and Pasquale De Fazio¹

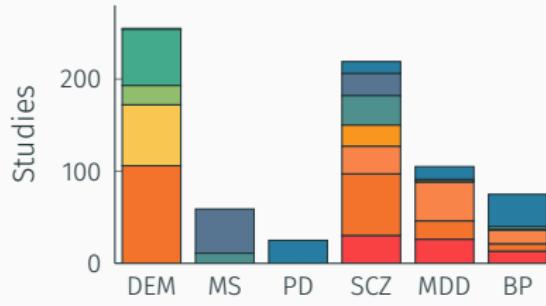
Machine learning techniques for the Schizophrenia diagnosis:
a comprehensive review and future research directions
Shradha Verma¹ · Tripti Goel¹ · M. Tanveer² · Weiping Ding³ · Rahul Sharma¹ · R. Murugan¹



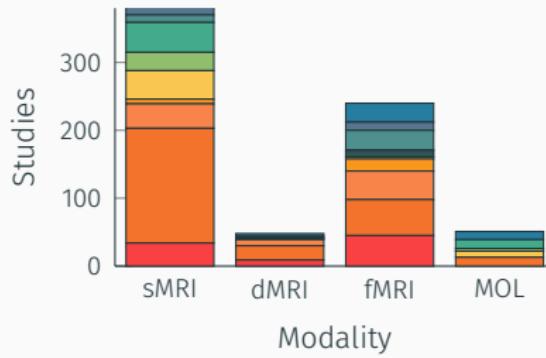
Diagnosis



Approach



Diagnosis

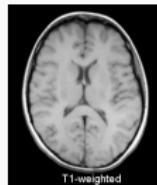


Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

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



Other structural MRI modalities



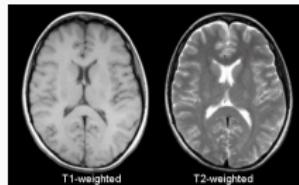
T1-weighted



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



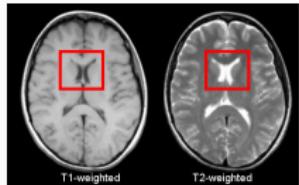
Other structural MRI modalities



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



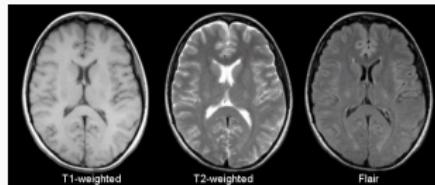
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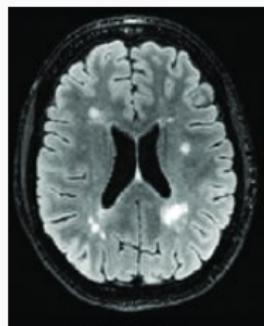
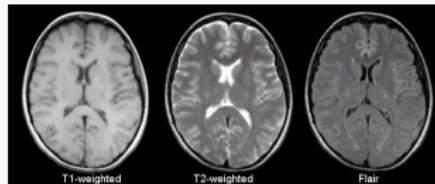
Other structural MRI modalities



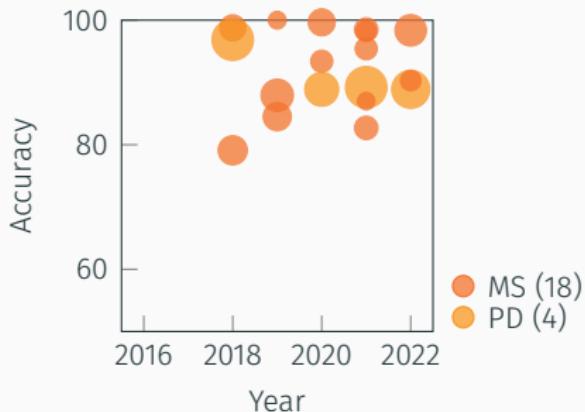
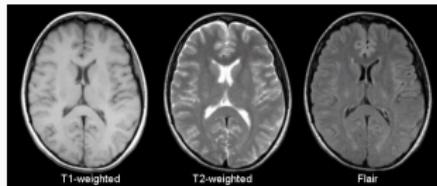
Preson D. C., (2006), MRI Basics, <https://case.edu/med/neurology/NR/MRI%20Basics>



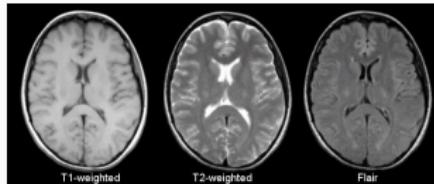
Other structural MRI modalities



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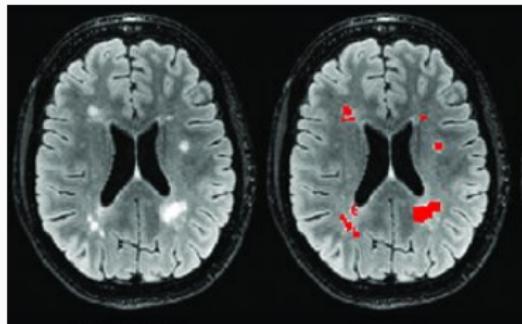
Other structural MRI modalities



T1-weighted

T2-weighted

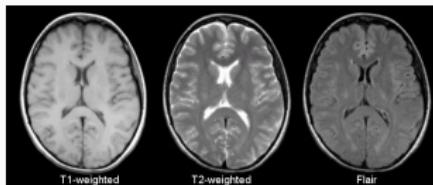
Flair



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.



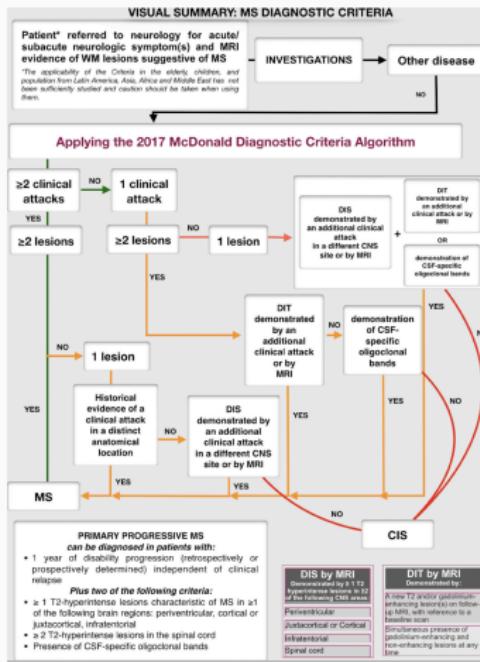
Other structural MRI modalities



T1-weighted

T2-weighted

Flair



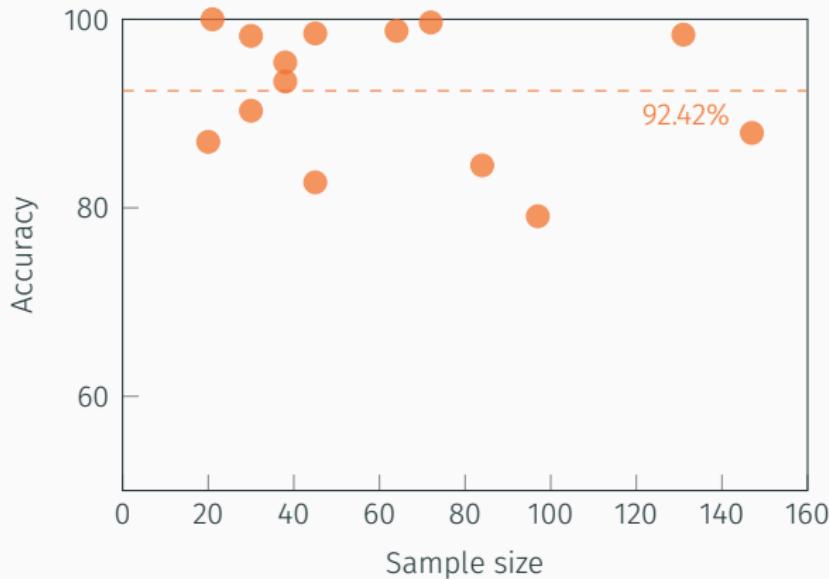
De Angelis, F., Brownlee, W. J., Chard, D. T., & Trip, S. A. (2019). New MS diagnostic criteria in practice. *Practical Neurology*, 19(1), 64-67



Other structural MRI modalities



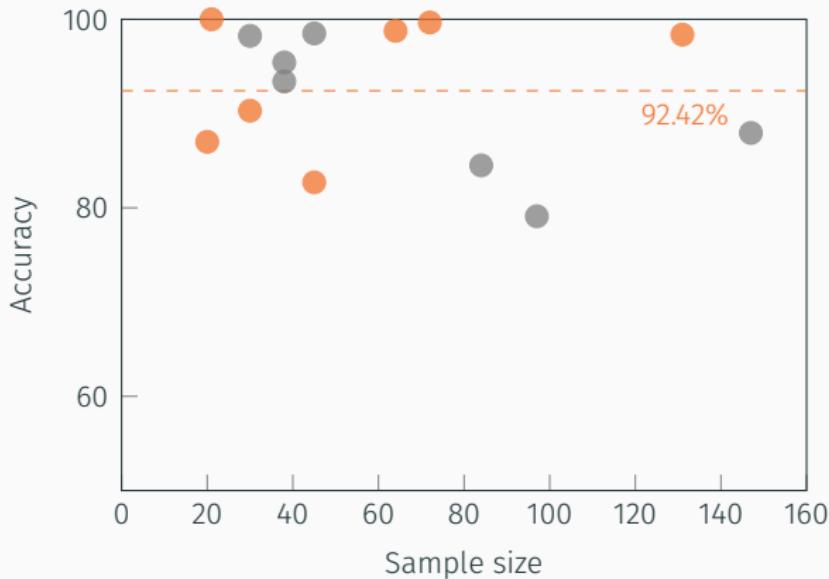
MS classification studies using non-T1w sMRI



Other structural MRI modalities



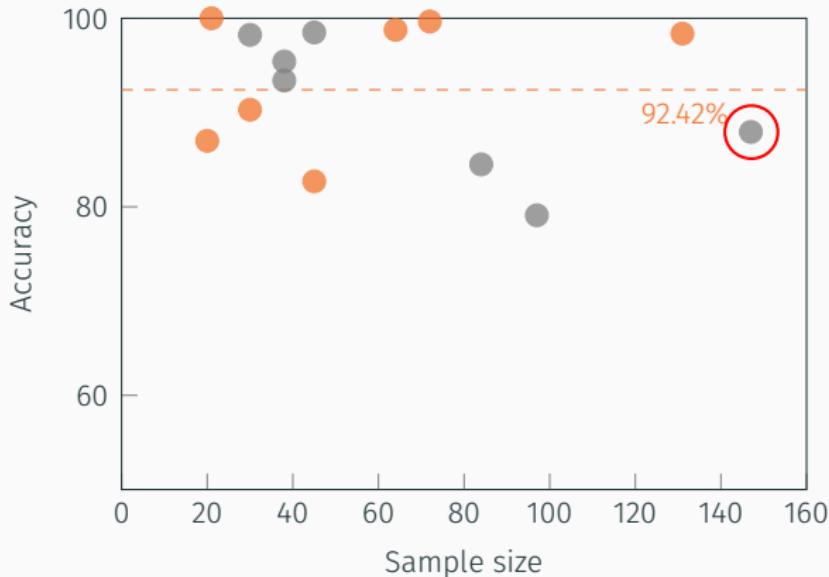
MS classification studies using non-T1w sMRI



Other structural MRI modalities



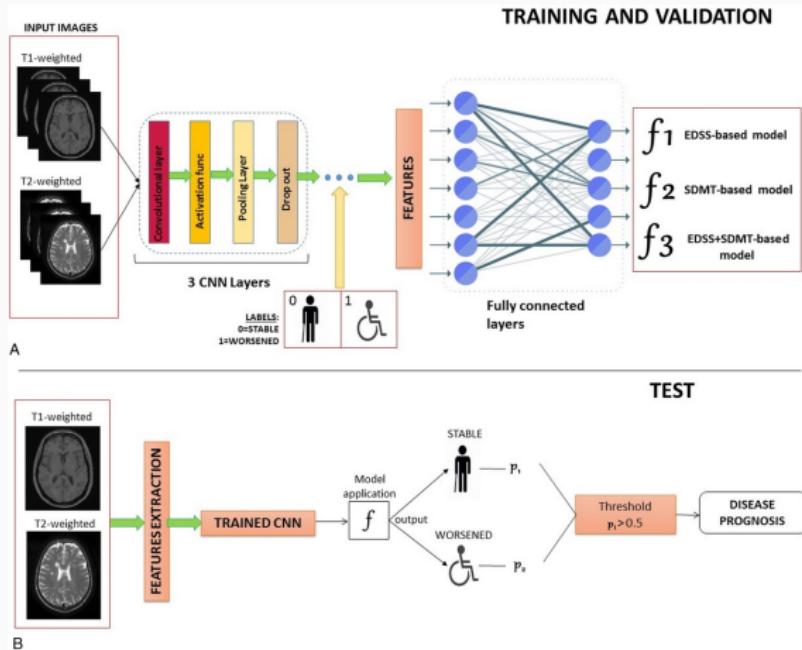
MS classification studies using non-T1w sMRI



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



Other structural MRI modalities



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



		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

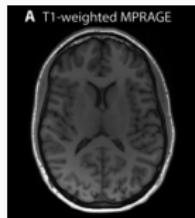


Other structural MRI modalities

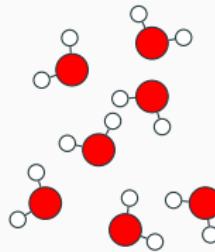
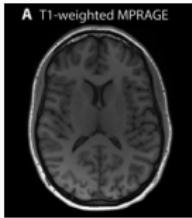
- (Non T1-weighted) structural MRI
 - Most prevalent in studies classifying MS and PD, yielding high accuracies (~90%).
 - T2 intimately linked with MS due to its efficacy at exposing characteristic lesions.
 - Machine learning models trained on T1 and T2-weighted scans shown by Storelli et al. to predict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



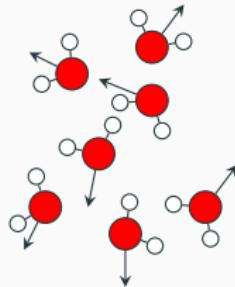
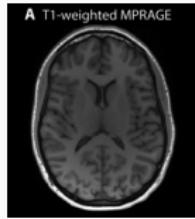
Diffusion MRI



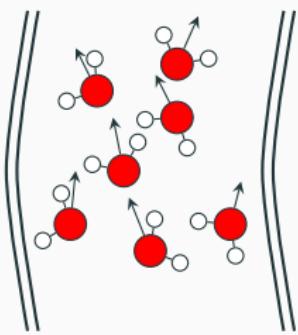
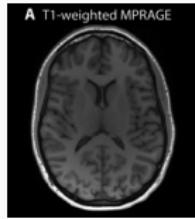
Diffusion MRI



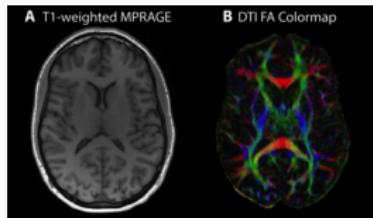
Diffusion MRI



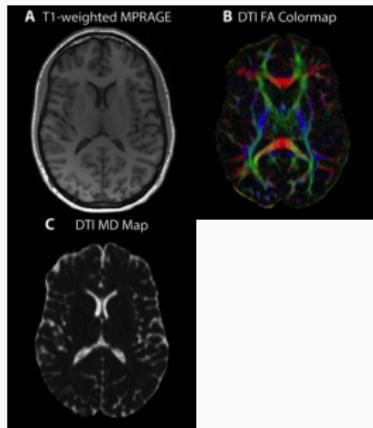
Diffusion MRI



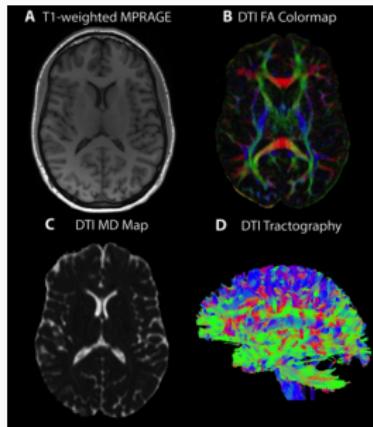
Diffusion MRI



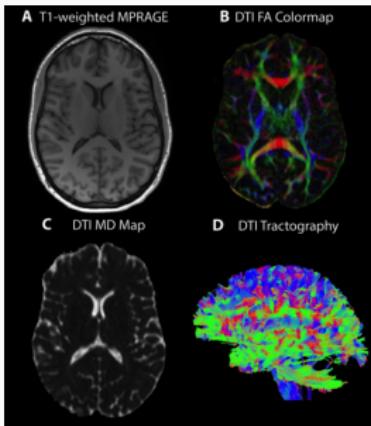
Diffusion MRI



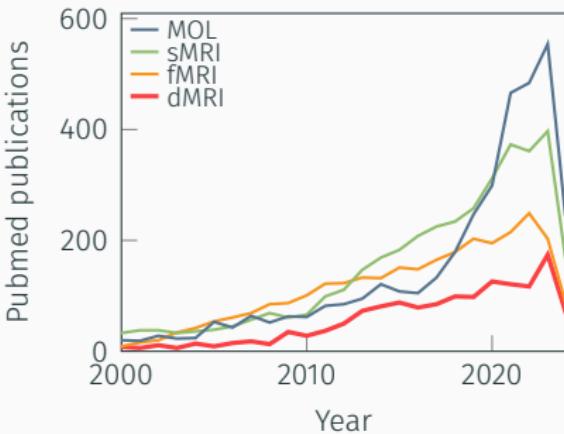
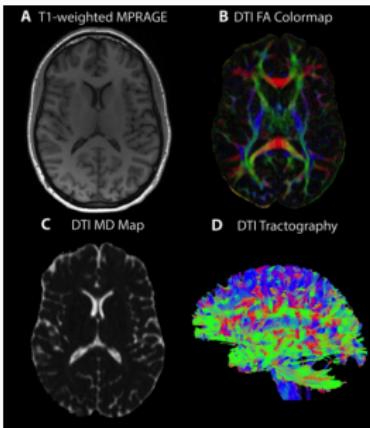
Diffusion MRI



Diffusion MRI



Diffusion MRI



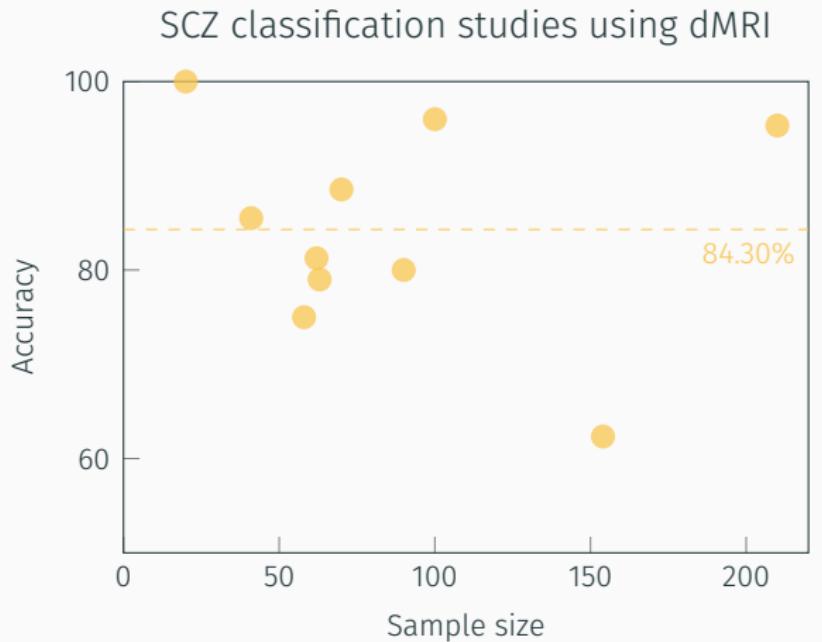
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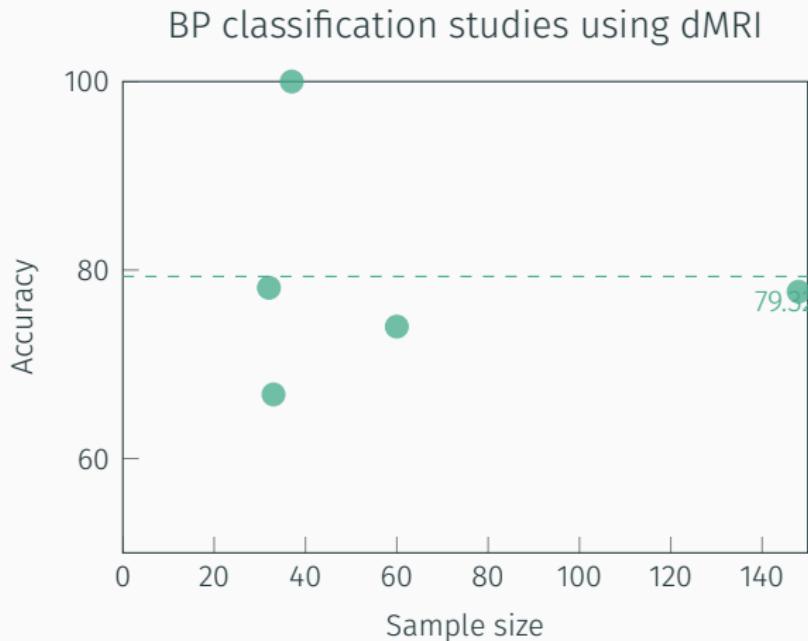
sMRI: ((structural[Title] AND MRI[Title]) OR smRI[Title] OR T1[Title] OR T2[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)

fMRI: ((functional[Title] AND MRI[Title]) OR fmRI[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)

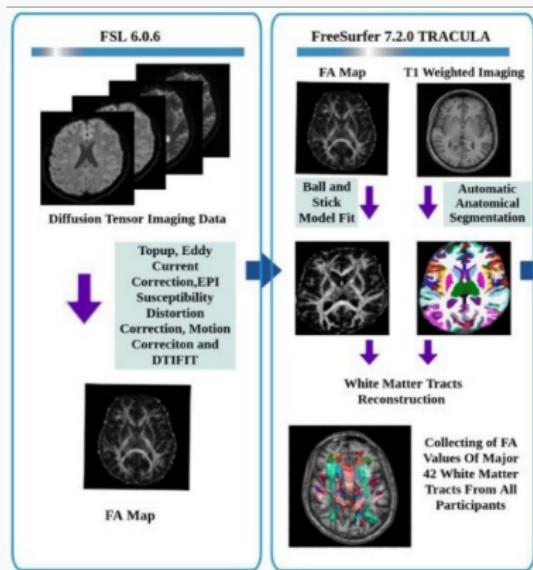
dMRI: ((diffusion[Title] AND MRI[Title]) OR dMRI[Title] OR DTI[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)







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

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

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

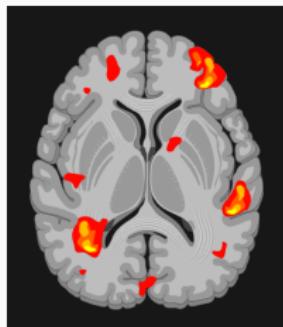
- (Non T1-weighted) structural MRI (T2/FLAIR)
 - Most prevalent in studies classifying MS and PD, yielding high accuracies (~90%).
 - Intimately linked with MS due to their efficacy at exposing characteristic lesions.
 - Potentially more useful than T1-weighted MRI for differentially diagnosing PD and PSP, as demonstrated by Talai et al.
- Diffusion MRI
 - Relatively few prediction studies found. Those that exist are for various disorders, mostly mental disorders (SCZ, MDD, BP) with varying accuracies (60-100%).
 - Used by Saglam et al. to differentially diagnose SCZ and BP with 80% accuracy.



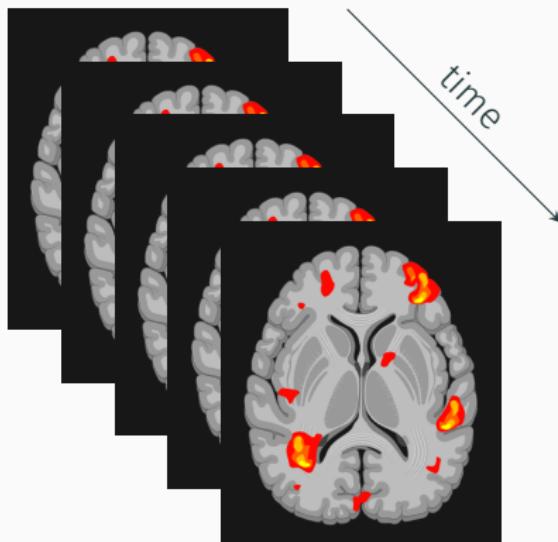
Functional Magnetic Resonance Imaging (fMRI)



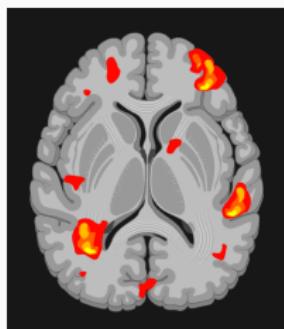
Functional Magnetic Resonance Imaging (fMRI)



Functional Magnetic Resonance Imaging (fMRI)



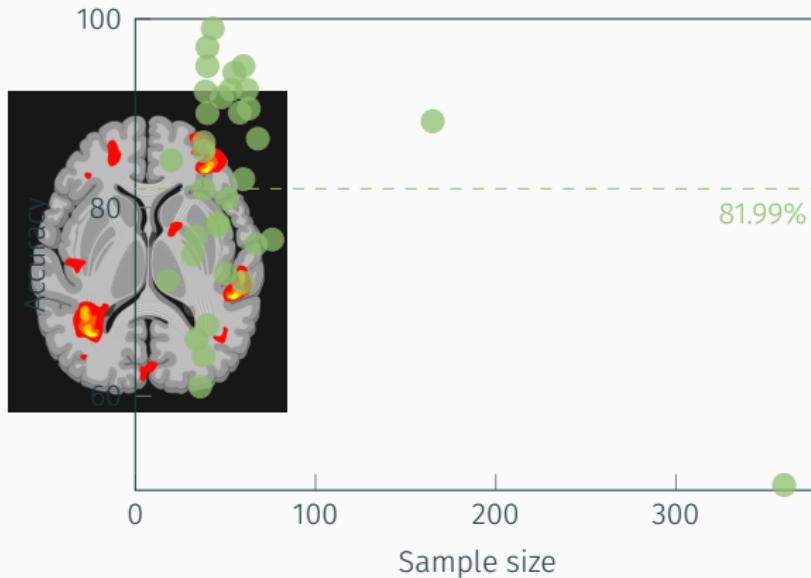
Functional Magnetic Resonance Imaging (fMRI)



Functional Magnetic Resonance Imaging (fMRI)



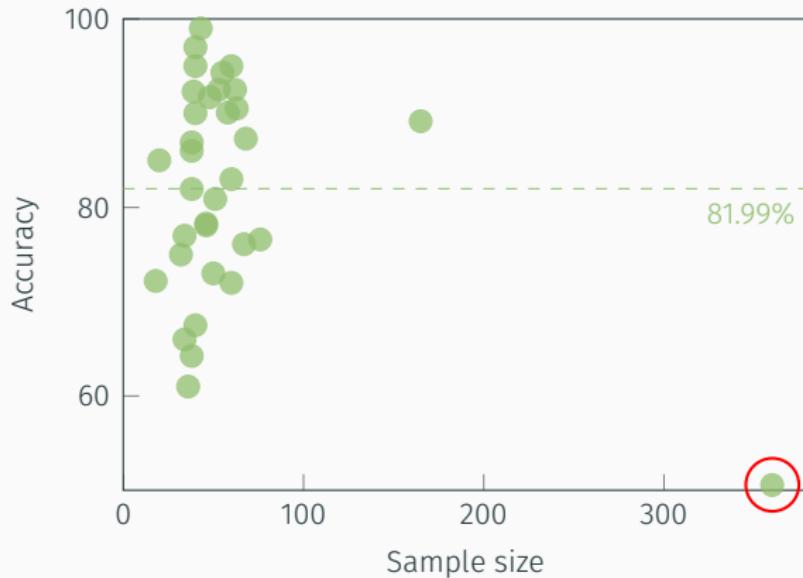
MDD classification studies using fMRI



Functional Magnetic Resonance Imaging (fMRI)



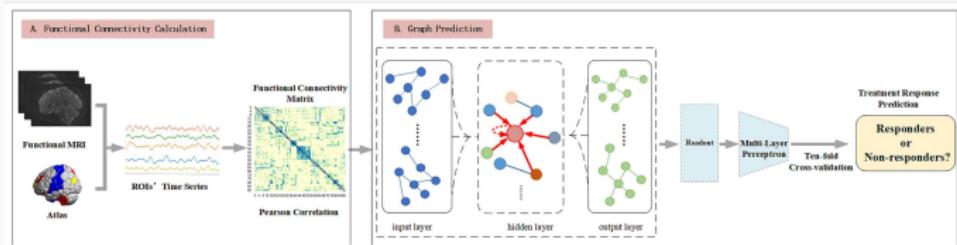
MDD classification studies using fMRI



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



Functional Magnetic Resonance Imaging (fMRI)



Duan, J., Li, Y., Zhang, X., Dong, S., Zhao, P., Liu, J., ... & Wang, F. (2023). Predicting treatment response in adolescents and young adults with major depressive episodes from fMRI using graph isomorphism network. *NeuroImage: Clinical*, 40, 103534



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
FDGN	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.



Duan, J., Li, Y., Zhang, X., Dong, S., Zhao, P., Liu, J., ... & Wang, F. (2023). Predicting treatment response in adolescents and young adults with major depressive episodes from fMRI using graph isomorphism network. *NeuroImage: Clinical*, 40, 103534

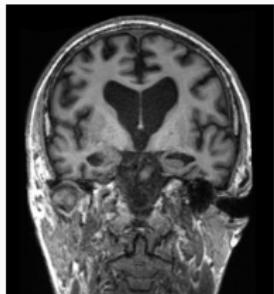


Functional Magnetic Resonance Imaging (fMRI)

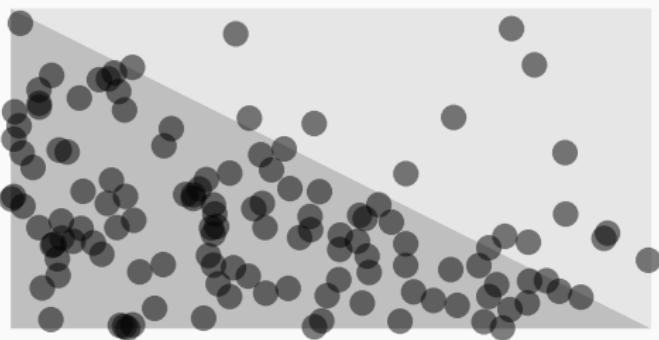
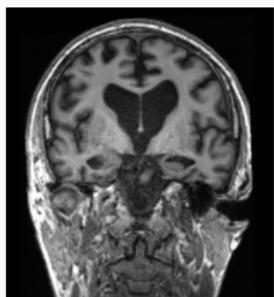
- (Non T1-weighted) structural MRI (T2/FLAIR)
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 - Potentially more useful than T1-weighted MRI for differentially diagnosing PD and PSP, as demonstrated by Talai et al.
- Diffusion MRI
 - Relatively few prediction studies found. Those that exist are for various disorders, mostly mental disorders (with varying 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 DEM with 81% accuracy.
- Functional MRI



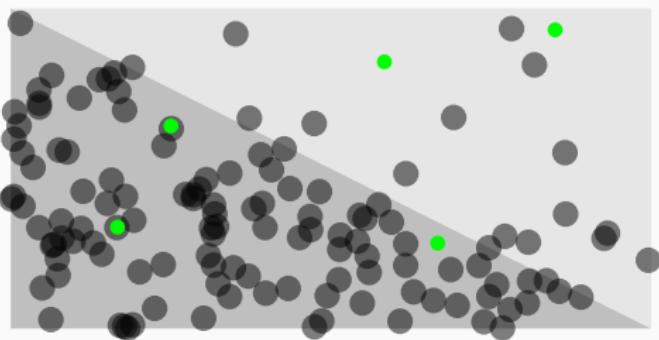
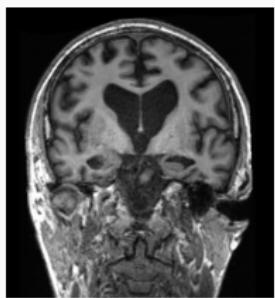
Molecular imaging



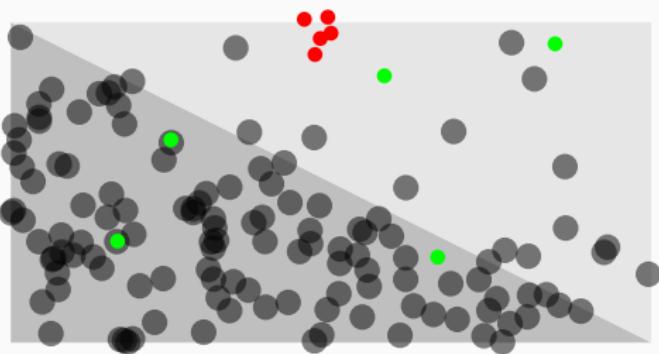
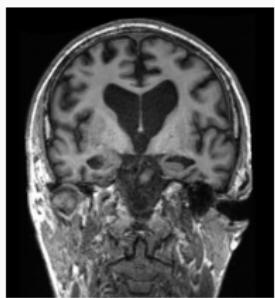
Molecular imaging



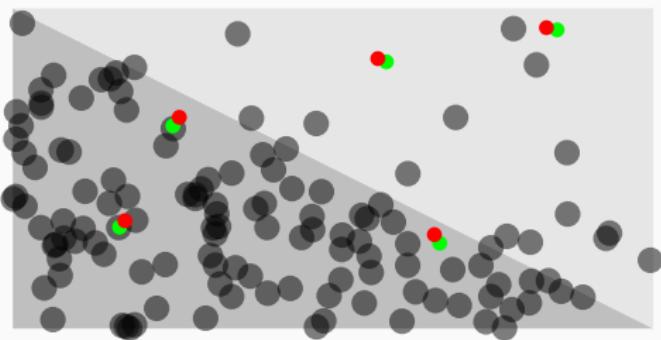
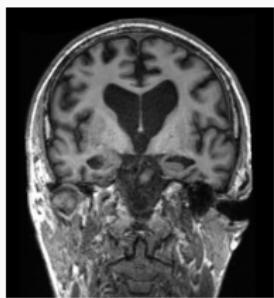
Molecular imaging



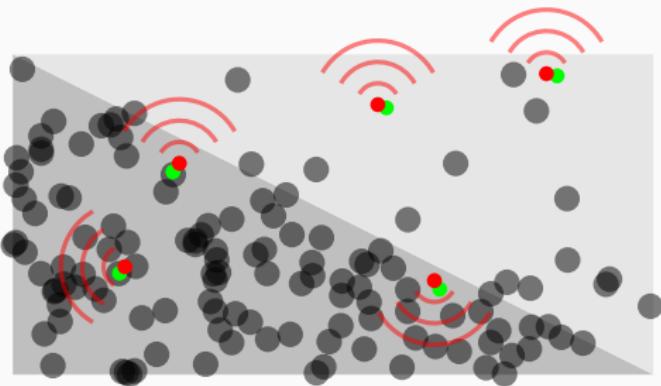
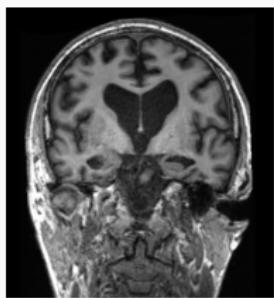
Molecular imaging



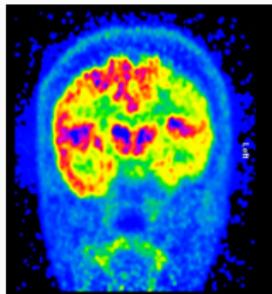
Molecular imaging



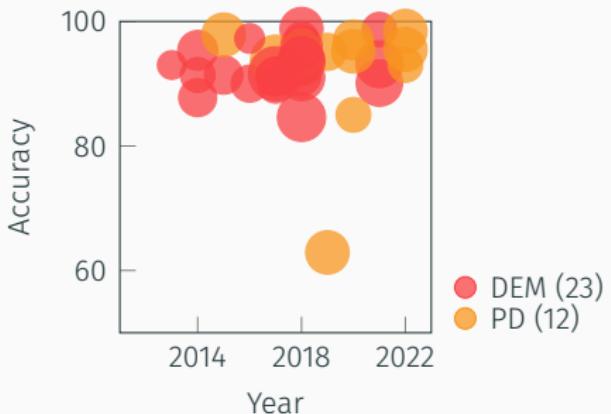
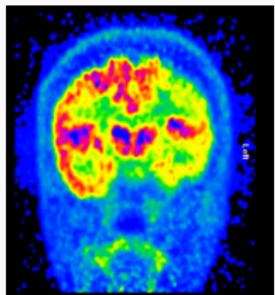
Molecular imaging



Molecular imaging

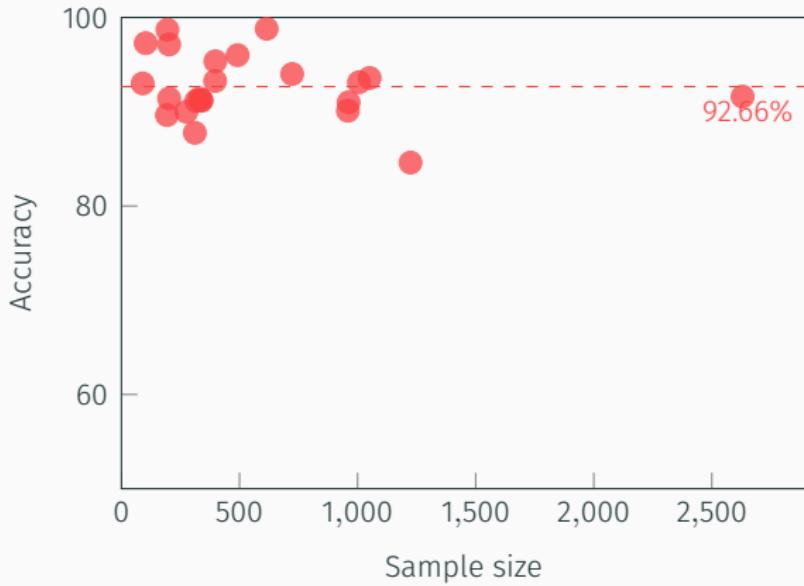


Molecular imaging

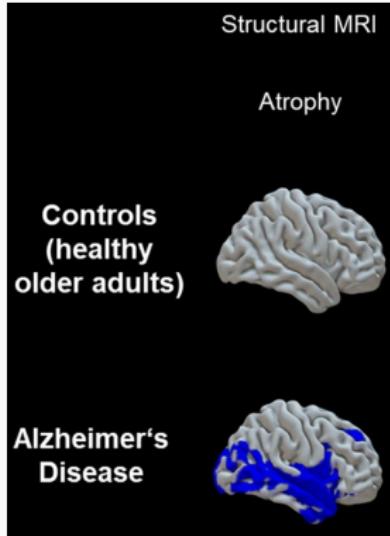


Molecular imaging

DEM classification studies using molecular imaging



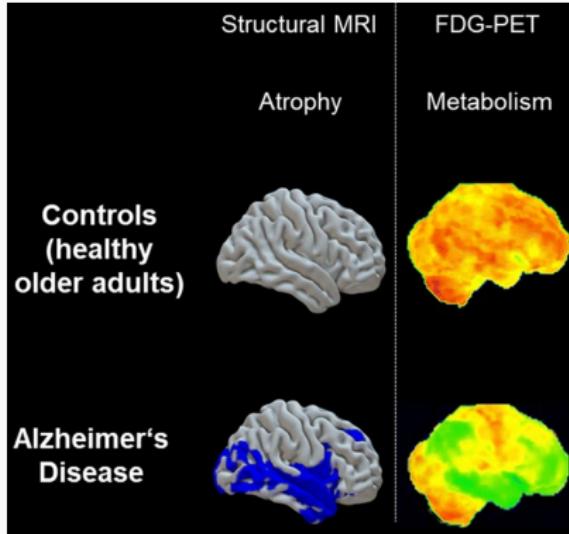
Molecular imaging



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



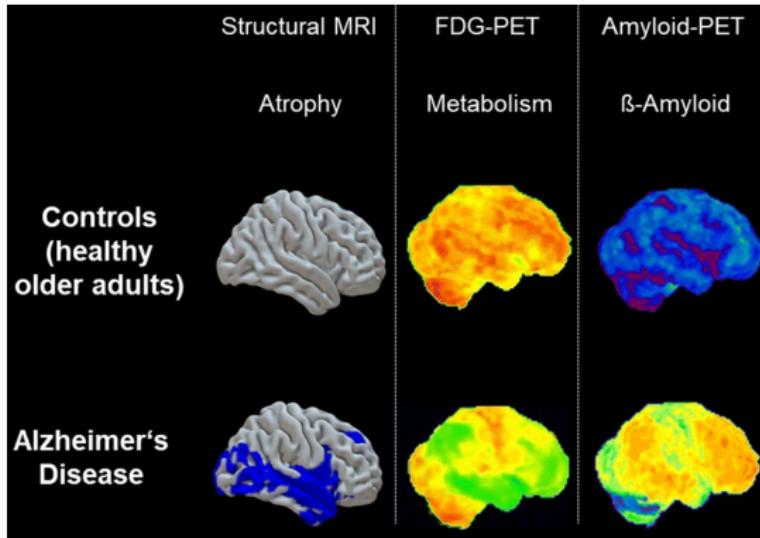
Molecular imaging



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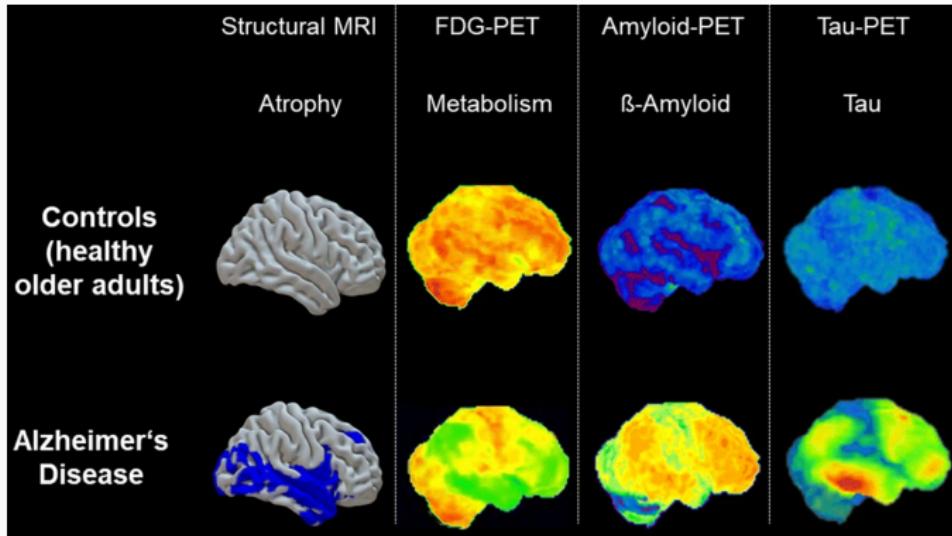
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Molecular imaging



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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

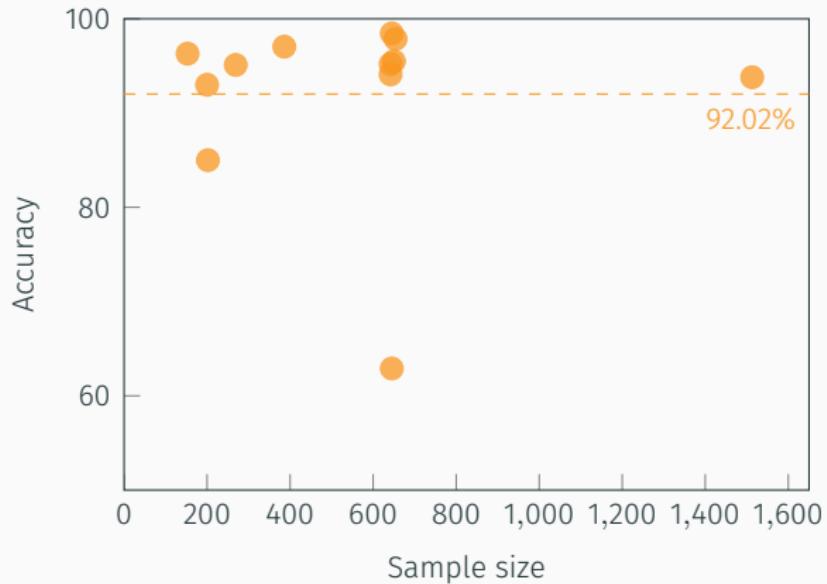
Clinical syndromes commonly seen with AD may also be caused by disorders other than AD and therefore clinical presentation alone is not diagnostic of AD

The same AD biology may result in different phenotypic presentations"

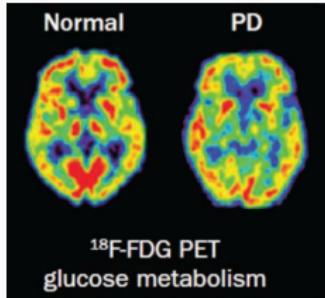


Molecular imaging

PD classification studies using molecular imaging

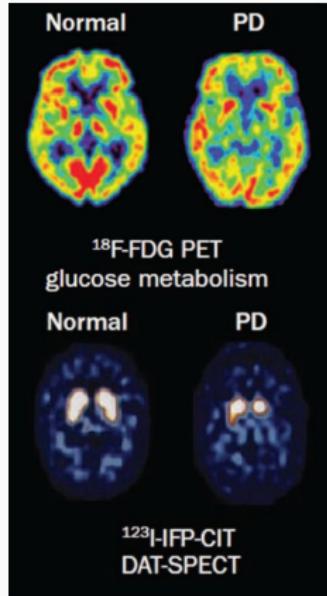


Molecular imaging



Pagano, G., Niccolini, F., & Politis, M. (2016). Imaging in Parkinson's disease. Clinical Medicine, 16(4), 371

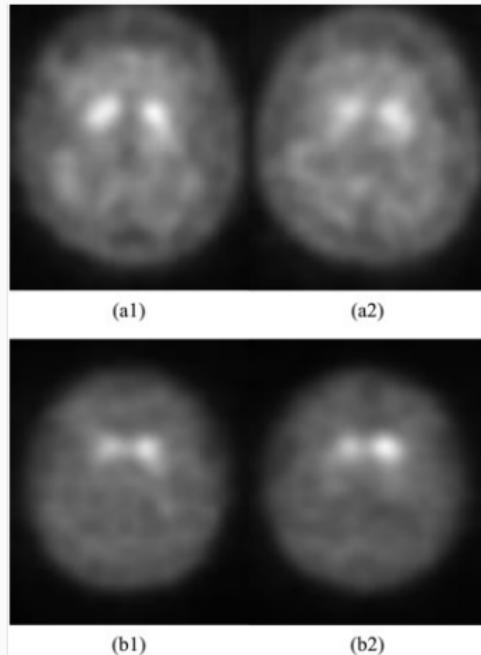
Molecular imaging



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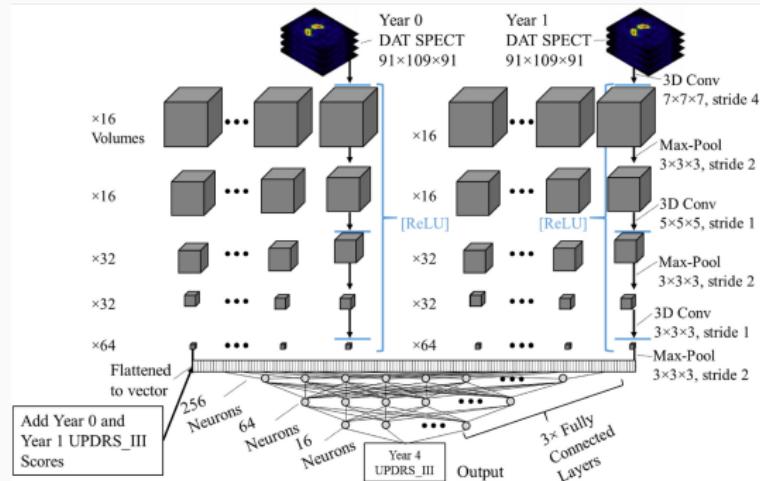
Molecular imaging



Adams, M. P., Rahmim, A., & Tang, J. (2021). Improved motor outcome prediction in Parkinson's disease applying deep learning to DaTscan SPECT images. *Computers in Biology and Medicine*, 132, 104312



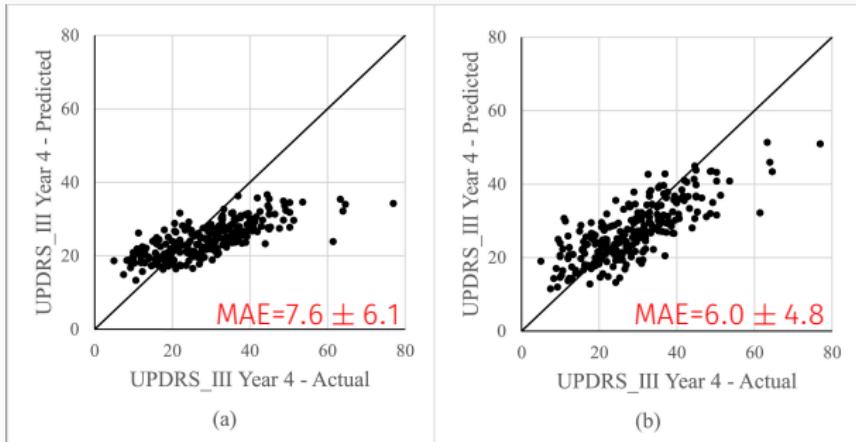
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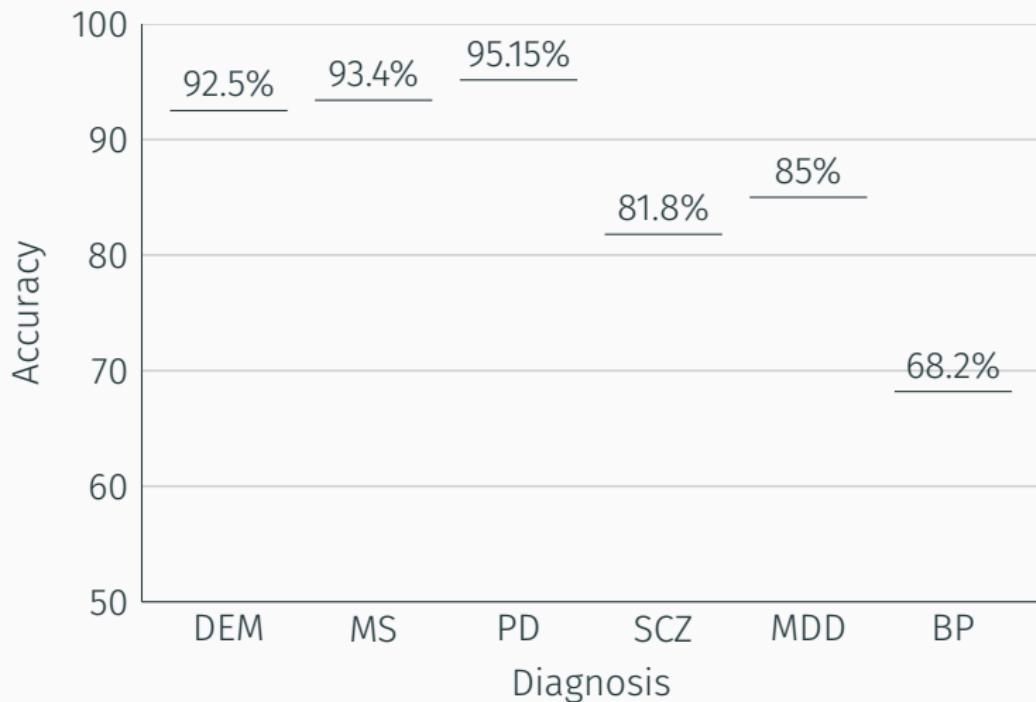


The future of neuroimaging-based prediction

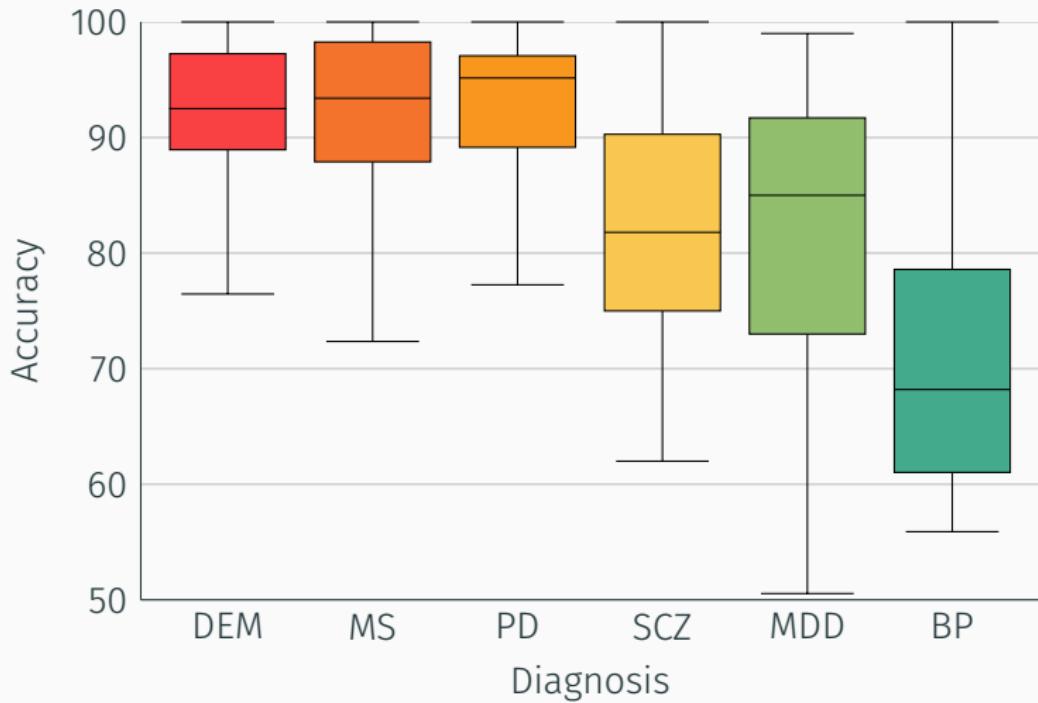


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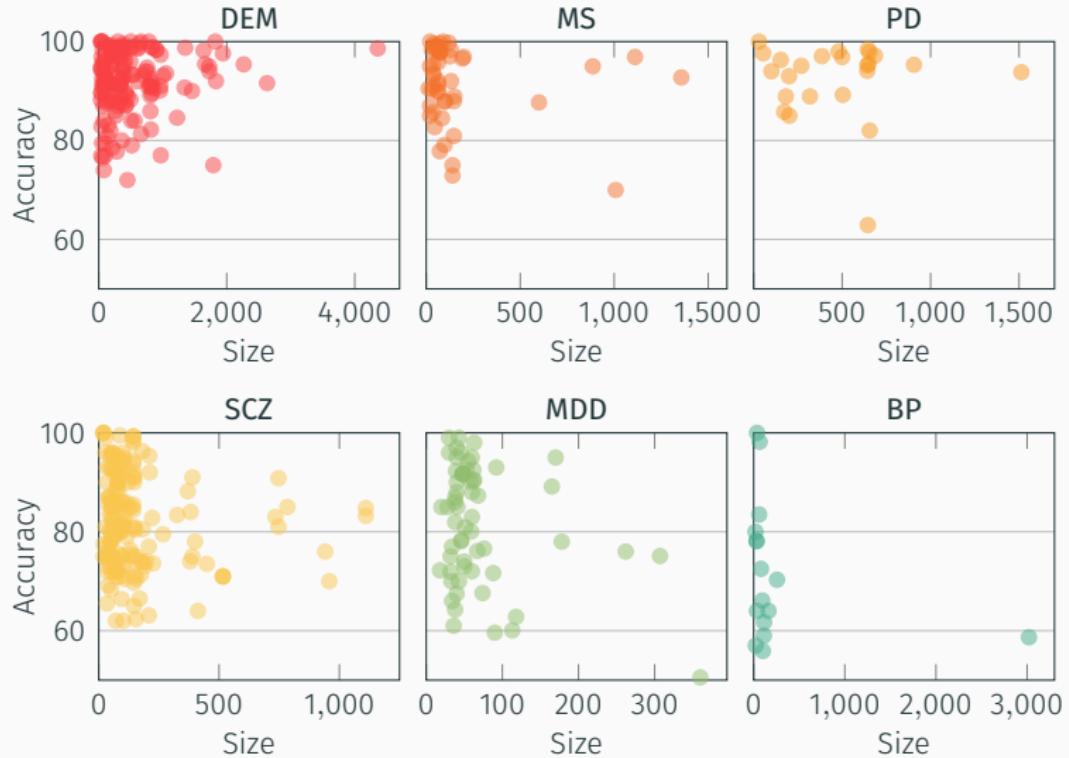
Challenges: Predictiveness



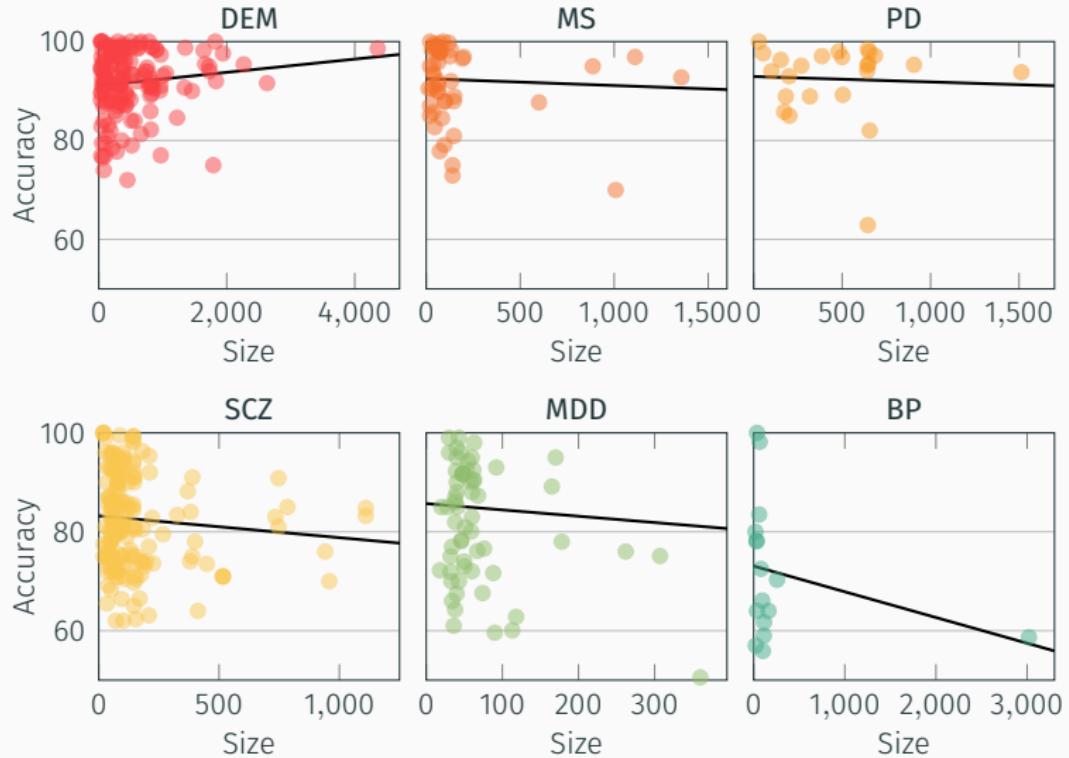
Challenges: Predictiveness



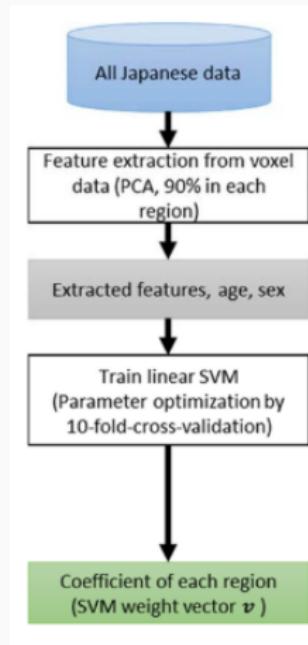
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Challenges: Predictiveness



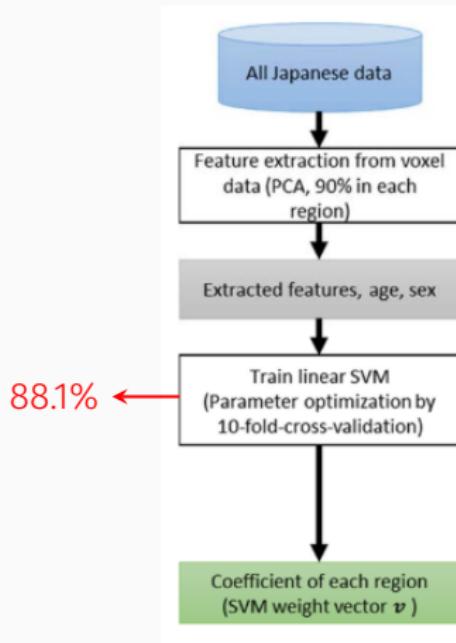
Challenges: Generalization



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



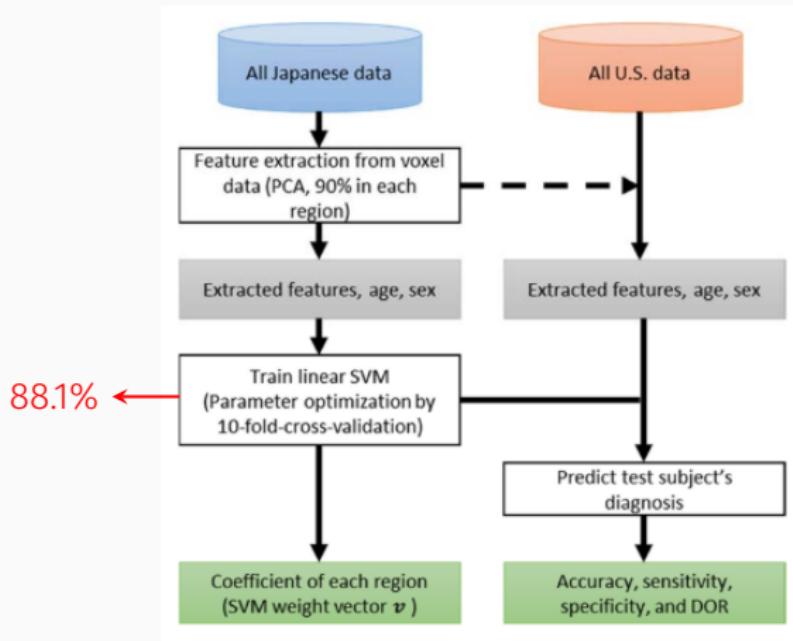
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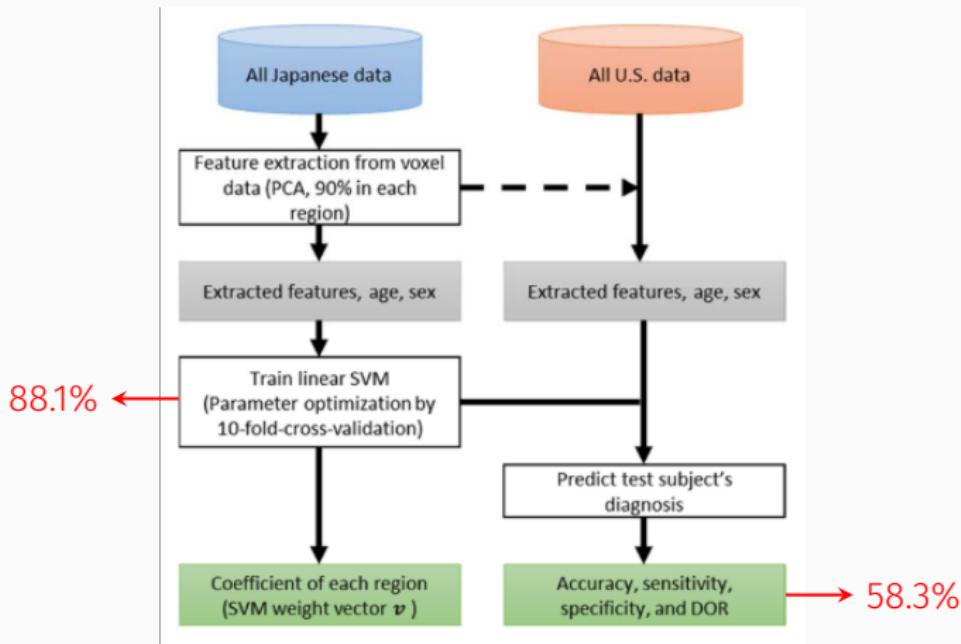
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Challenges: Generalization



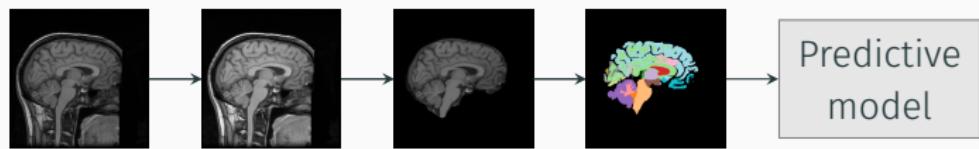
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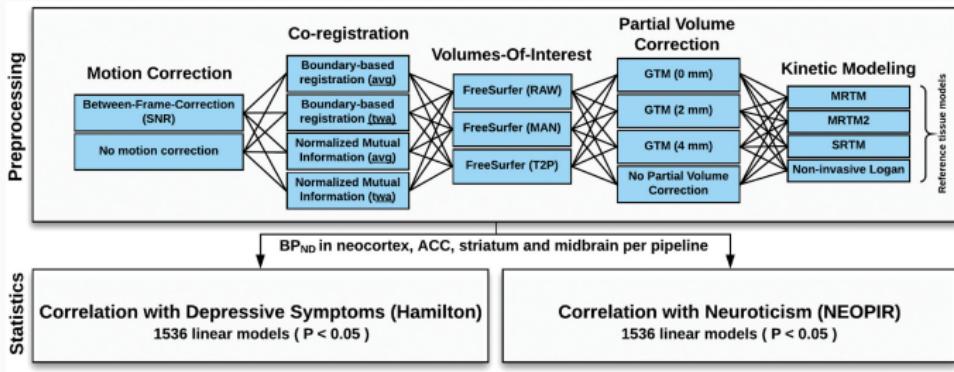
Challenges: Researcher degrees of freedom



Challenges: Researcher degrees of freedom



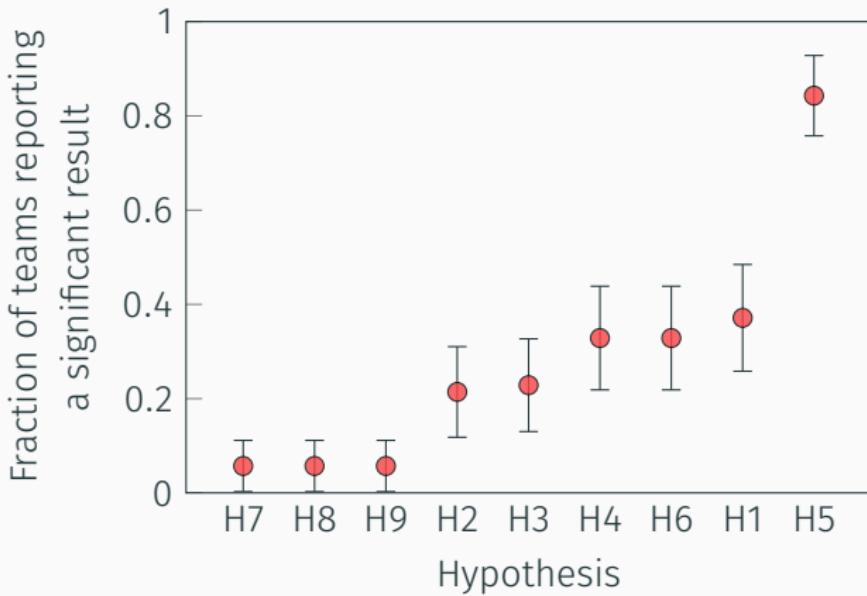
Challenges: Researcher degrees of freedom



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

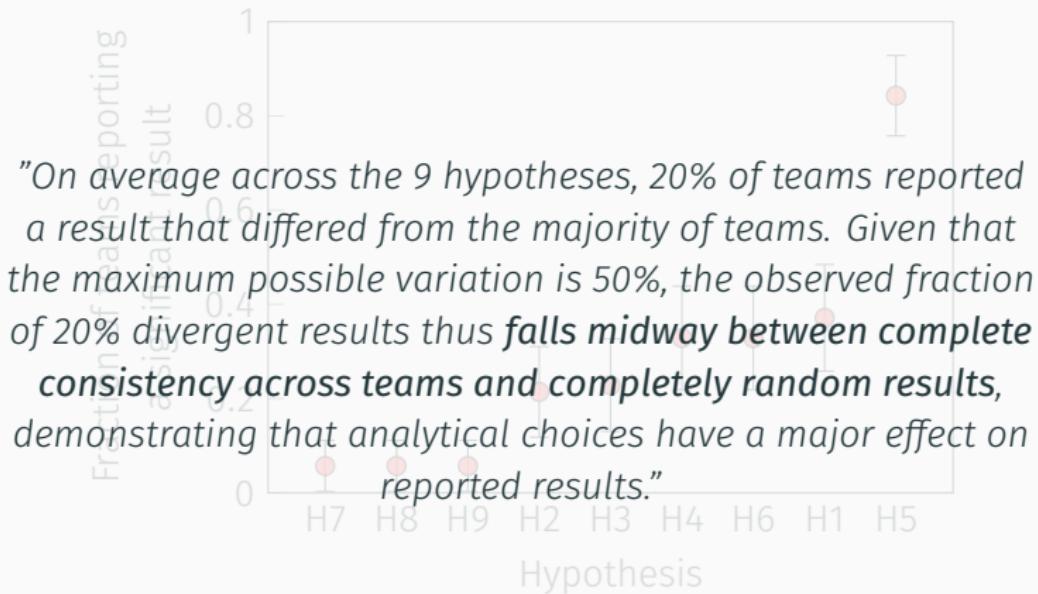


Adapted from Botvinik-Nezer et al., 2020

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



Adapted from Botvinik-Nezer et al., 2020

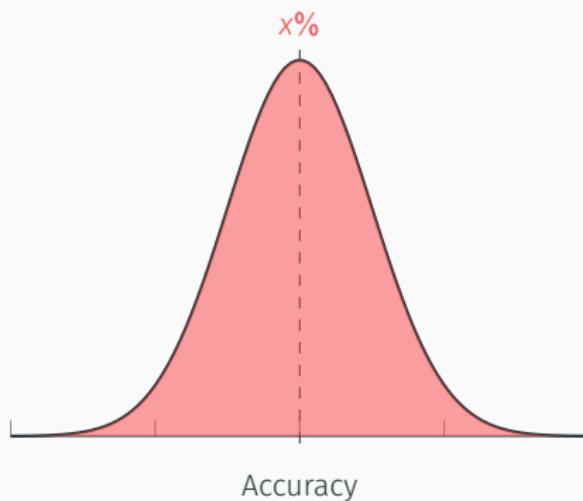
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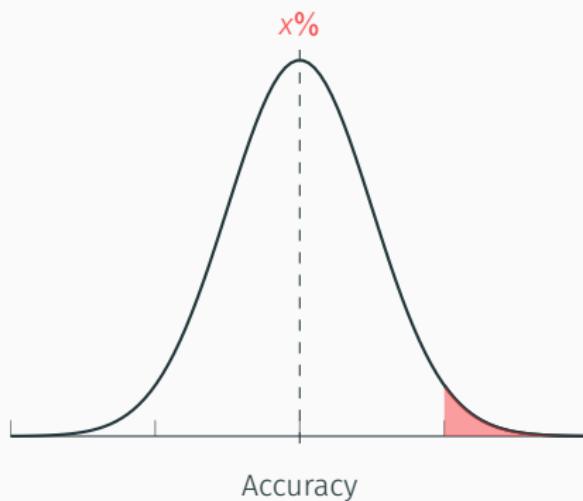
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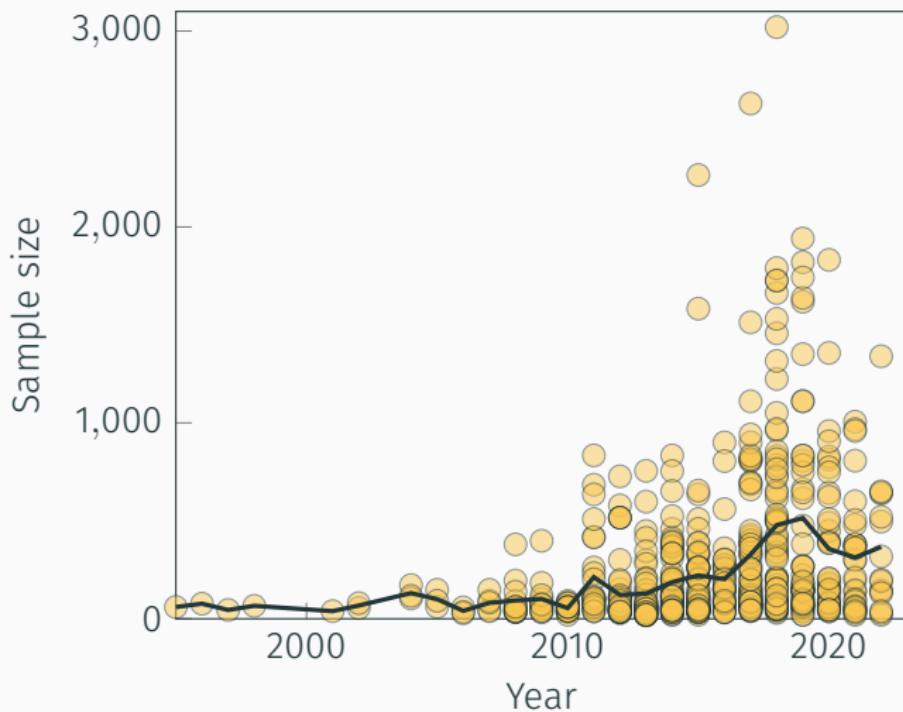
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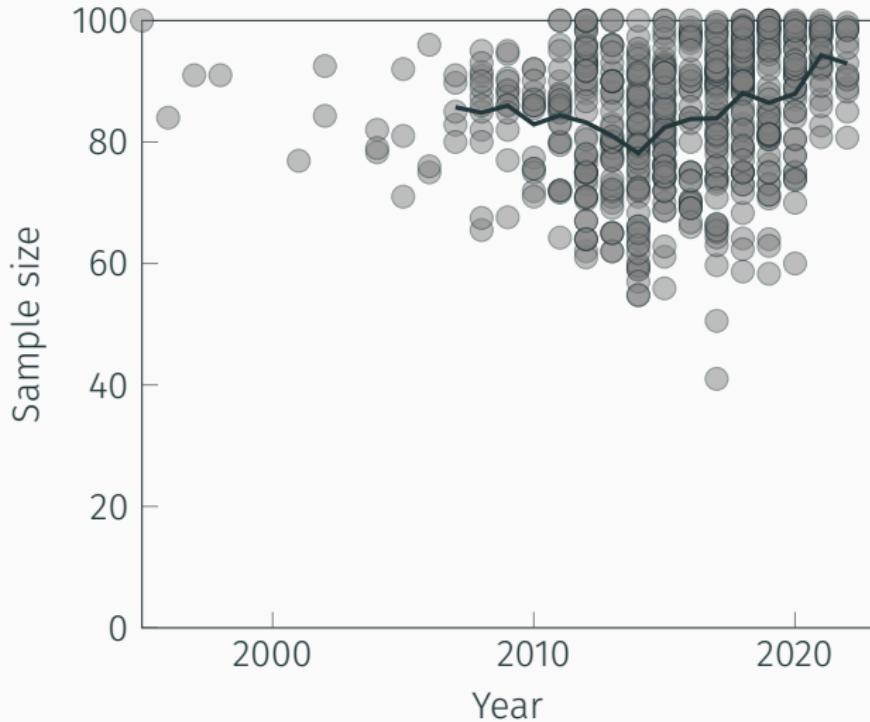
Challenges: Researcher degrees of freedom



Opportunities: Larger datasets



Opportunities: Better methods



Opportunities: Better methods

