

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

Esten H. Leonardsen

26.10.23



**UNIVERSITETET
I OSLO**

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



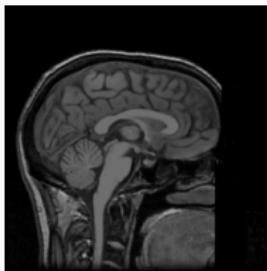
Background

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



Background

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



Bert from FreeSurfer 7.3

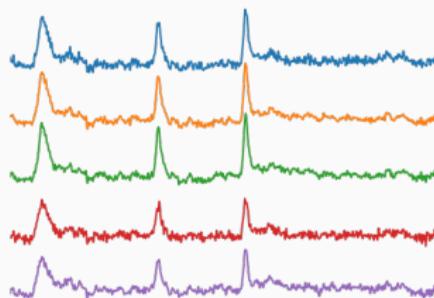


Background

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



Bert from FreeSurfer 7.3



Sample from the MNE library



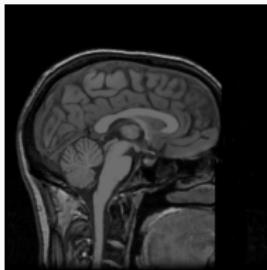
Background

- 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

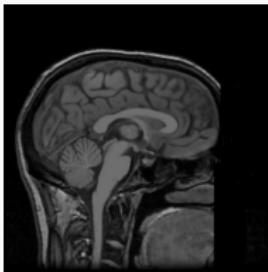


Bert from FreeSurfer 7.3

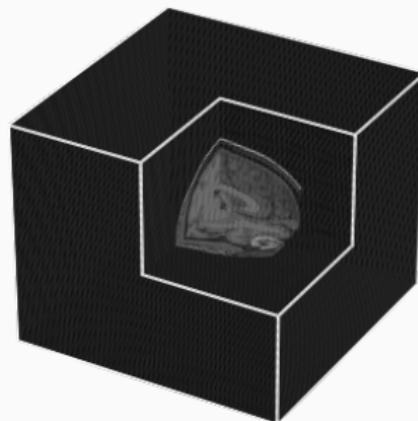


Background

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

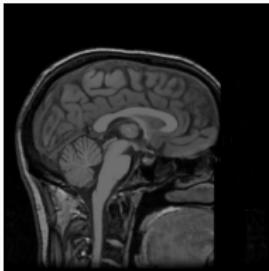


Bert from FreeSurfer 7.3

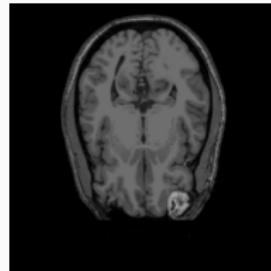
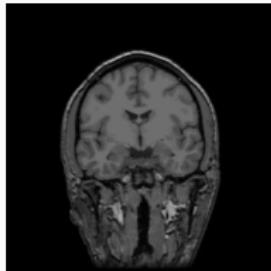


Background

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



Bert from FreeSurfer 7.3

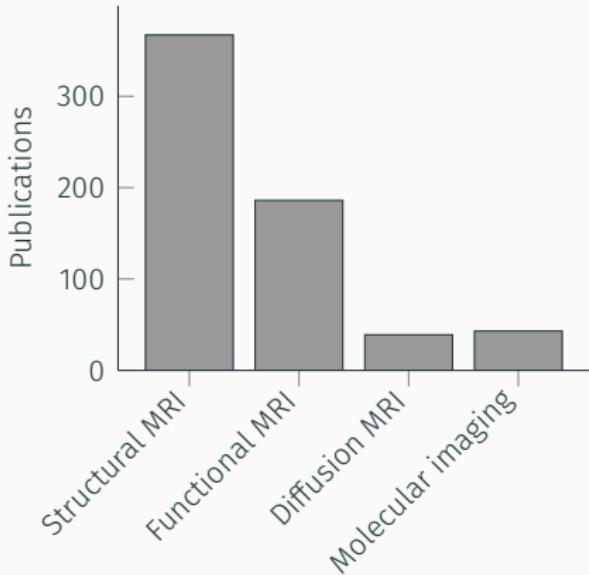


Background

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



Bert from FreeSurfer 7.3



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

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

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



Background

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

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)



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

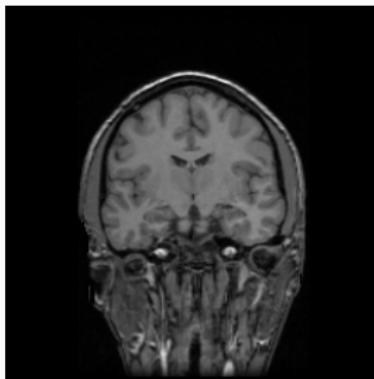


Generated by DALL-E 3



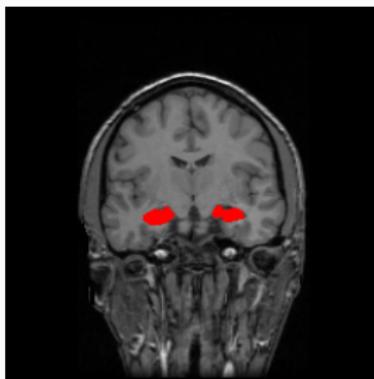
Background

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



Background

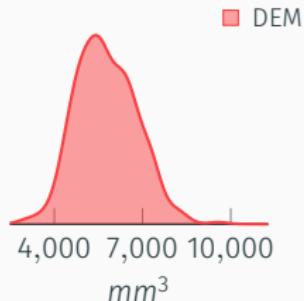
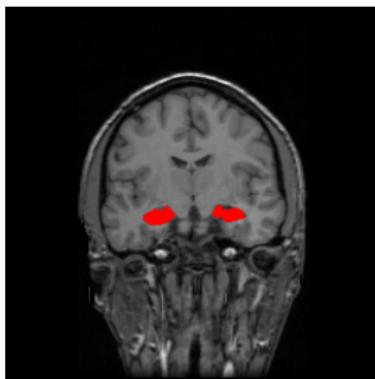
- The role of neuroimaging beyond T1-weighted MRI in the diagnosis and prediction of neuropsychiatric disorders



Background



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



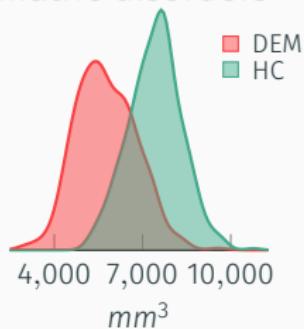
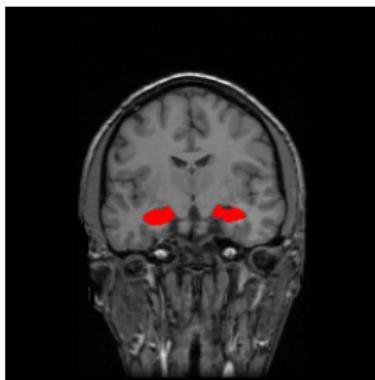
Data from ADNI

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.



Background

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



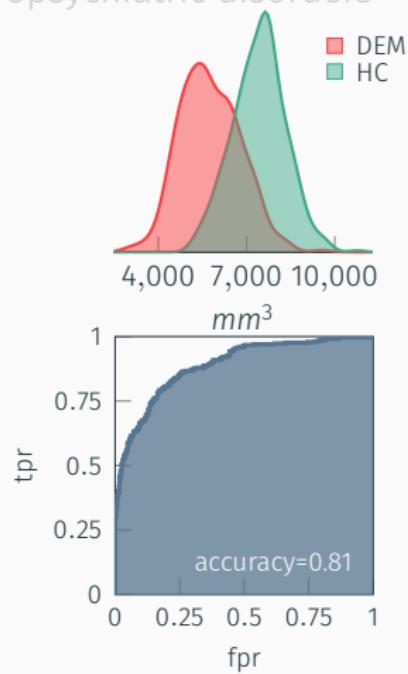
Data from ADNI

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



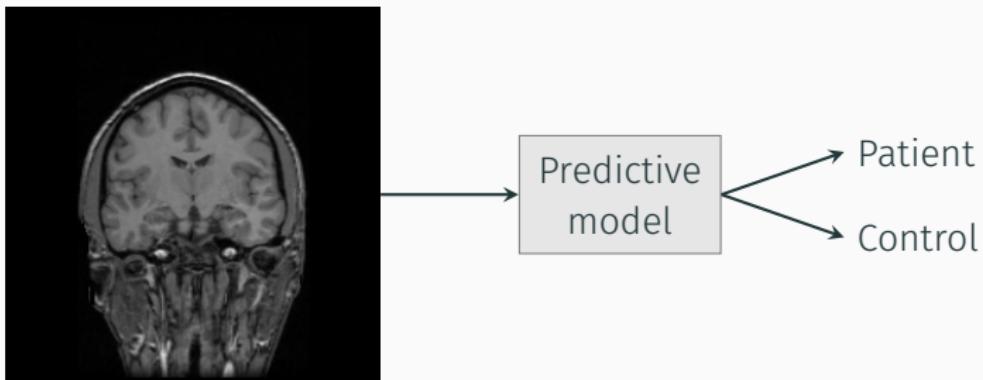
Background

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



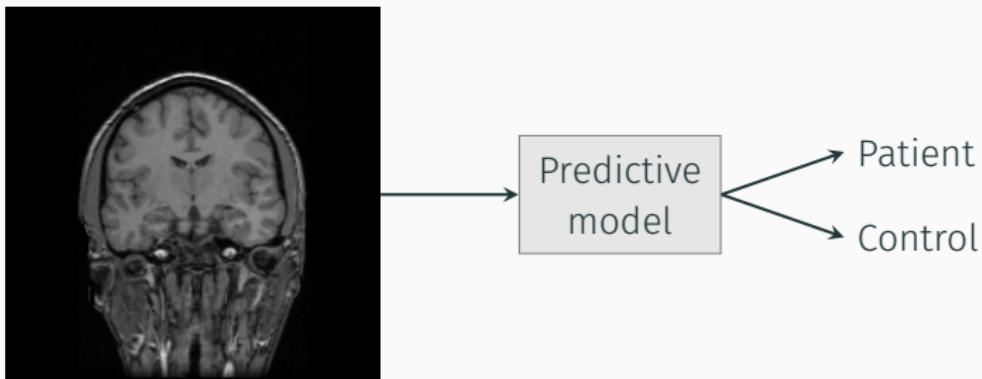
Background

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



Background

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



$$\text{accuracy} = \frac{\text{correct predictions}}{\text{all predictions}}$$



Neuroimaging modalities for diagnostic predictions



UNIVERSITETET
I OSLO

Approach

(Non-T1) structural MRI (sMRI)

Diffusion MRI (dMRI)

Functional MRI (fMRI)

Molecular imaging (MOL)



Approach

(Non-T1) structural MRI (sMRI)

Diffusion MRI (dMRI)

Functional MRI (fMRI)

Molecular imaging (MOL)

DEM MS PD SCZ MDD BP



Approach

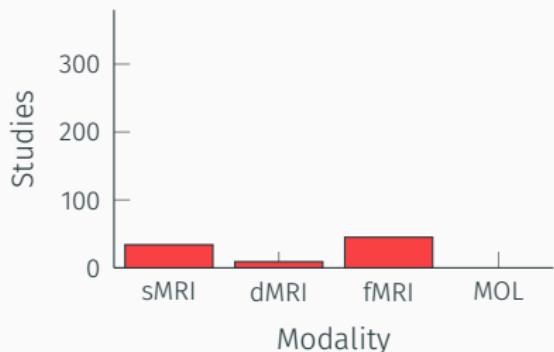
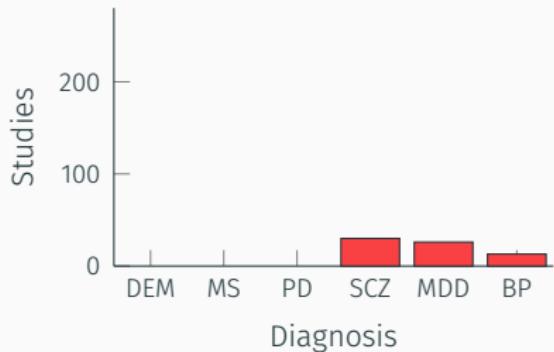
(Non-T1) structural MRI (sMRI)						
Diffusion MRI (dMRI)						
Functional MRI (fMRI)						
Molecular imaging (MOL)						

Data



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

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



Data

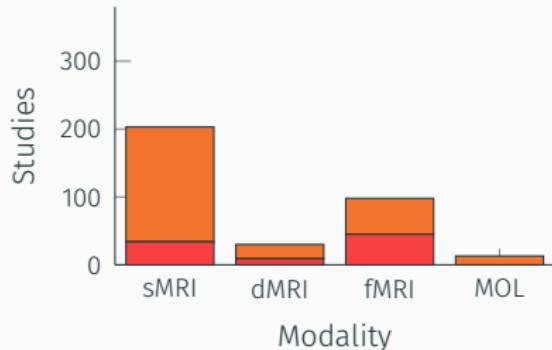
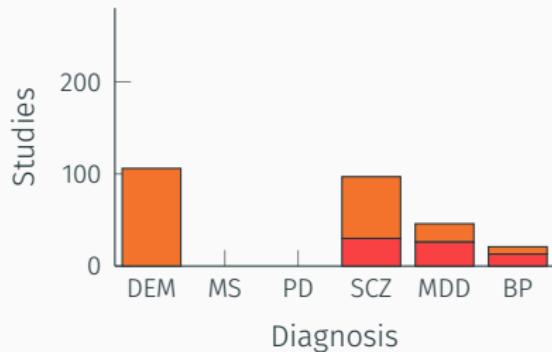


From estimating activation locality to predicting disorder: A review of pattern recognition for neuroimaging-based psychiatric diagnostics

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

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

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



Data



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

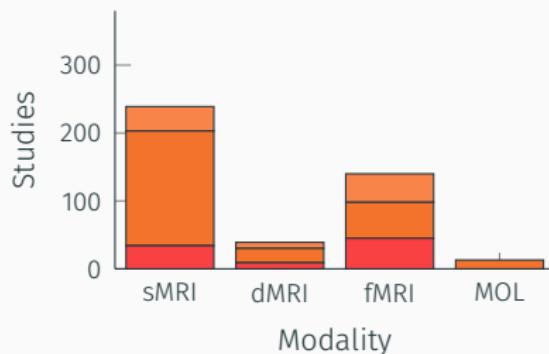
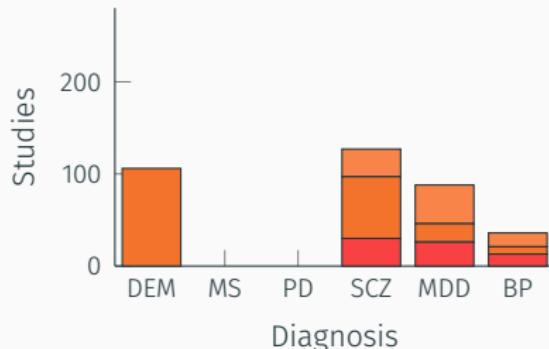
Thomas Wolters ^{a b} , Jan K. Buitelaar ^{c d}, Christian F. Beckmann ^{b c e}, Barbara Franke ^{a f}, Andre F. Marquand ^{a g}

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

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

Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun



Data



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

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

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

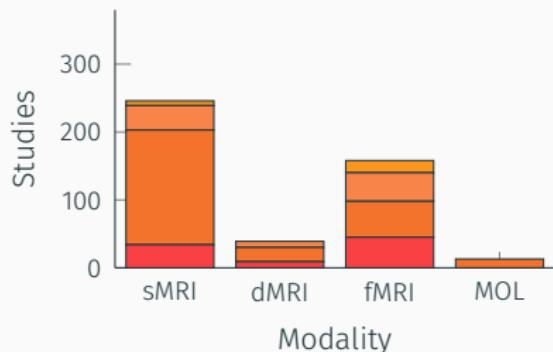
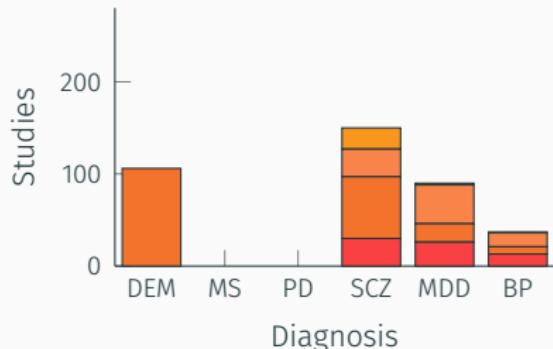
Mohammad R. ArbabiShirani^{a,b}, , Sergey Pliushch^a, Jing Sui^{a,c}, Vince D. Calhoun^{a,d}

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 Quaak³, Laurens van de Mortel³, Rajat Mani Thomas³, Guido van Wingen²



Data



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

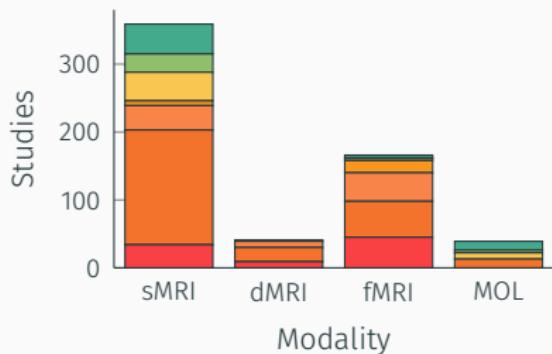
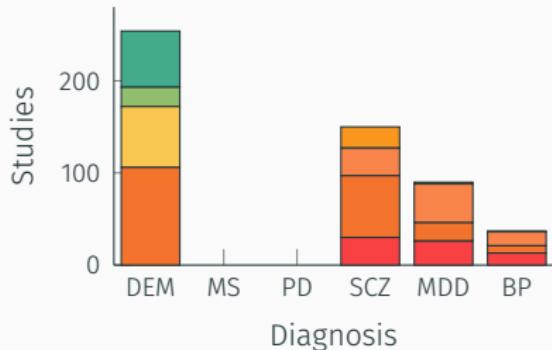
Mr Amir Ebrahimghahnavieh ³, Suhuai Luo ³, Raymond Chiong ²

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

Golrokh Mirzaei ², R., Hojjat Adeli ³

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

Sina Fathi ¹, Maryam Ahmadi ², Afshaneh Dehnad ³

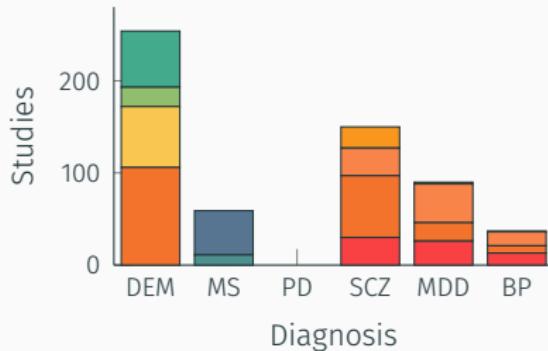


Data



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

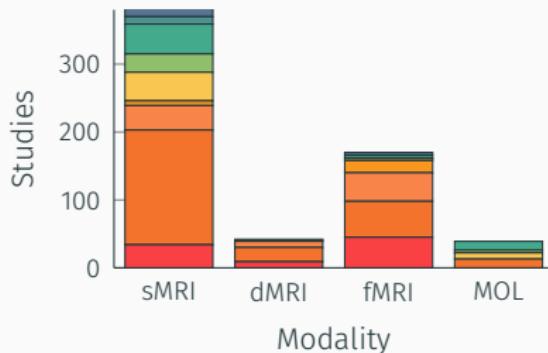
Afshin Shoebi¹, Marjane Khodatari², Mahboobeh Jafari³, Parisa Mordinian⁴, Mitra Rezaei⁵, Roohallah Alzadehsani⁶, Fahime Khozeimeh⁶, Juan Manuel Gorri⁷, Jonathan Heras⁸, Maryam Panahiazar⁹, Saeid Nahavandi⁸, U Rajendra Acharya¹⁰



Diagnosis

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

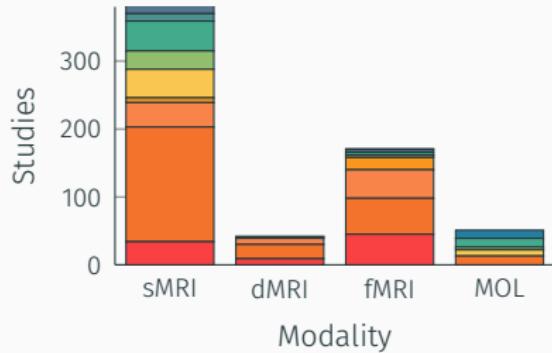
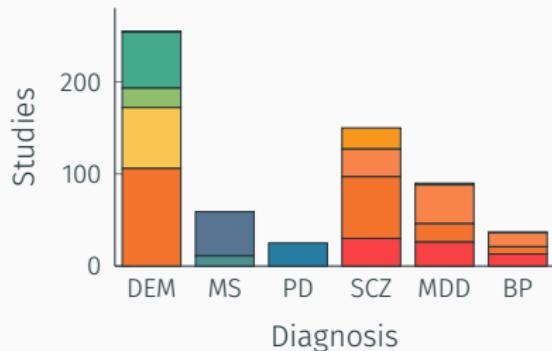
by Nida Aslam¹ , Irfan Ulah Khan¹ , Asma Basharat¹, Fatima A. Alghoot¹, Meena Aboulhous¹ , Noorah M. Alsuwayyid¹, Rawa'a K. Alturais¹, Samira Brahim², Sumayyah S. Aljanees¹ and Kholeoud Al Ghendi³



Modality



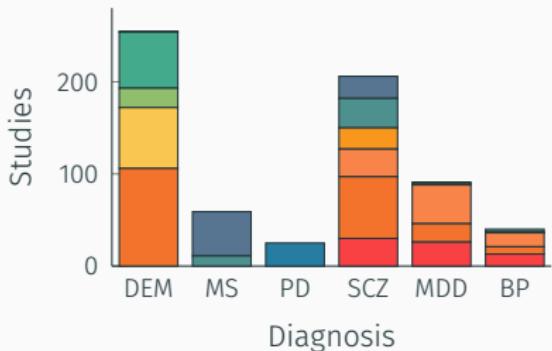
Data



Role of Artificial Intelligence Techniques and Neuroimaging Modalities in Detection of Parkinson's Disease: A Systematic Review
Nikita Aggarwal¹ • B. S. Saini¹ • Savita Gupta²

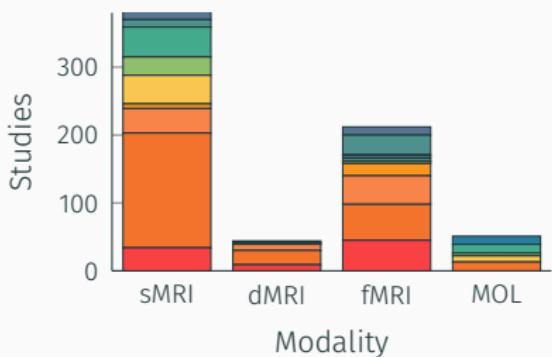


Data

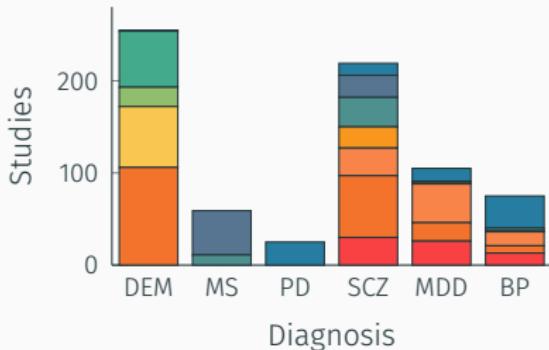


Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review
Renato de Faria,^{1*} Elvira Anna Carboni,^{1†} Raffaele Gastone,¹ Antonella Brusa,¹ Valentina Pugliese,¹ Cristina Segura-García,² and Pasquale De Fazio¹

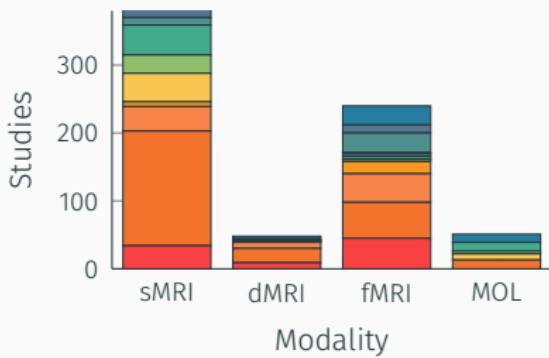
Machine learning techniques for the Schizophrenia diagnosis:
a comprehensive review and future research directions
Shradha Verma¹ · Tripti Goel¹ · M. Tanveer² · Weiping Ding³ · Rahul Sharma¹ · R. Murugan¹



Data



Diagnosis

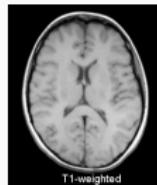


Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

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



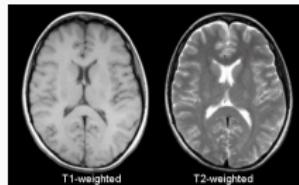
Other structural MRI modalities



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



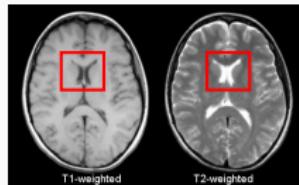
Other structural MRI modalities



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



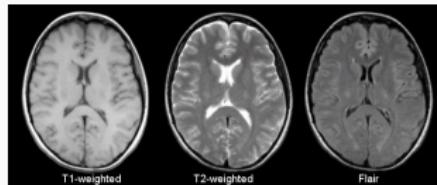
Other structural MRI modalities



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



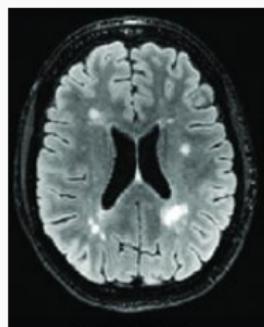
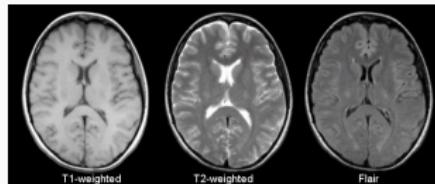
Other structural MRI modalities



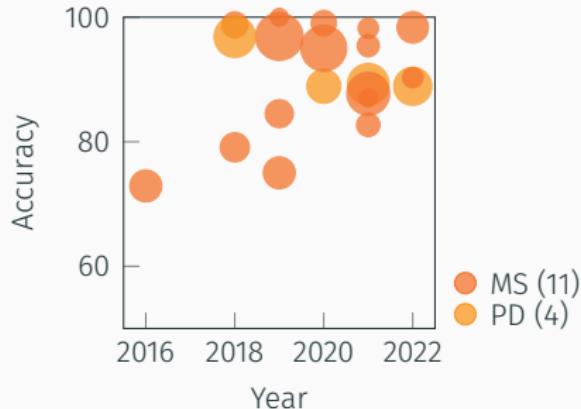
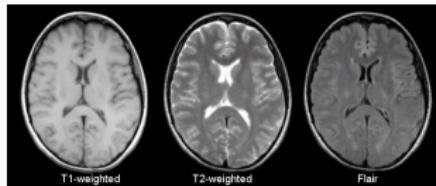
Preson D. C., (2006), MRI Basics, <https://case.edu/med/neurology/NR/MRI%20Basics>



Other structural MRI modalities



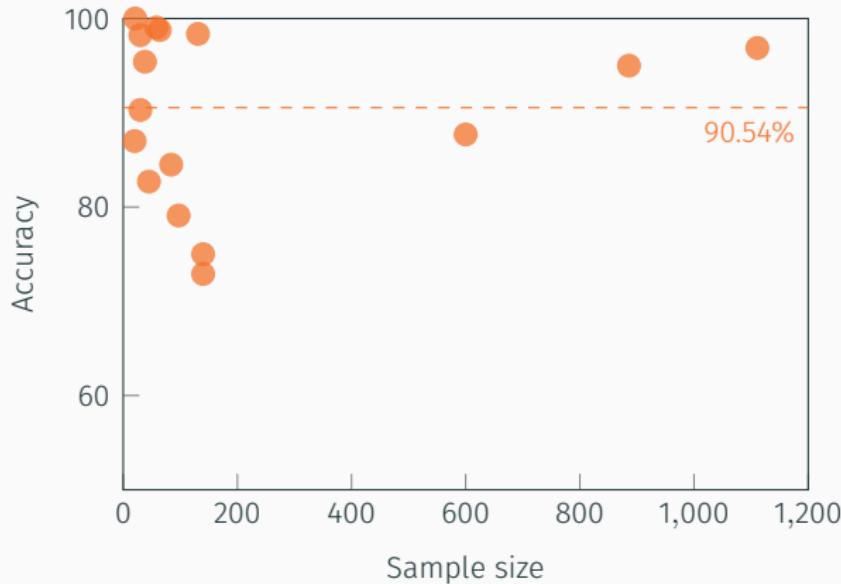
Other structural MRI modalities



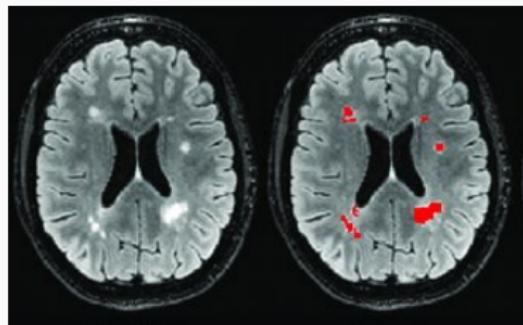
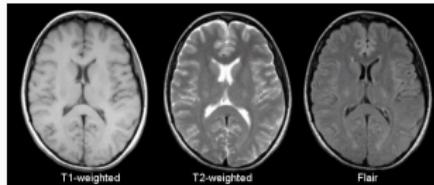
Other structural MRI modalities



MS classification studies using non-T1w sMRI



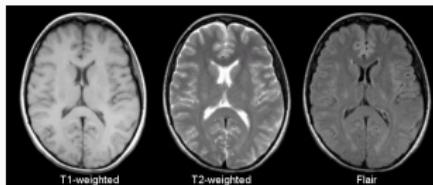
Other structural MRI modalities



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



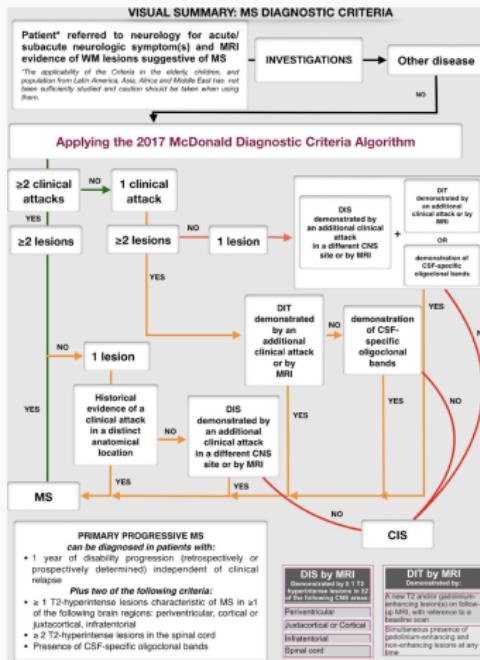
Other structural MRI modalities



T1-weighted

T2-weighted

Flair



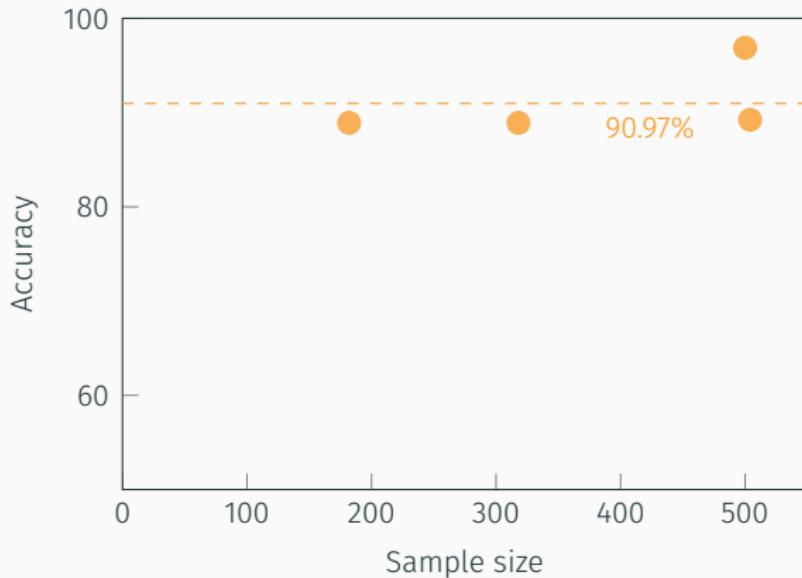
De Angelis, F., Brownlee, W. J., Chard, D. T., & Trip, S. A. (2019). New MS diagnostic criteria in practice. *Practical Neurology*, 19(1), 64-67



Other structural MRI modalities



PD classification studies using non-T1w sMRI



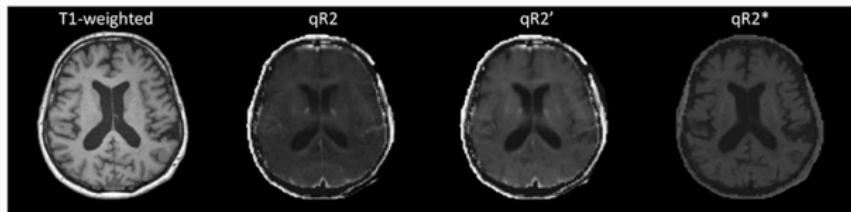
Other structural MRI modalities



T2/T2*



Other structural MRI modalities



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



Other structural MRI modalities



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

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

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

Morphology Features (Surface area, Volume, and Surface-Area-to-Volume Ratio Features)

Class	TP Rate	FP Rate	Precision	Recall	F-Measure	MCC	ROC Area	Confusion Matrix			Accuracy
								HC	PD	PSP-RS	
HC	0.605	0.185	0.657	0.605	0.630	0.429	0.710	23	12	3	65.0%
PD	0.622	0.241	0.667	0.622	0.644	0.384	0.690	10	28	7	
PSP-RS	0.800	0.120	0.615	0.800	0.696	0.619	0.840	2	2	16	

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



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

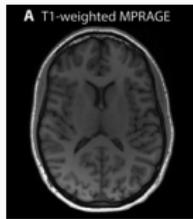


Other structural MRI modalities

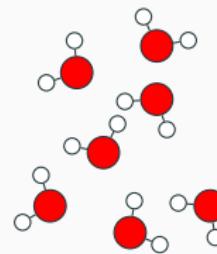
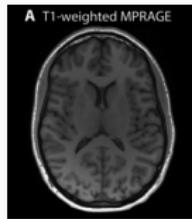
- (Non T1-weighted) structural MRI
 - Most prevalent in studies classifying MS and PD, yielding high accuracies (~90%).
 - Intimately linked with MS due to their efficacy at exposing characteristic lesions.
 - Potentially more useful than T1-weighted MRI for differentially diagnosing PD and PSP, as demonstrated by Talai et al.



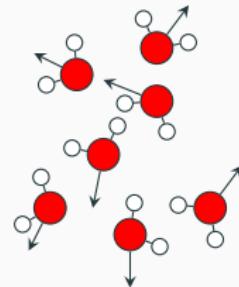
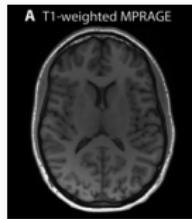
Diffusion MRI



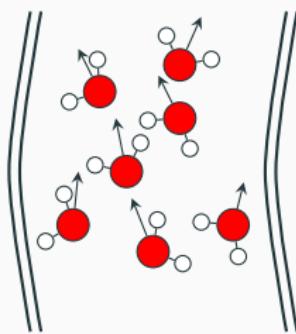
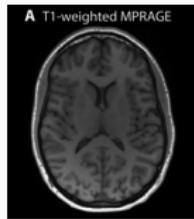
Diffusion MRI



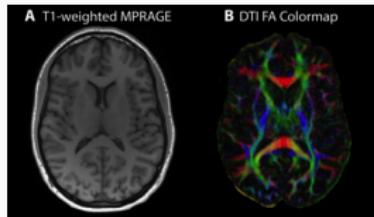
Diffusion MRI



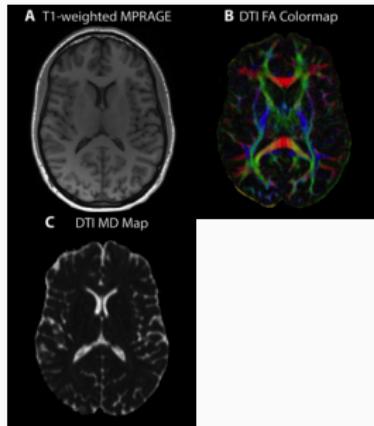
Diffusion MRI



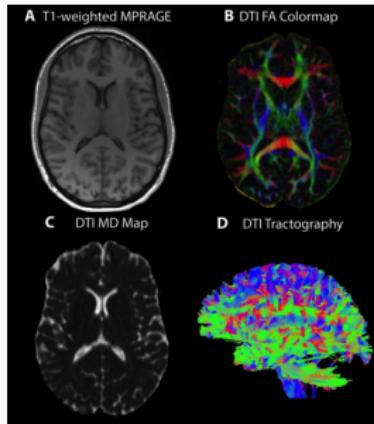
Diffusion MRI



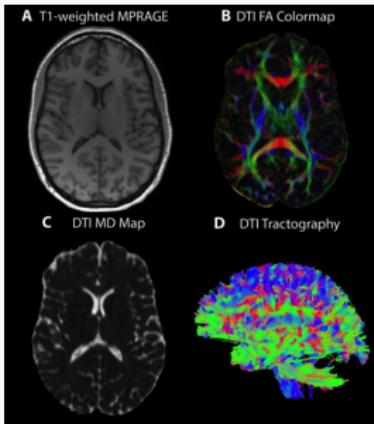
Diffusion MRI



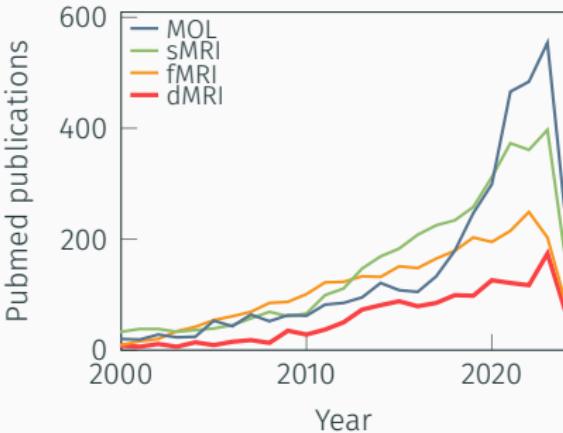
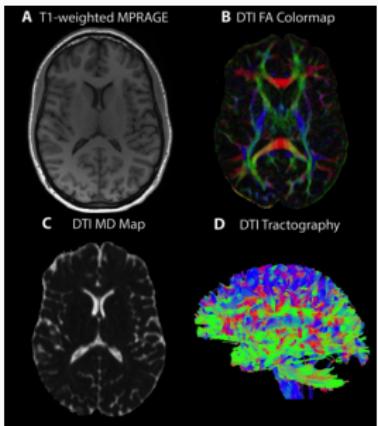
Diffusion MRI



Diffusion MRI



Diffusion MRI

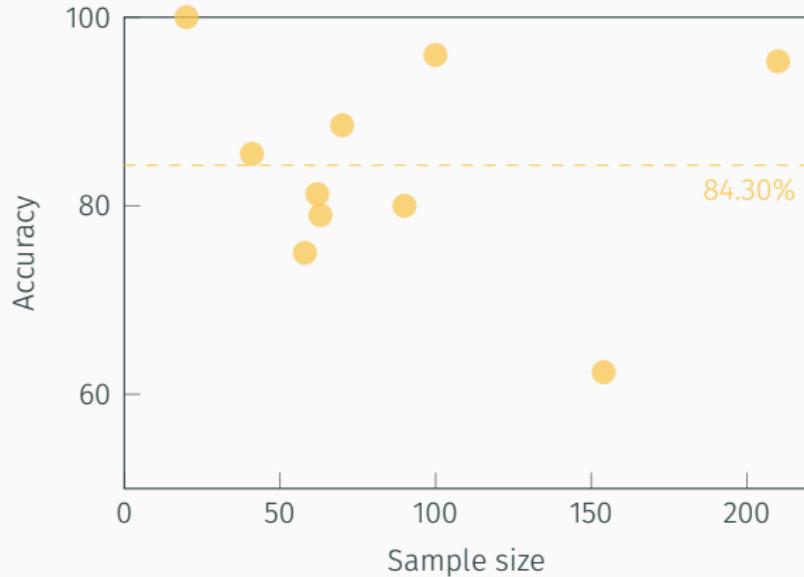


- MOL: ((molecular[Title] AND imaging[Title]) OR PET[Title] OR SPECT[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)"
- sMRI: ((structural[Title] AND MRI[Title]) OR smRI[Title] OR T1[Title] OR T2[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)
- fMRI: ((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)

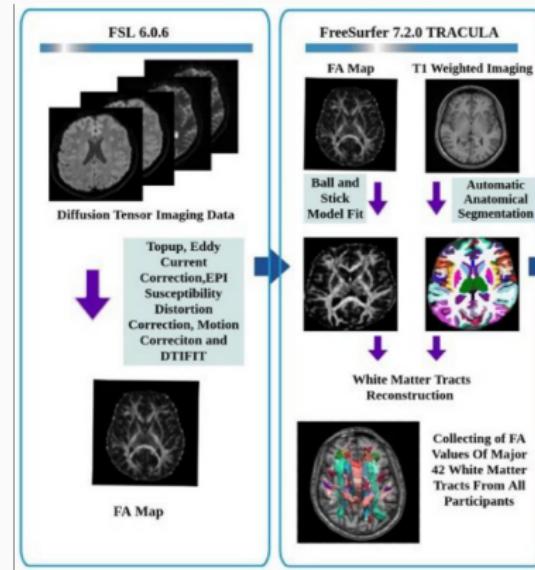




SCZ classification studies using dMRI



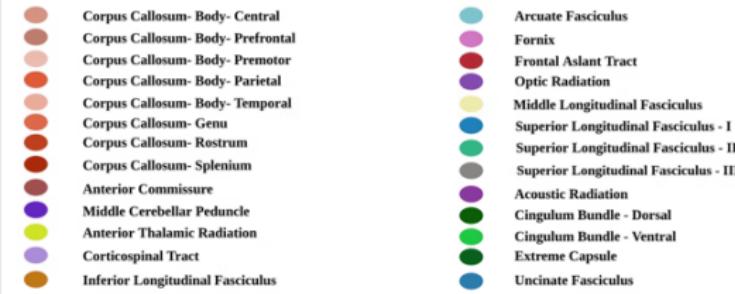
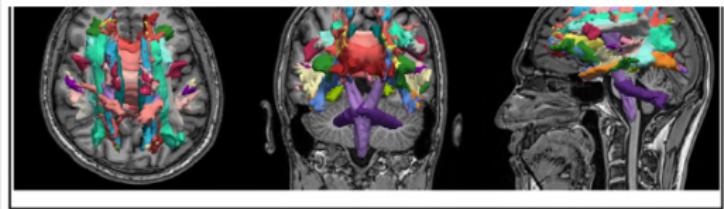
Diffusion MRI



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



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



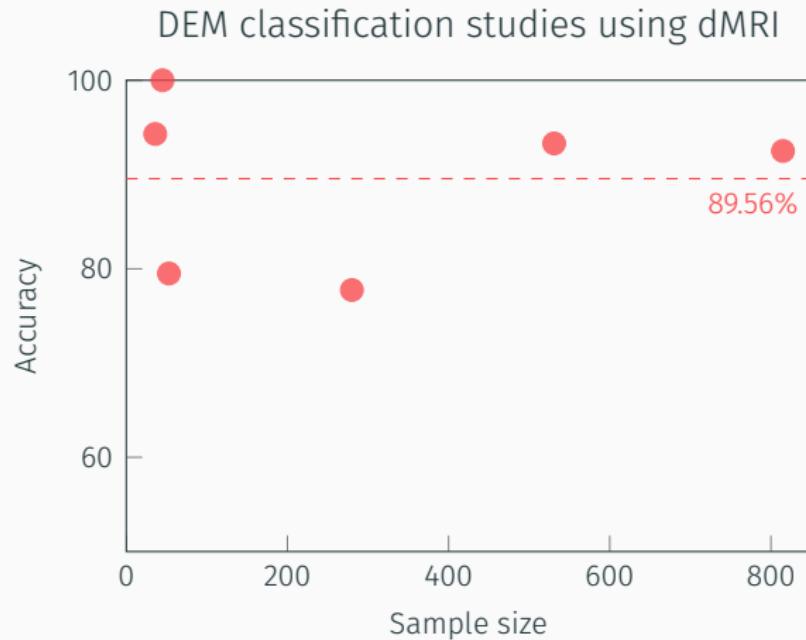
Diffusion MRI



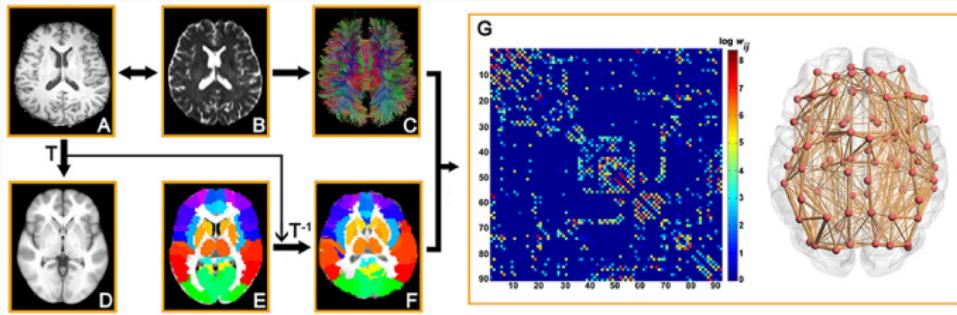
Classifier	AUC	Accuracy	Sensitivity	Specificity	Precision	F1 score	MCC
SVM-linear	0.85	0.80	0.75	0.86	0.79	0.77	0.74
Random forest	0.82	0.79	0.72	0.81	0.76	0.74	0.70
SVM-Gaussian	0.83	0.78	0.71	0.80	0.75	0.73	0.70
LR	0.78	0.76	0.70	0.79	0.73	0.71	0.68
Naive Bayes	0.75	0.72	0.65	0.74	0.68	0.66	0.62

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





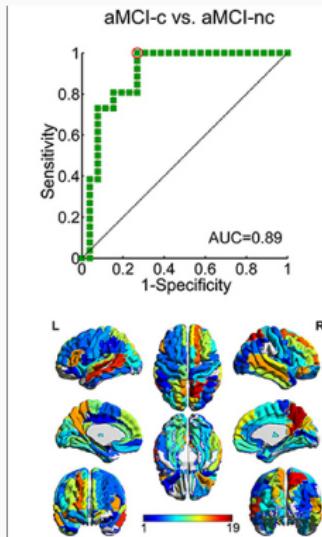
Diffusion MRI



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



Diffusion MRI



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



Diffusion MRI



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	0.106	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.

Morphology Features (Surface area, Volume, and Surface-Area-to-Volume Ratio Features)											
Class	TP Rate	FP Rate	Precision	Recall	F-Measure	MCC	ROC Area	Confusion Matrix			Accuracy
								HC	PD	PSP-RS	
HC	0.605	0.185	0.657	0.605	0.630	0.429	0.710	23	12	3	65.0%
PD	0.622	0.241	0.667	0.622	0.644	0.384	0.690	10	28	7	
PSP-RS	0.800	0.120	0.615	0.800	0.896	0.619	0.840	2	2	16	

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.

Diffusion Tensor Imaging Features (MD, FA, RD, AD Features)											
Class	TP Rate	FP Rate	Precision	Recall	F-Measure	MCC	ROC Area	Confusion Matrix			Accuracy
								HC	PD	PSP-RS	
HC	1.000	0.000	1.000	1.000	1.000	1.000	1.000	38	0	0	95.1%
PD	0.933	0.034	0.955	0.933	0.944	0.901	0.975	0	42	3	
PSP-RS	0.900	0.036	0.857	0.900	0.878	0.848	0.968	0	2	18	

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; MD, Mean diffusivity; FA, Fractional anisotropy; RD, Radial diffusivity; AD, Axial diffusivity.



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



Diffusion MRI

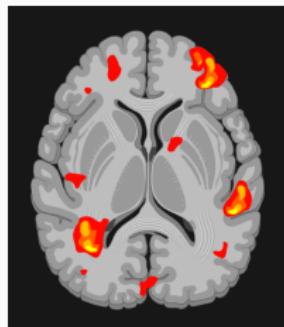
- (Non T1-weighted) structural MRI (T2/FLAIR)
 - Most prevalent in studies classifying MS and PD, yielding high accuracies (~90%).
 - Intimately linked with MS due to their efficacy at exposing characteristic lesions.
 - Potentially more useful than T1-weighted MRI for differentially diagnosing PD and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



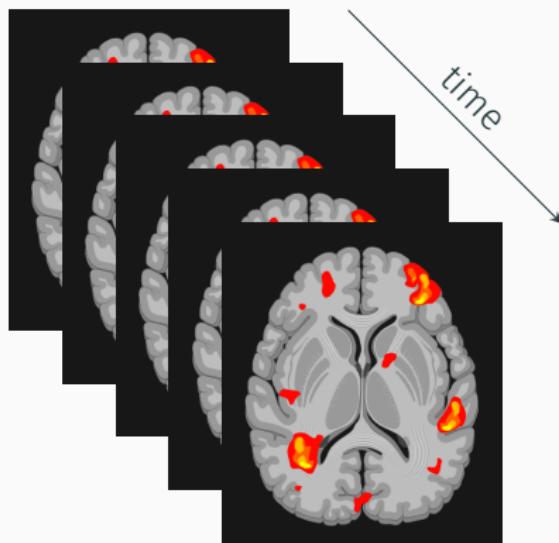
Functional Magnetic Resonance Imaging (fMRI)



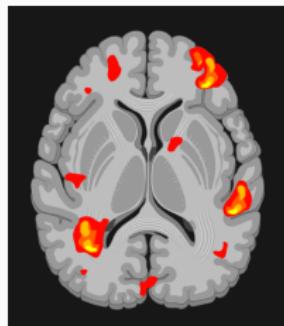
Functional Magnetic Resonance Imaging (fMRI)



Functional Magnetic Resonance Imaging (fMRI)

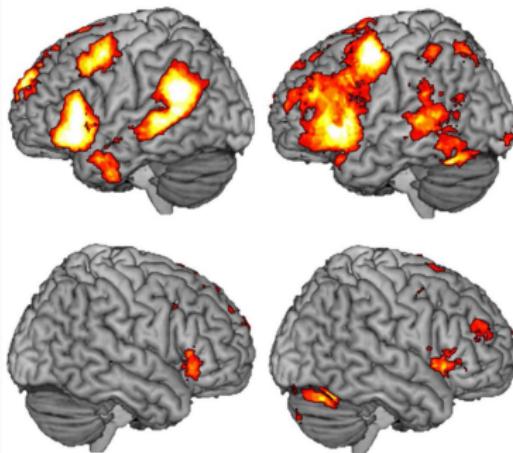


Functional Magnetic Resonance Imaging (fMRI)



rs-fMRI

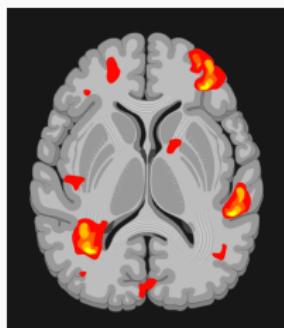
task-fMRI



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



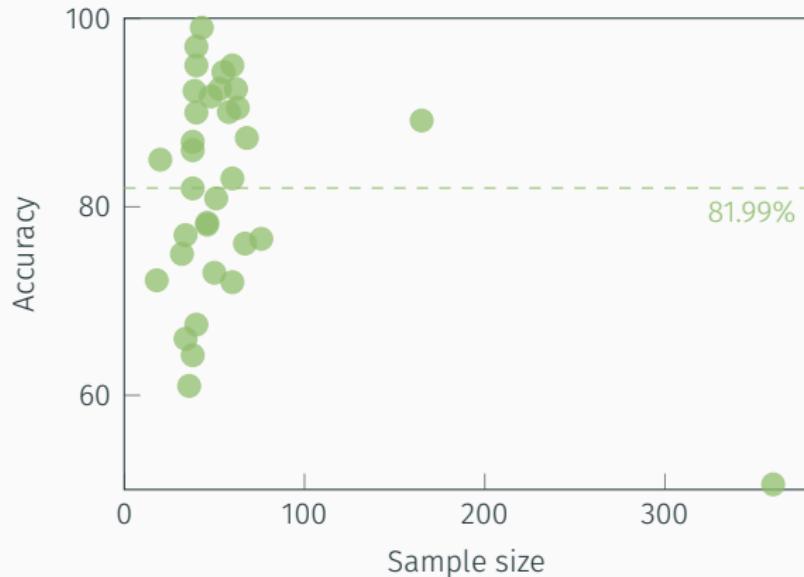
Functional Magnetic Resonance Imaging (fMRI)



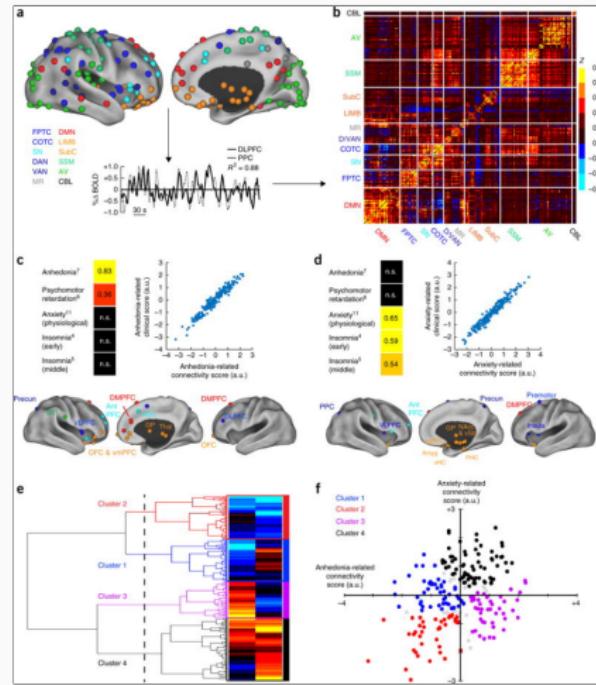
Functional Magnetic Resonance Imaging (fMRI)



MDD classification studies using fMRI



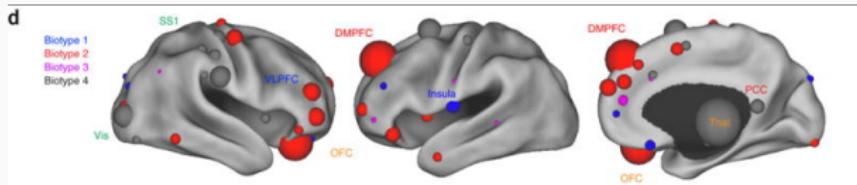
Functional Magnetic Resonance Imaging (fMRI)



Drysdale, A. T., Gosenick, L., Downar, J., Dunlop, K., Mansouri, F., Meng, Y., ... & Liston, C. (2017). Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nature medicine*, 23(1), 28-38



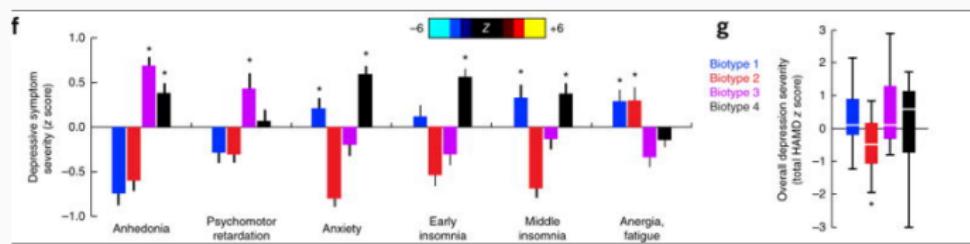
Functional Magnetic Resonance Imaging (fMRI)



Drysdale, A. T., Gosenick, L., Downar, J., Dunlop, K., Mansouri, F., Meng, Y., ... & Liston, C. (2017). Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nature medicine*, 23(1), 28-38



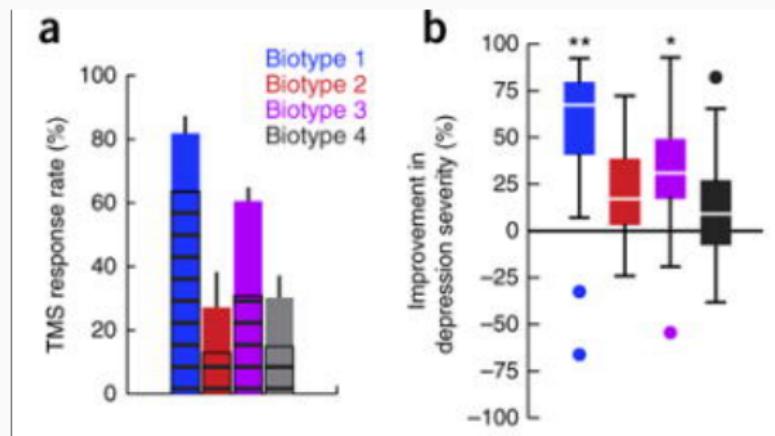
Functional Magnetic Resonance Imaging (fMRI)



Drysdale, A. T., Gosenick, L., Downar, J., Dunlop, K., Mansouri, F., Meng, Y., ... & Liston, C. (2017). Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nature medicine*, 23(1), 28-38



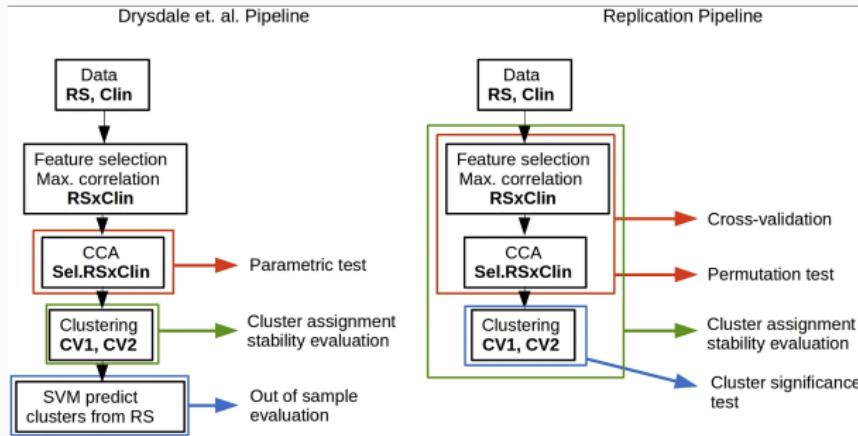
Functional Magnetic Resonance Imaging (fMRI)



Drysdale, A. T., Gosenick, L., Downar, J., Dunlop, K., Mansouri, F., Meng, Y., ... & Liston, C. (2017). Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nature medicine*, 23(1), 28-38



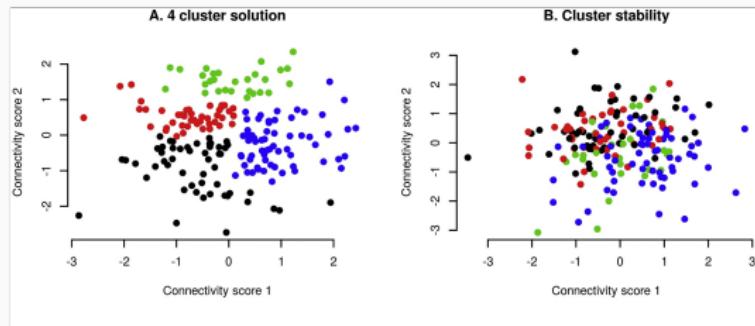
Functional Magnetic Resonance Imaging (fMRI)



Dinga, R., Schmaal, L., Penninx, B. W., van Tol, M. J., Veltman, D. J., van Velzen, L., ... & Marquand, A. F. (2019). Evaluating the evidence for biotypes of depression: Methodological replication and extension of Drysdale et al. (2017). *NeuroImage: Clinical*, 22, 101796



Functional Magnetic Resonance Imaging (fMRI)



Dinga, R., Schmaal, L., Penninx, B. W., van Tol, M. J., Veltman, D. J., van Velzen, L., ... & Marquand, A. F. (2019). Evaluating the evidence for biotypes of depression: Methodological replication and extension of Drysdale et al. (2017). *NeuroImage: Clinical*, 22, 101796

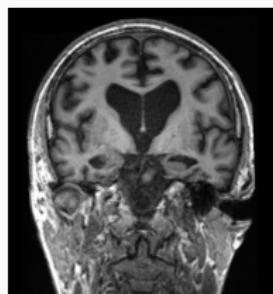


Functional Magnetic Resonance Imaging (fMRI)

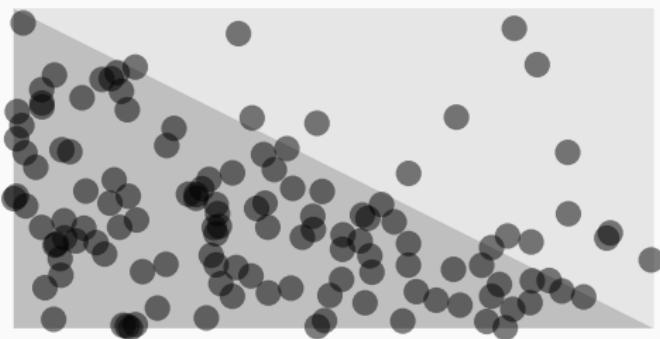
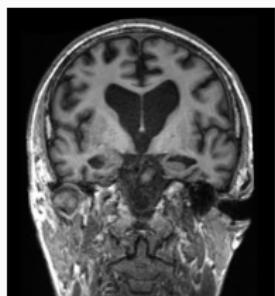
- (Non T1-weighted) structural MRI (T2/FLAIR)
 - Most prevalent in studies classifying MS and PD, yielding high accuracies (~90%).
 - Intimately linked with MS due to their efficacy at exposing characteristic lesions.
 - Potentially more useful than T1-weighted MRI for differentially diagnosing PD and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



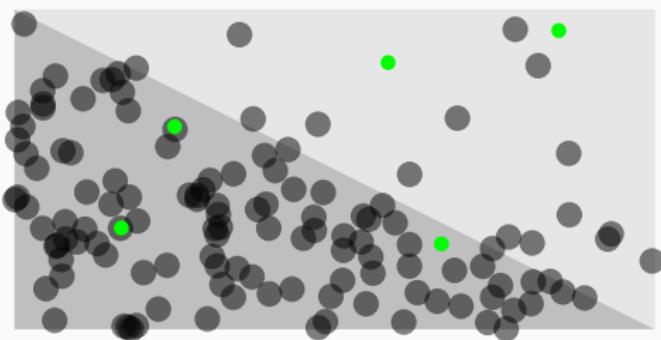
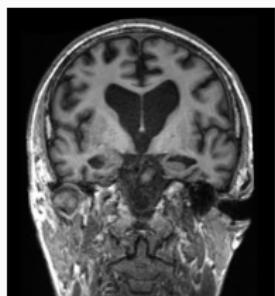
Molecular imaging (PET/SPECT)



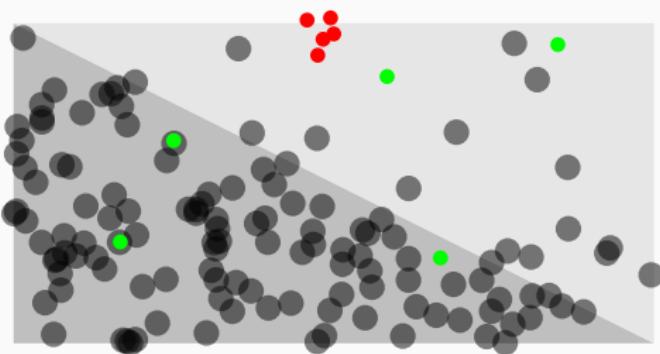
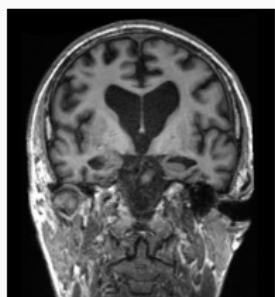
Molecular imaging (PET/SPECT)



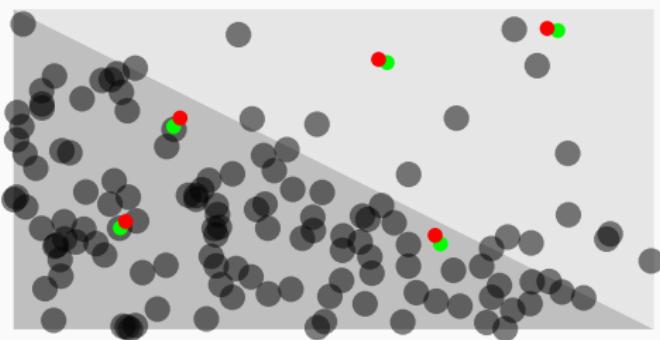
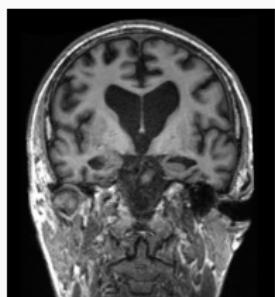
Molecular imaging (PET/SPECT)



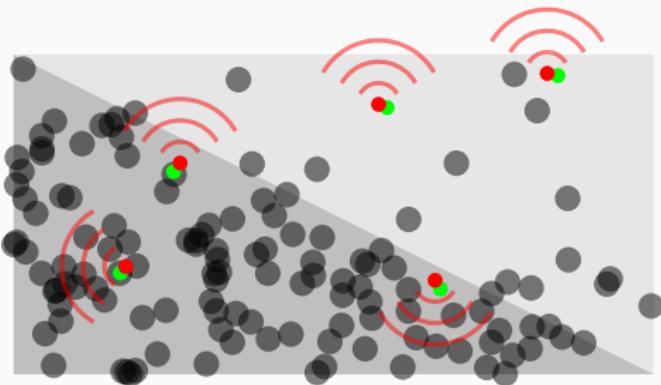
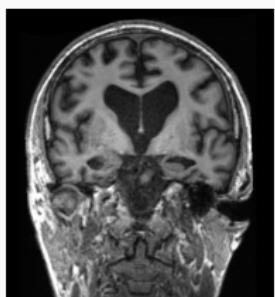
Molecular imaging (PET/SPECT)



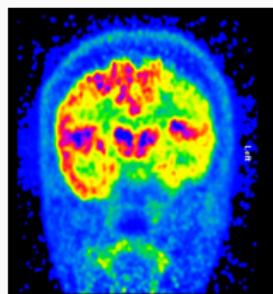
Molecular imaging (PET/SPECT)



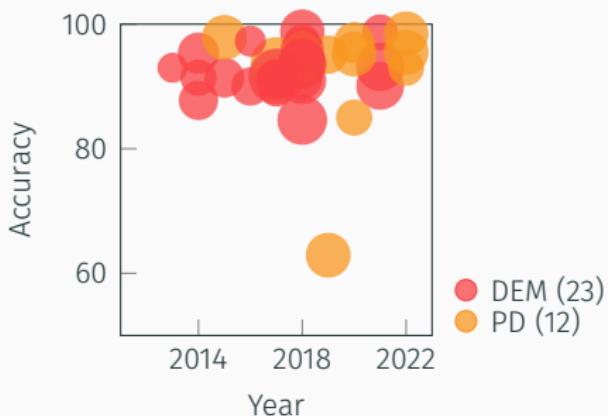
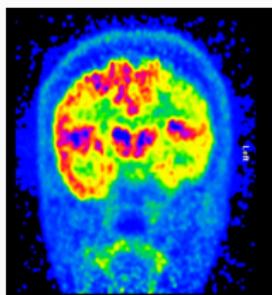
Molecular imaging (PET/SPECT)



Molecular imaging (PET/SPECT)



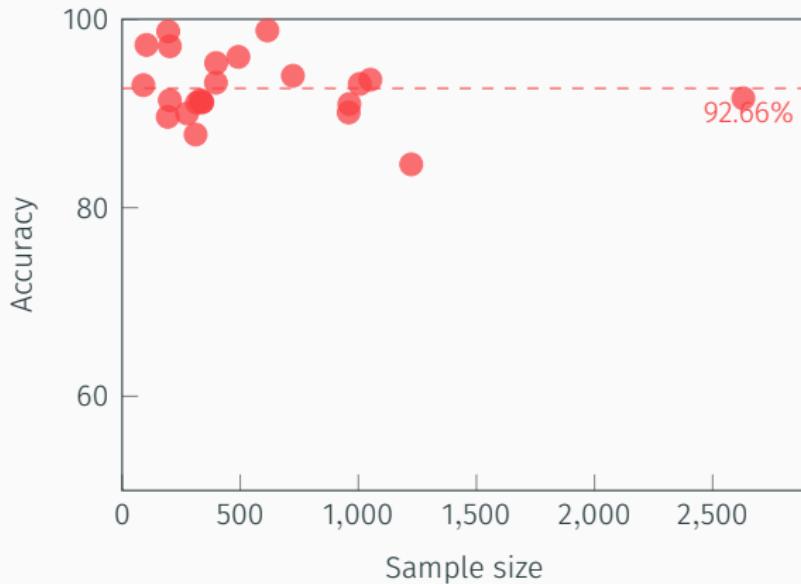
Molecular imaging (PET/SPECT)



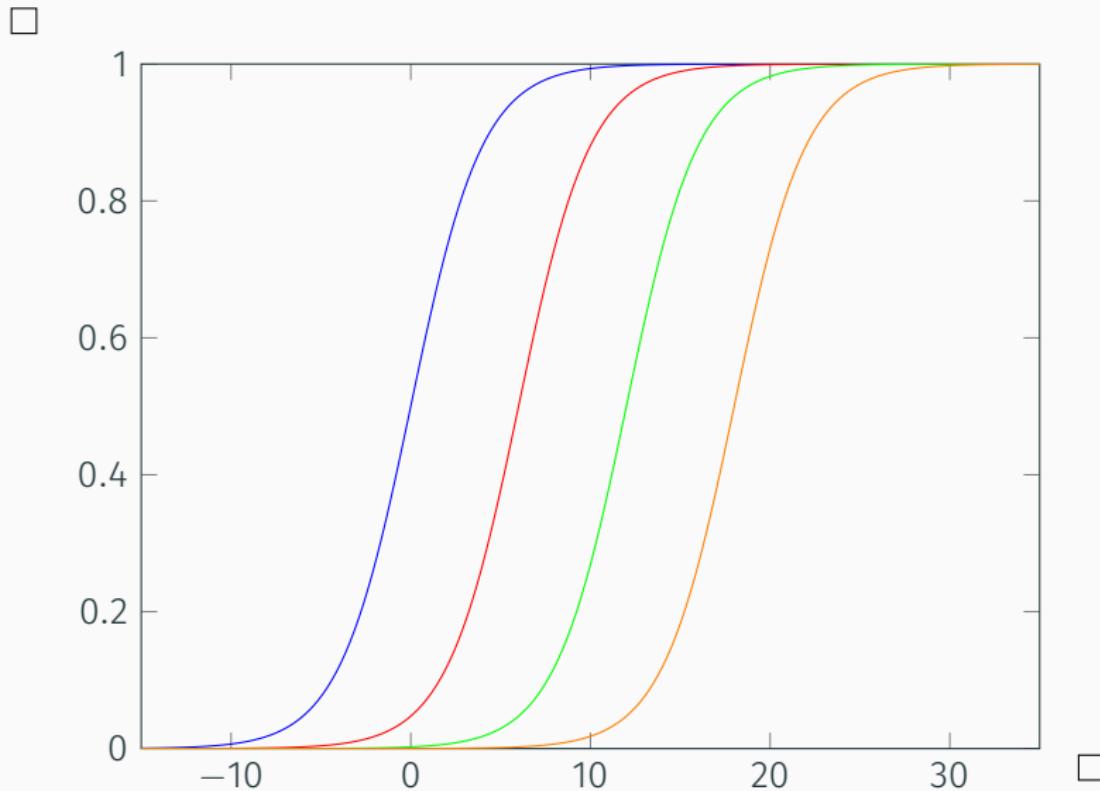
Molecular imaging (PET/SPECT)



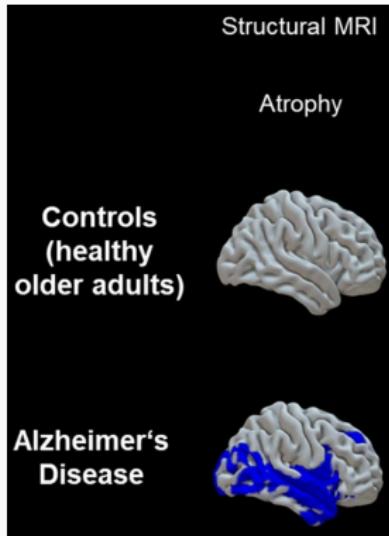
DEM classification studies using molecular imaging



Molecular imaging (PET/SPECT)



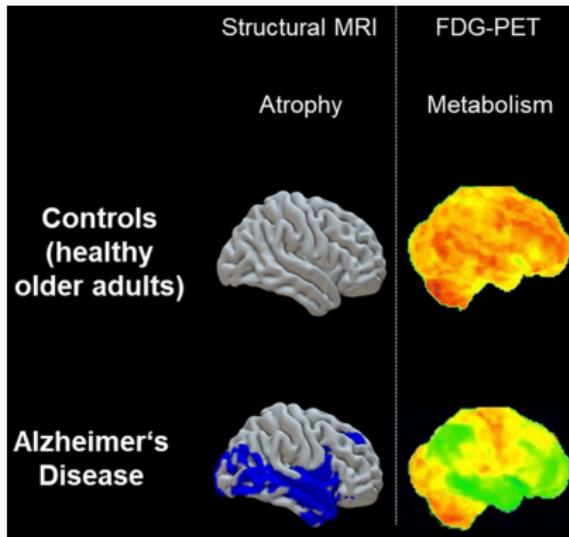
Molecular imaging (PET/SPECT)



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



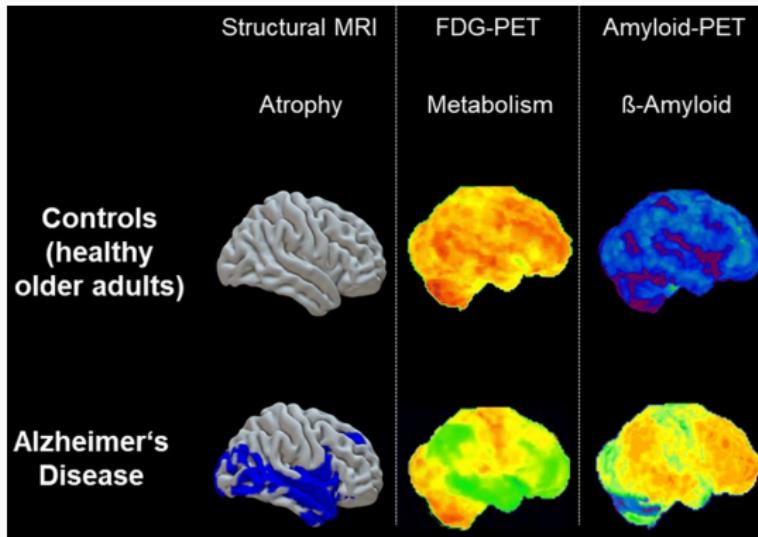
Molecular imaging (PET/SPECT)



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



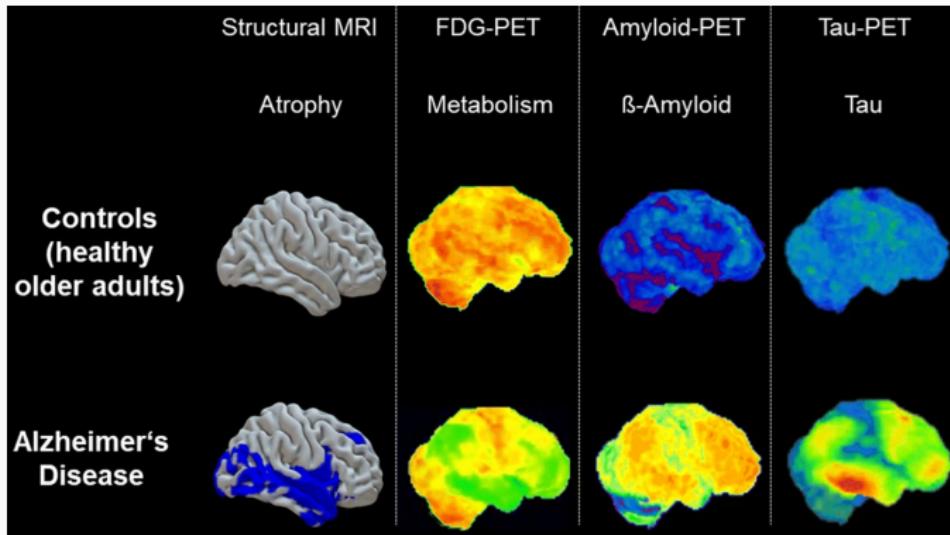
Molecular imaging (PET/SPECT)



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



Molecular imaging (PET/SPECT)



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



Molecular imaging (PET/SPECT)



"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

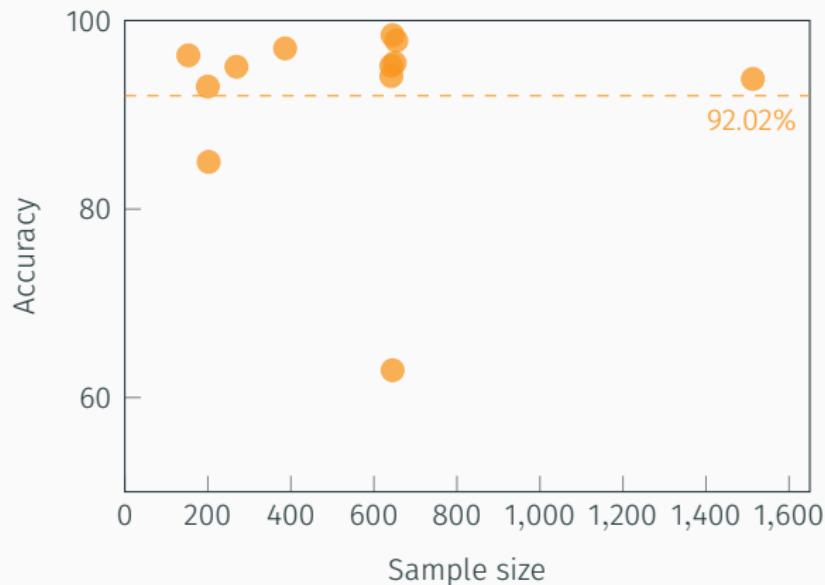
The same AD biology may result in different phenotypic presentations"



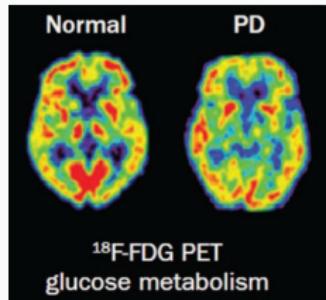
Molecular imaging (PET/SPECT)



PD classification studies using molecular imaging



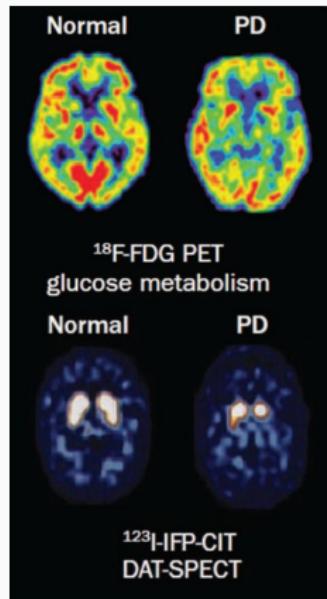
Molecular imaging (PET/SPECT)



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



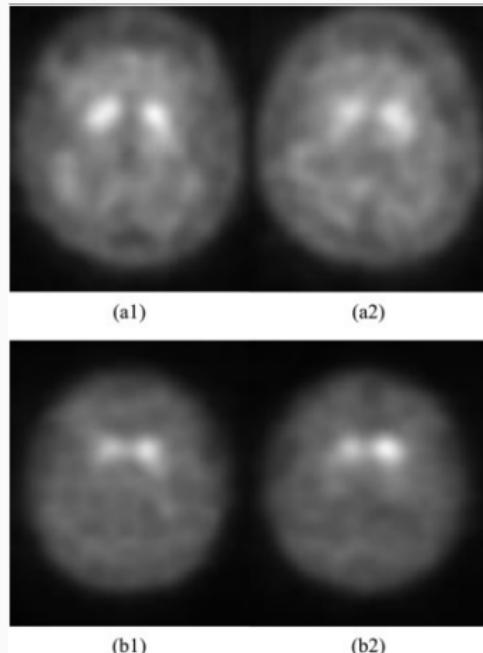
Molecular imaging (PET/SPECT)



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



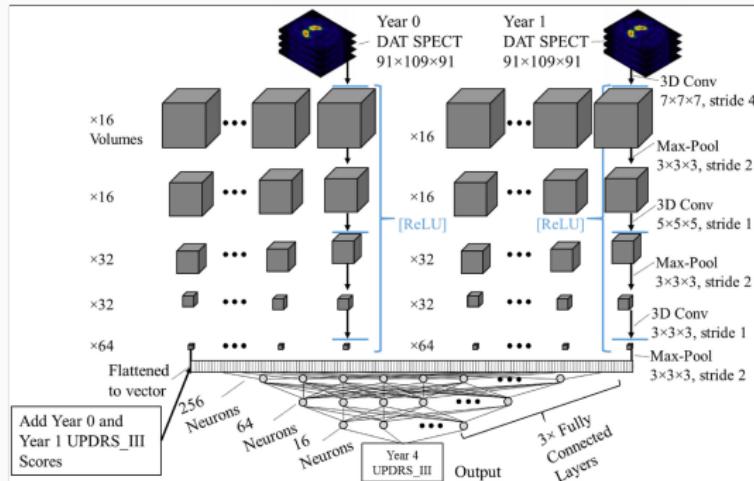
Molecular imaging (PET/SPECT)



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



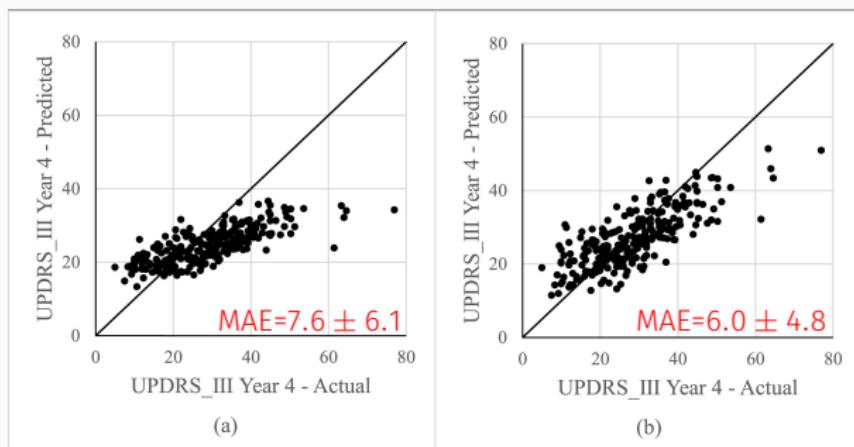
Molecular imaging (PET/SPECT)



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



Molecular imaging (PET/SPECT)



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



Molecular imaging (PET/SPECT)

- (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 (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
 - 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 A β plaques 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.

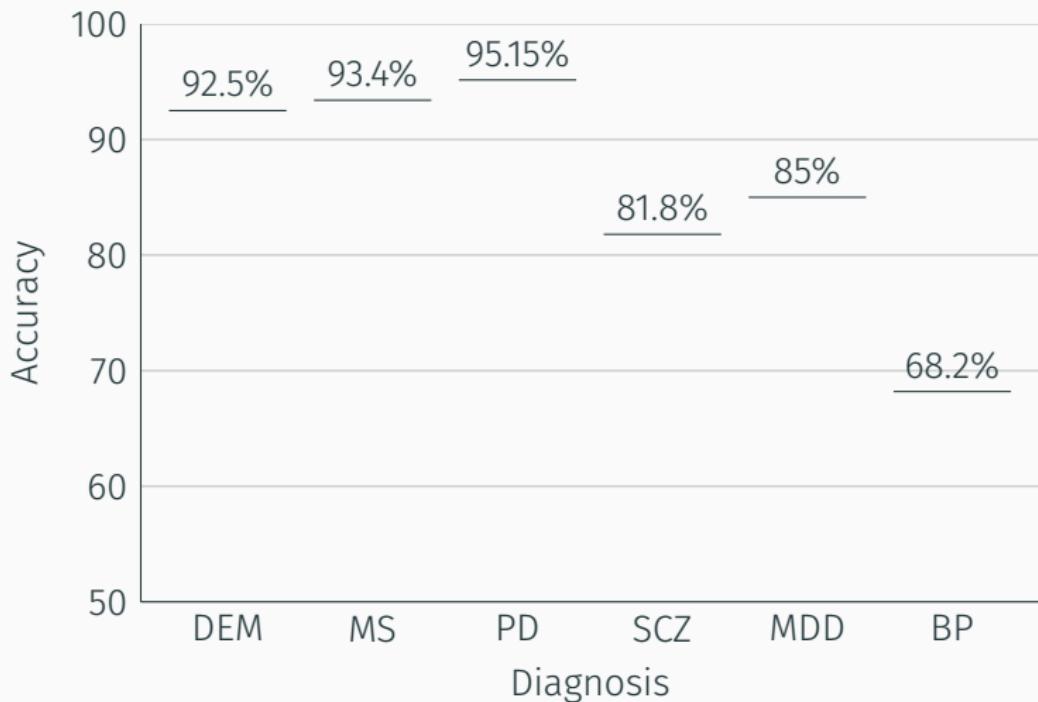


The future of neuroimaging-based prediction

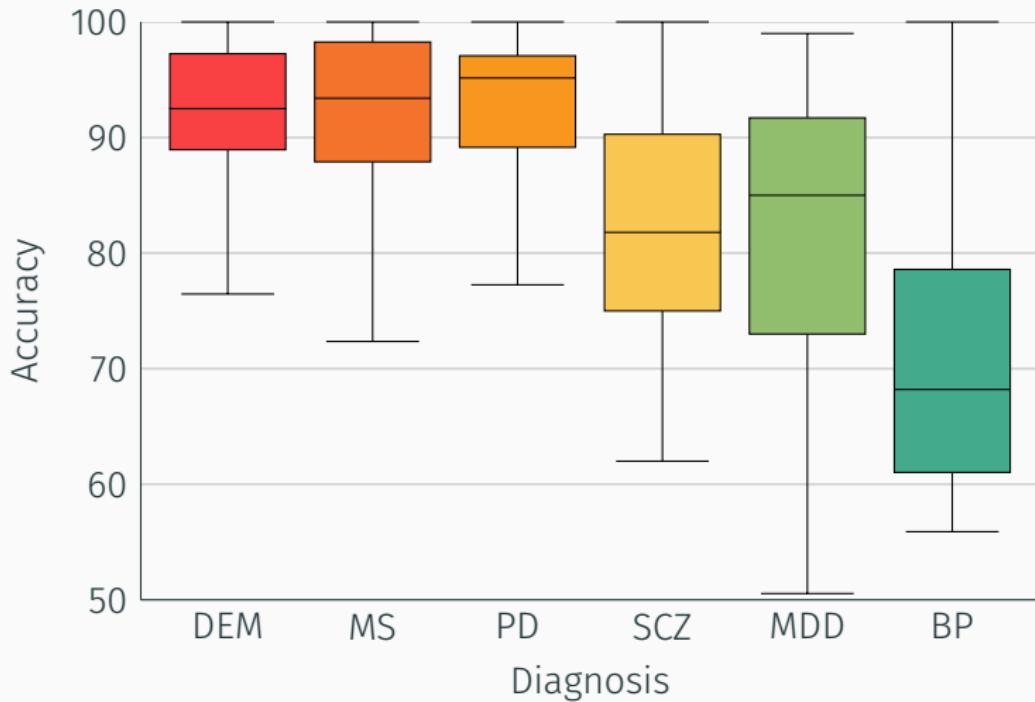


UNIVERSITETET
I OSLO

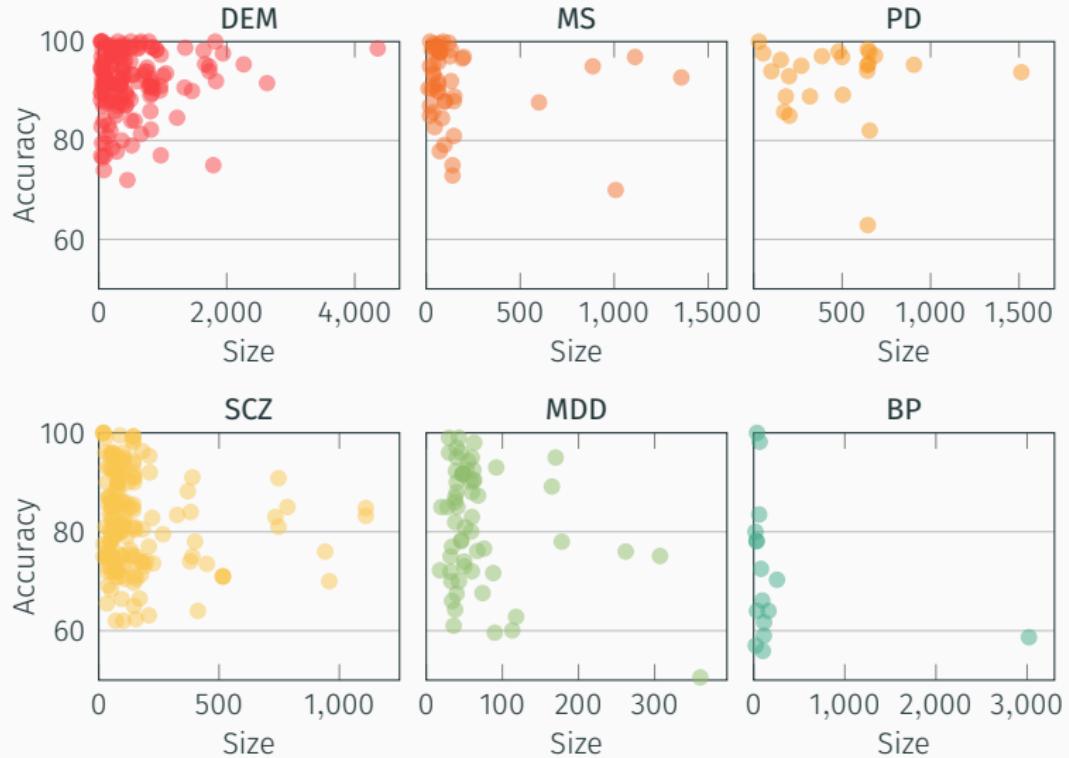
Challenges: Predictiveness



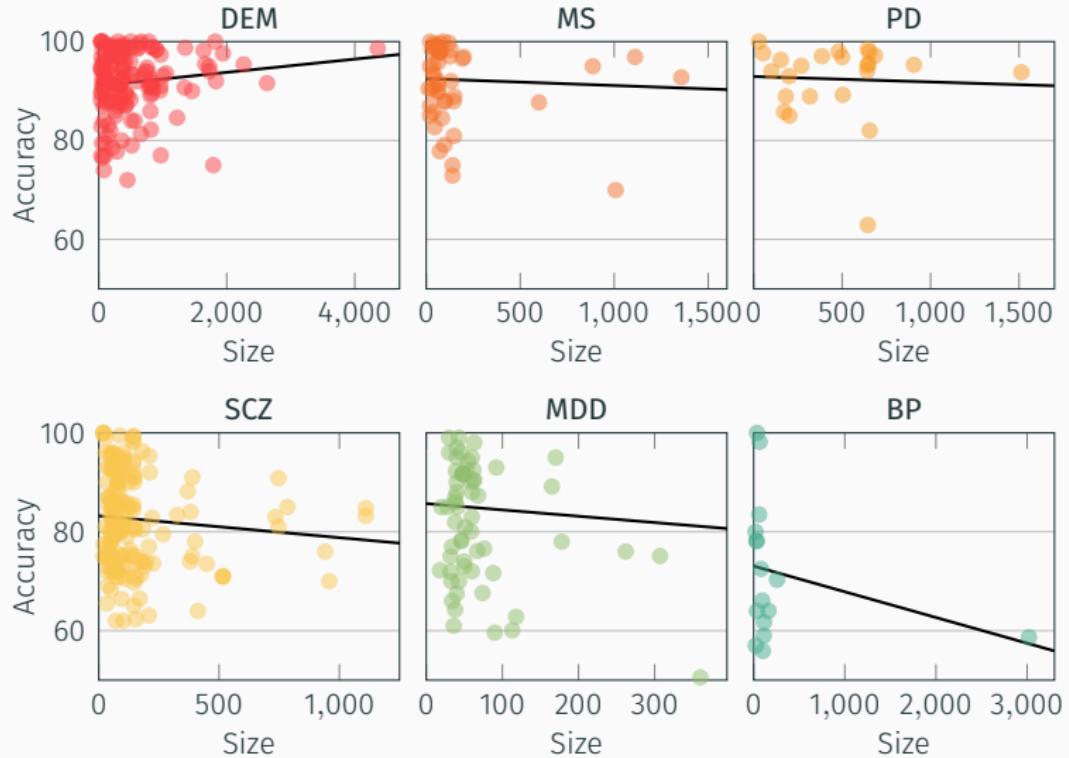
Challenges: Predictiveness



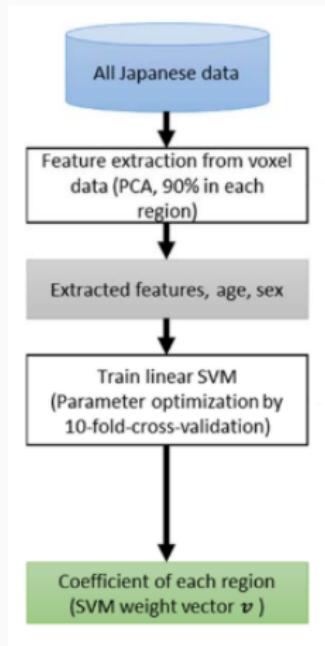
Challenges: Predictiveness



Challenges: Predictiveness



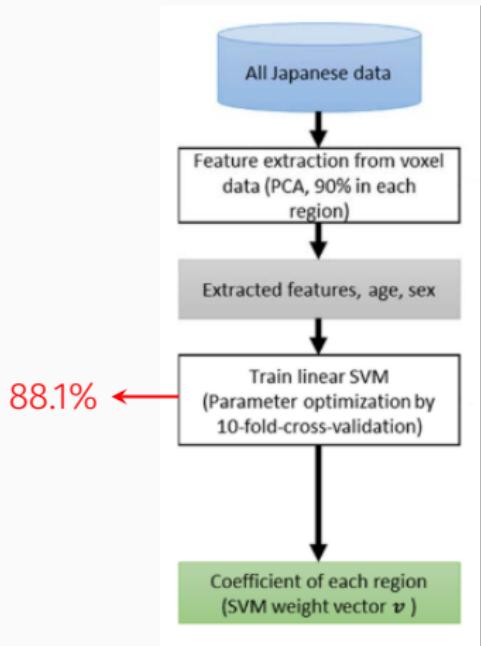
Challenges: Generalization



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



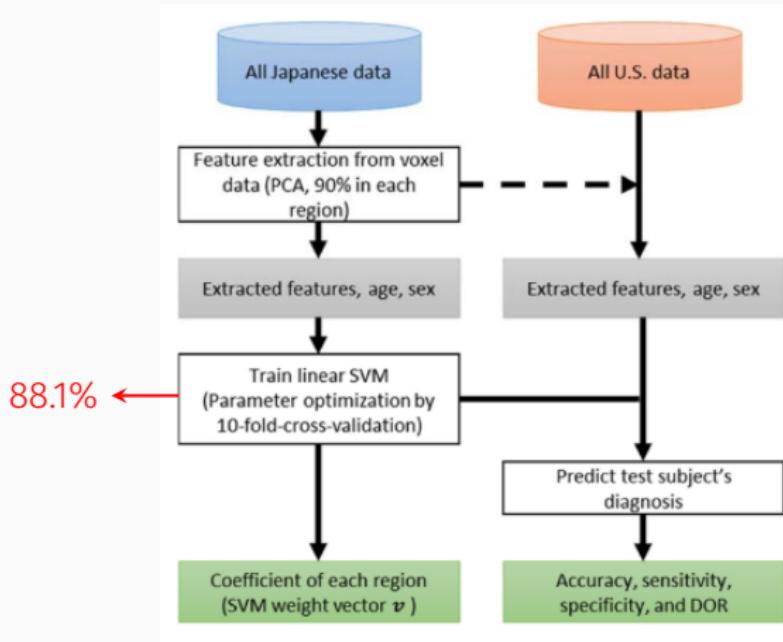
Challenges: Generalization



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



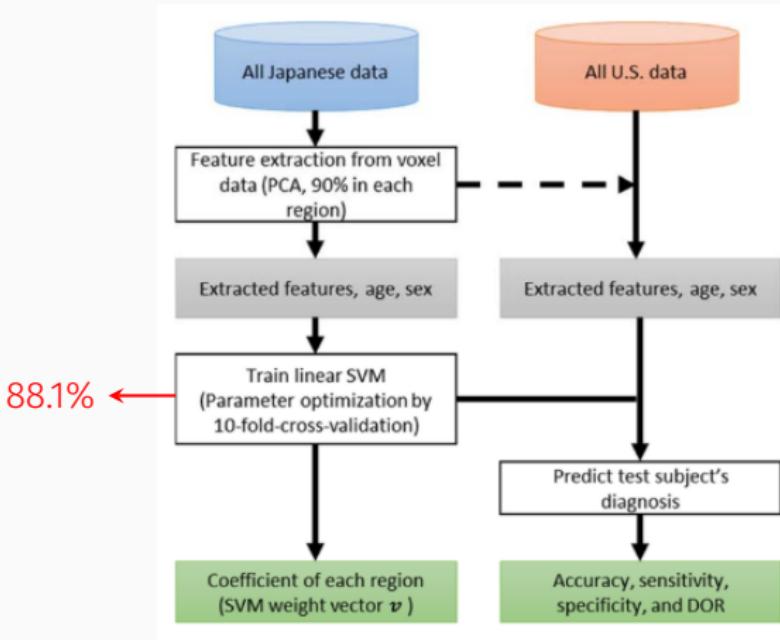
Challenges: Generalization



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



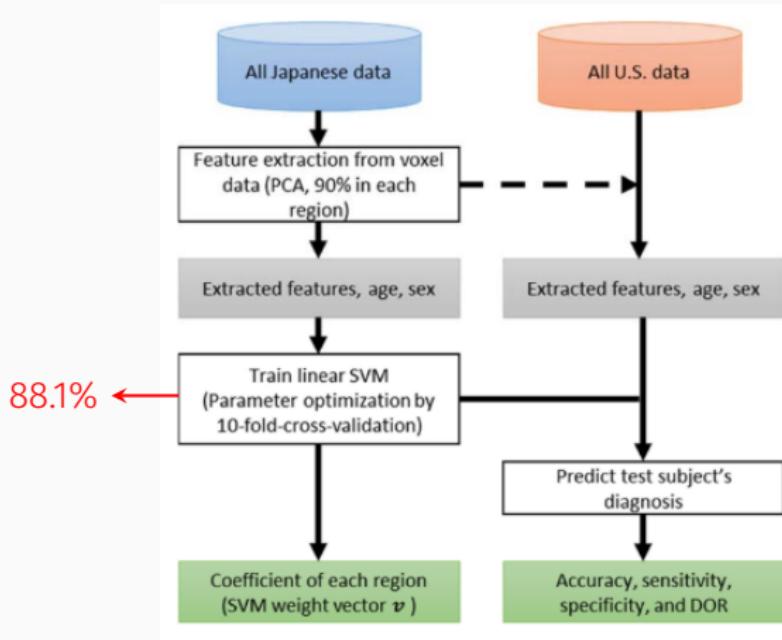
Challenges: Generalization



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



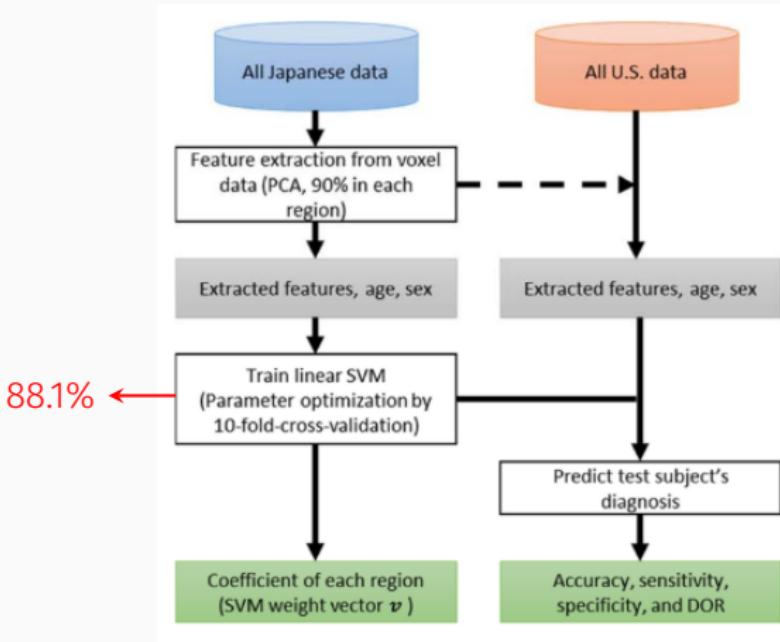
Challenges: Generalization



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



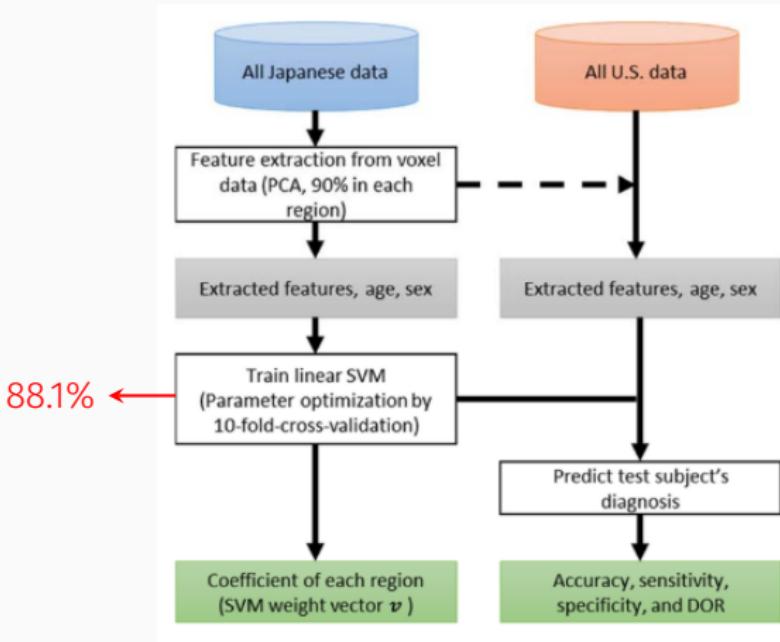
Challenges: Generalization



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



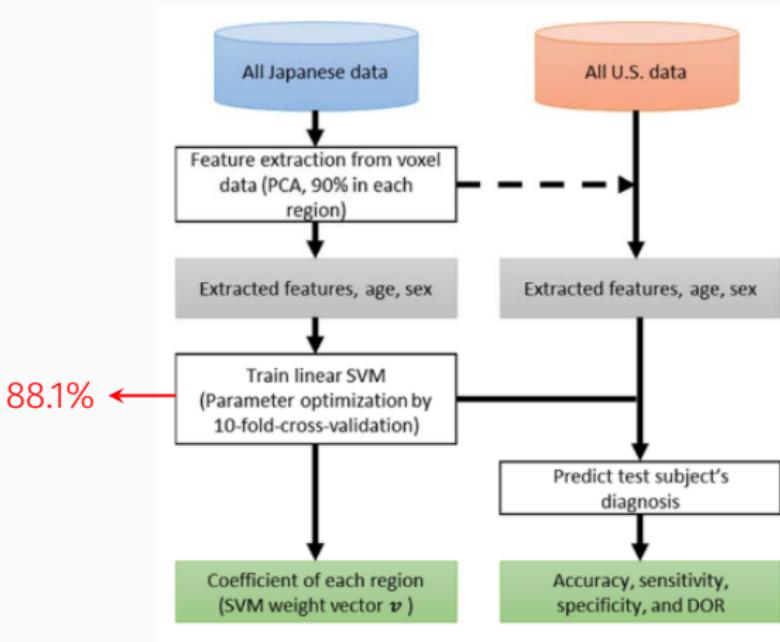
Challenges: Generalization



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



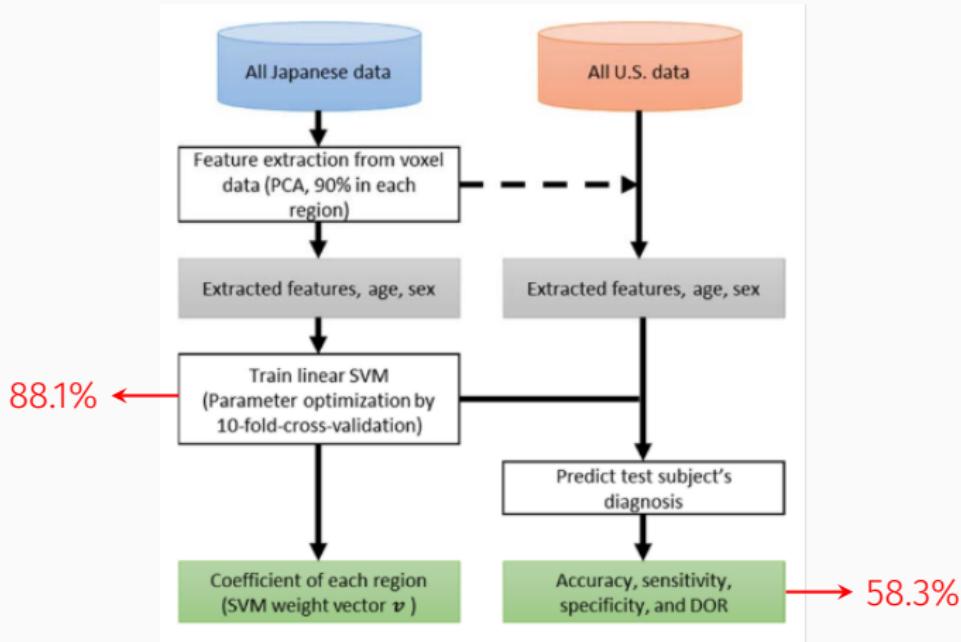
Challenges: Generalization



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



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



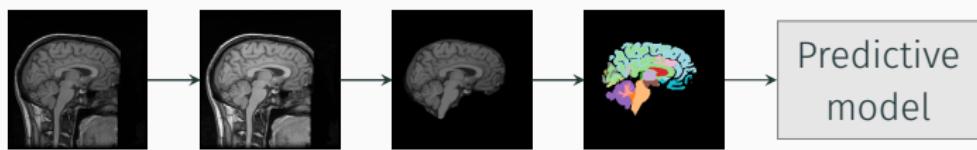
Challenges: Researcher degrees of freedom



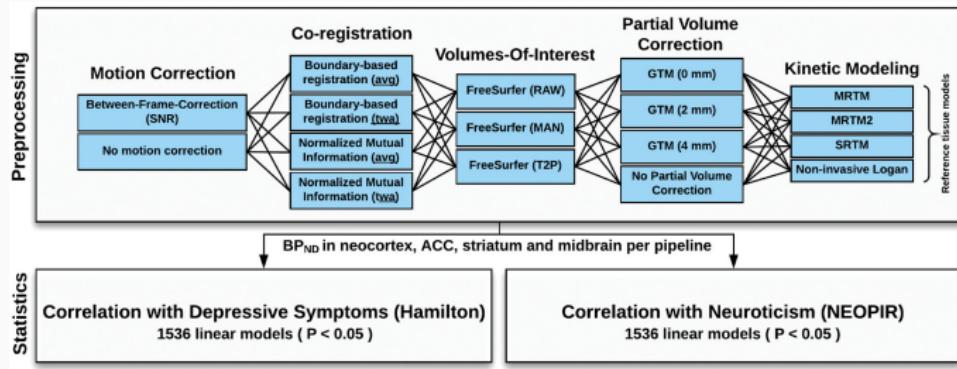
Predictive
model



Challenges: Researcher degrees of freedom



Challenges: Researcher degrees of freedom



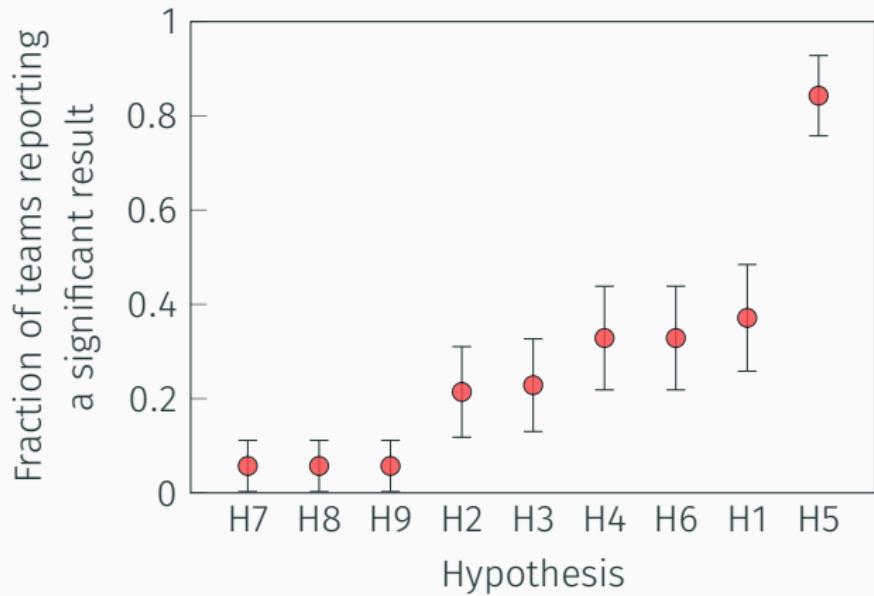
Nørgaard et al., 2020



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

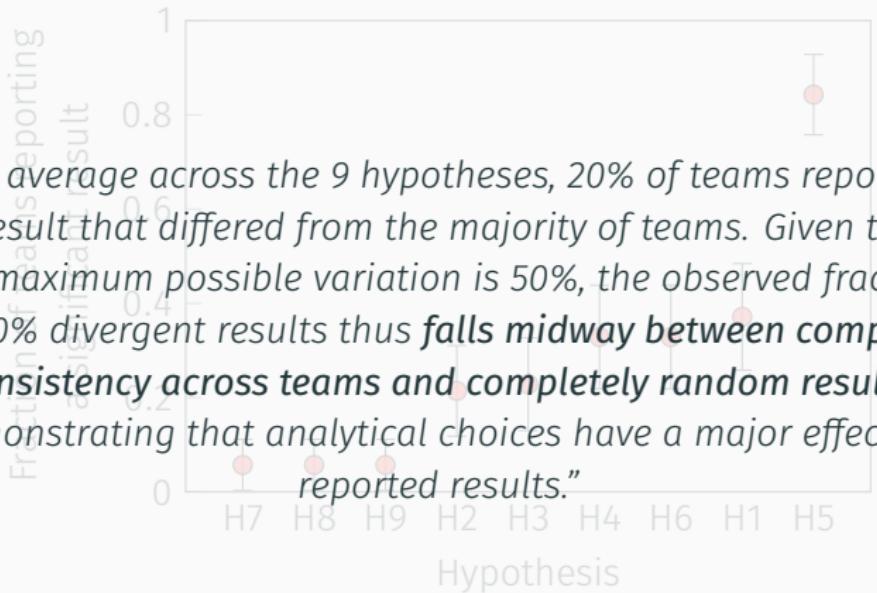


Adapted from Botvinik-Nezer et al., 2020

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



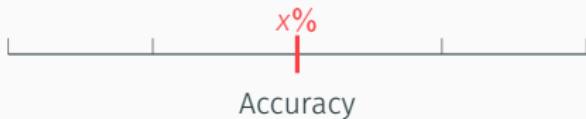
Adapted from Botvinik-Nezer et al., 2020



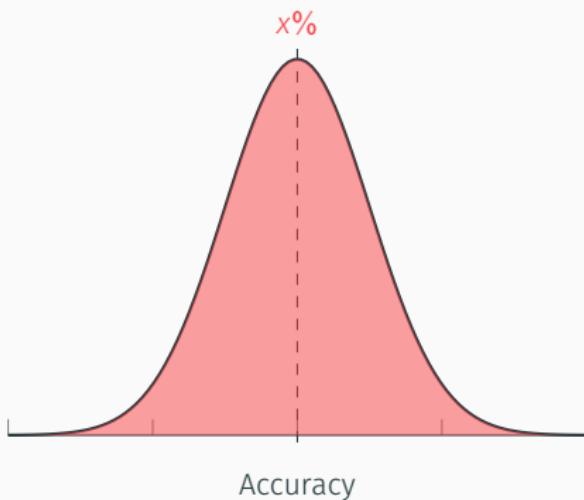
Botvinik-Nezer, R., Holzmeister, F., Camerer, C. F., Dreber, A., Huber, J., Johannesson, M., ... & Rieck, J. R. (2020). Variability in the analysis of a single neuroimaging dataset by many teams. *Nature*, 582(7810), 84-88



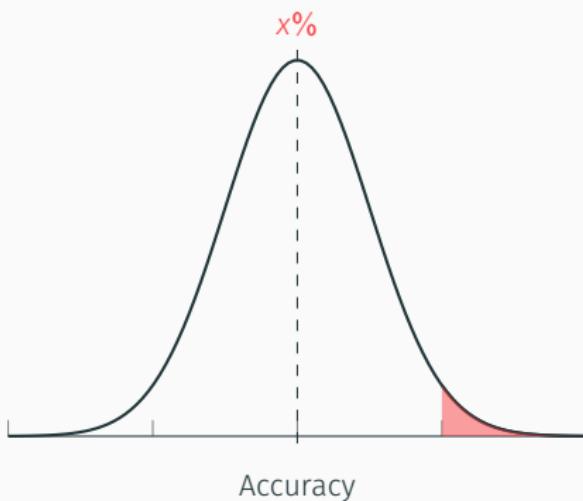
Challenges: Researcher degrees of freedom



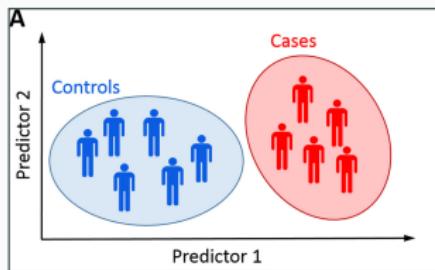
Challenges: Researcher degrees of freedom



Challenges: Researcher degrees of freedom



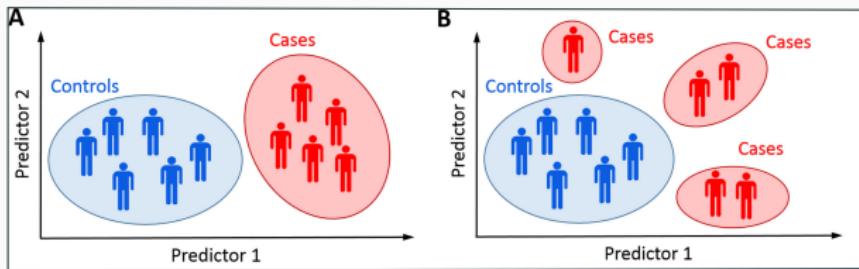
Challenges: Predictive targets



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



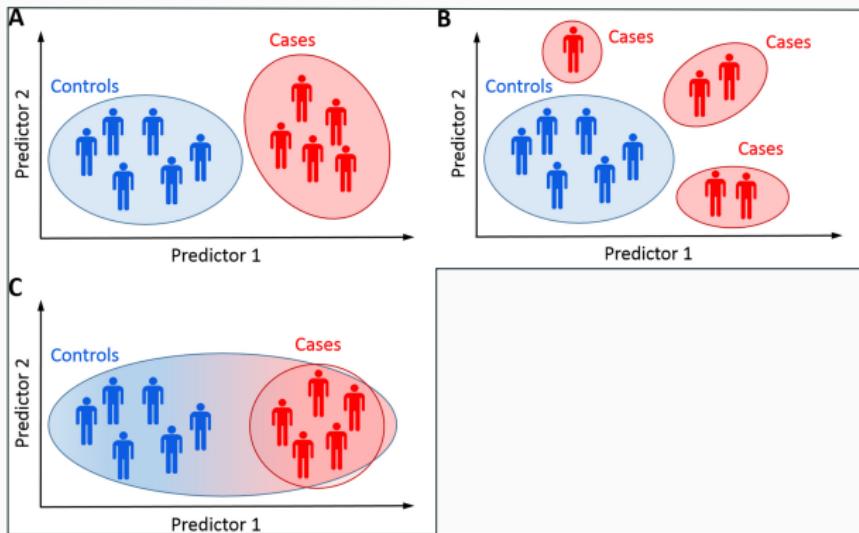
Challenges: Predictive targets



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



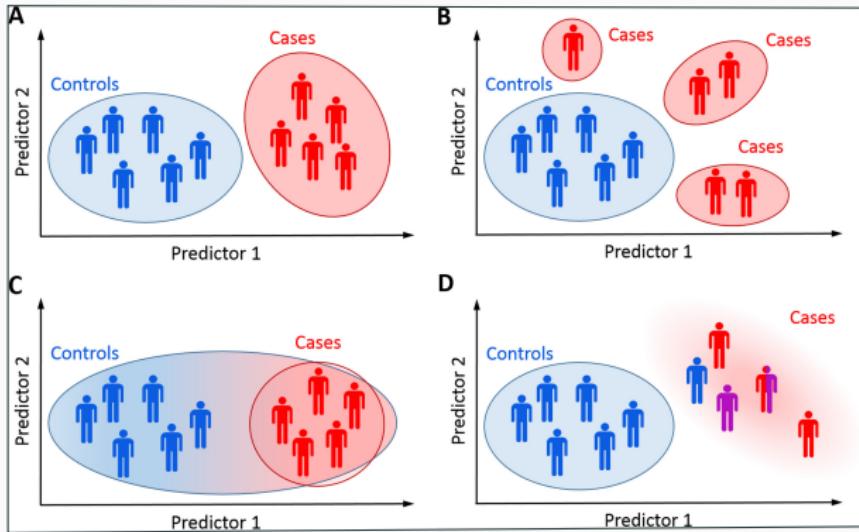
Challenges: Predictive targets



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



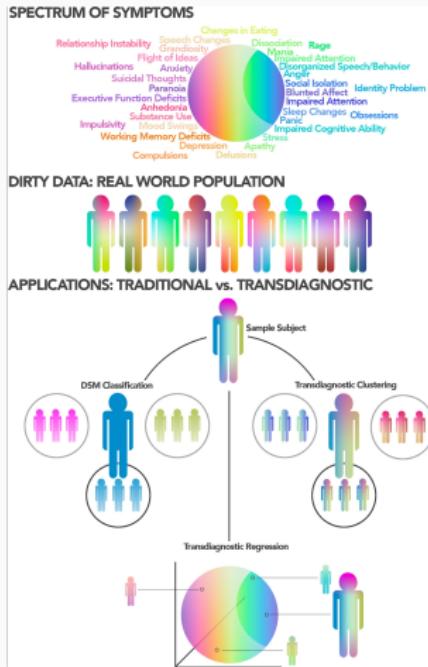
Challenges: Predictive targets



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

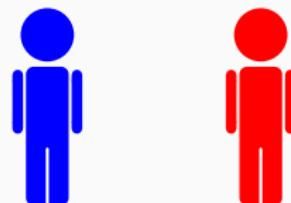


Challenges: Predictive targets

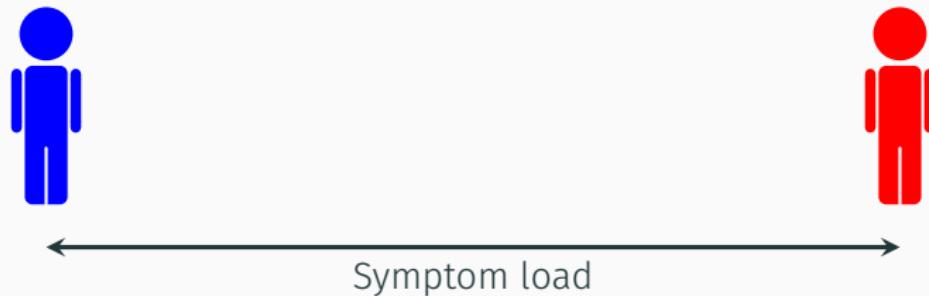


Vogel & Black (2024)

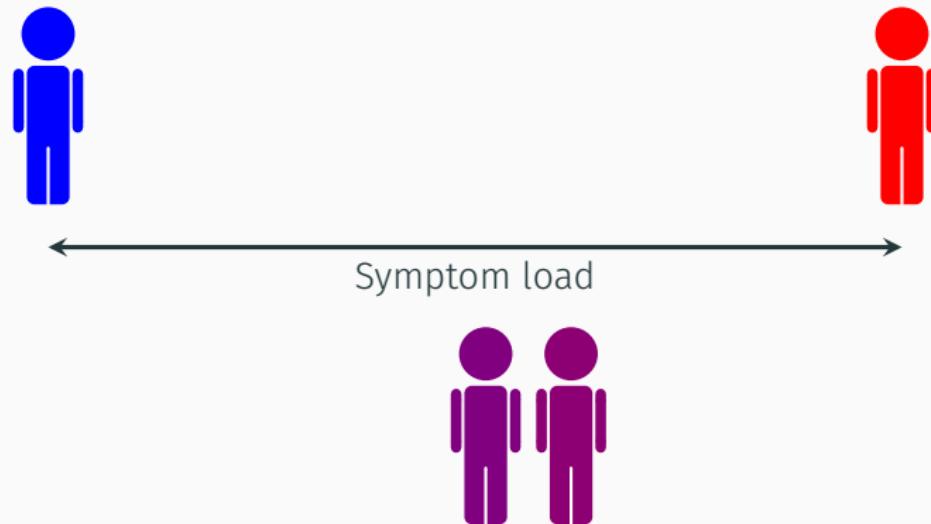
Challenges: Predictive targets



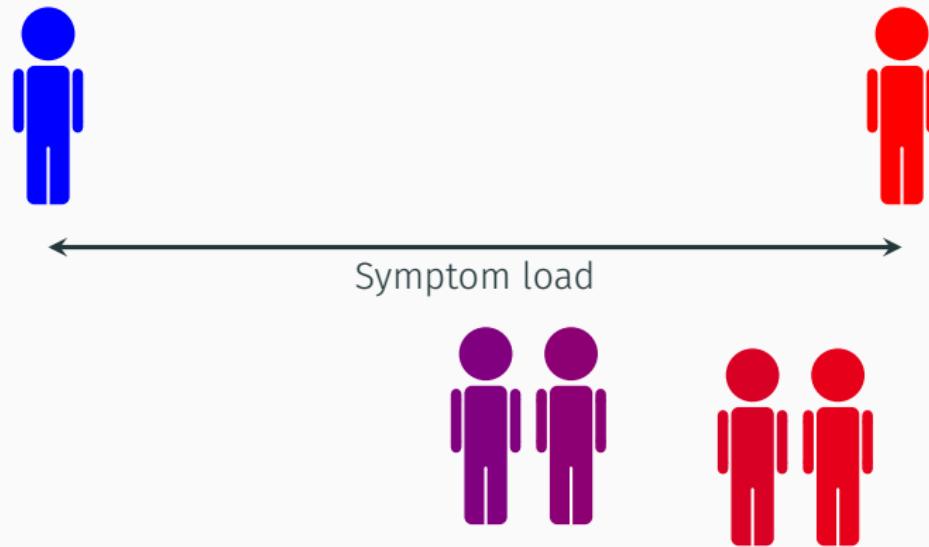
Challenges: Predictive targets



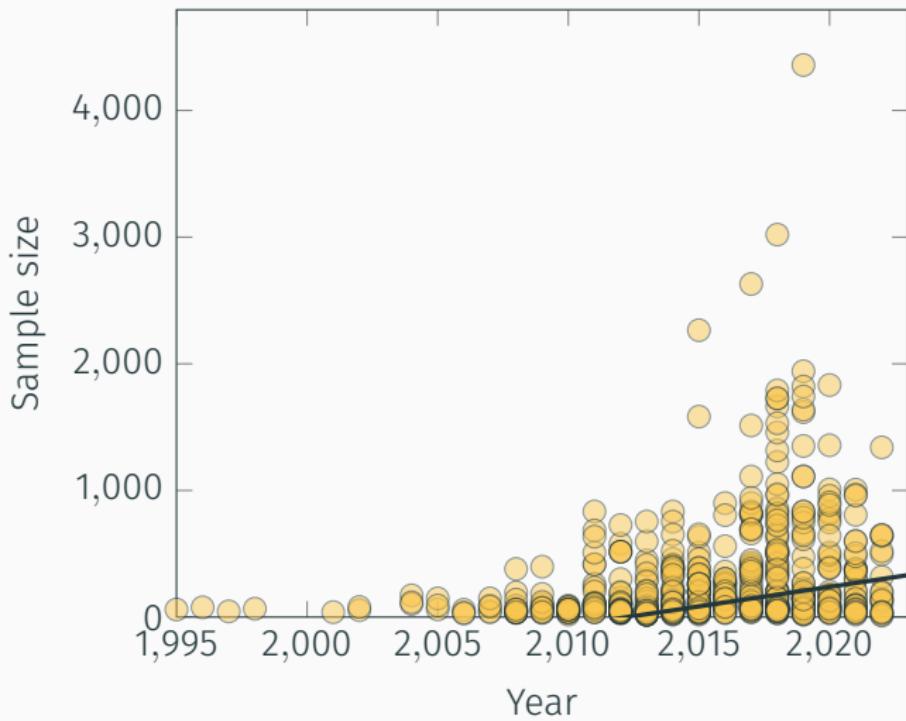
Challenges: Predictive targets



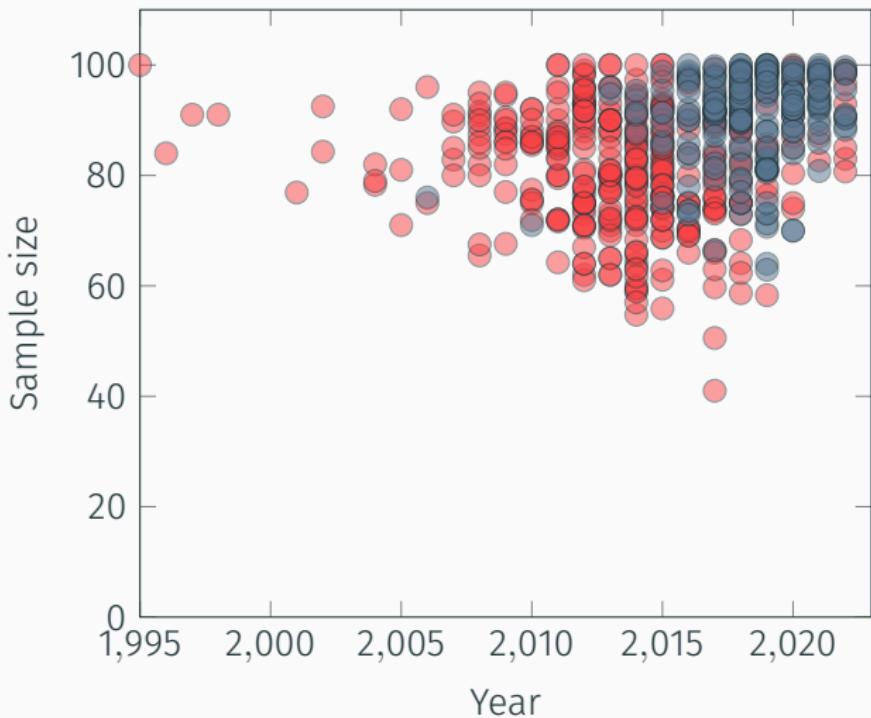
Challenges: Predictive targets



Opportunities: Larger datasets



Opportunities: Better methods



Opportunities: Better methods

