

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

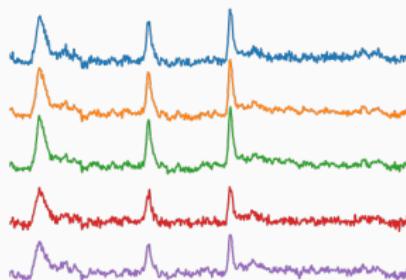


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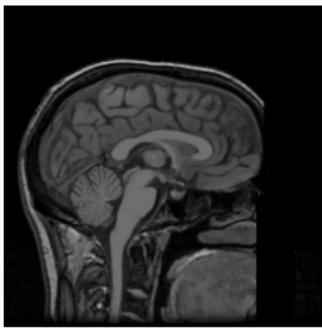


Sample from the MNE library

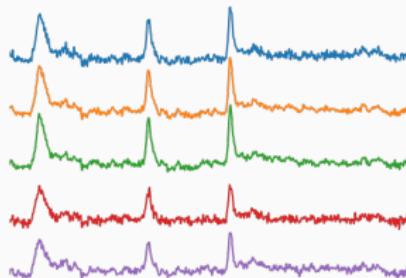


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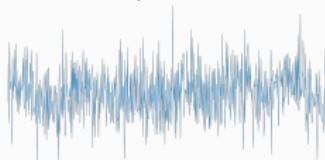
- The role of neuroimaging beyond T1-weighted MRI in the diagnosis and prediction of neuropsychiatric disorders



Bert from FreeSurfer 7.3



Sample from the MNE library



Sample from Tremlay et al., 2016

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

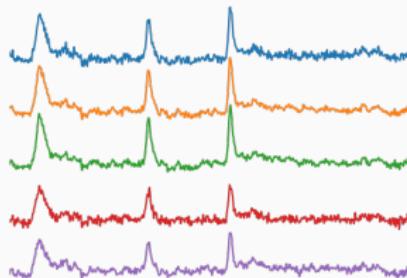


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Bert from FreeSurfer 7.3



Sample from the MNE library



Sample from Tremblay et al., 2016



Meta Quest Pro

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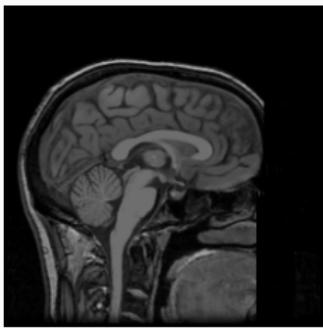
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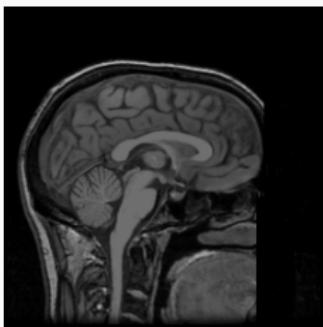


Bert from FreeSurfer 7.3



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3D

Bert from FreeSurfer 7.3



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Sagittal, axial

Bert from FreeSurfer 7.3

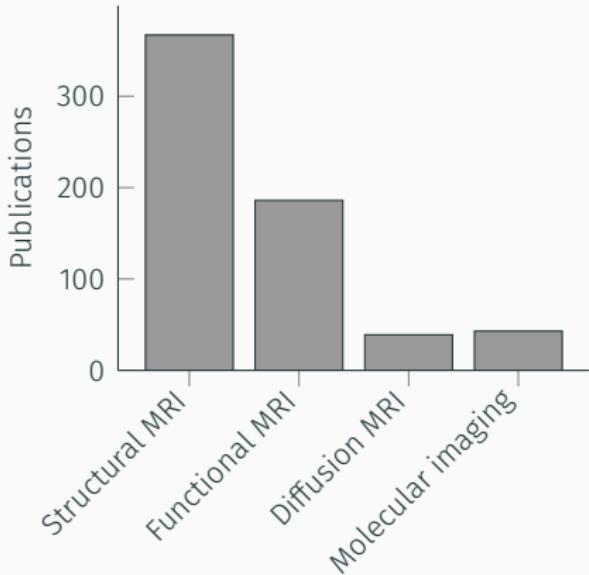


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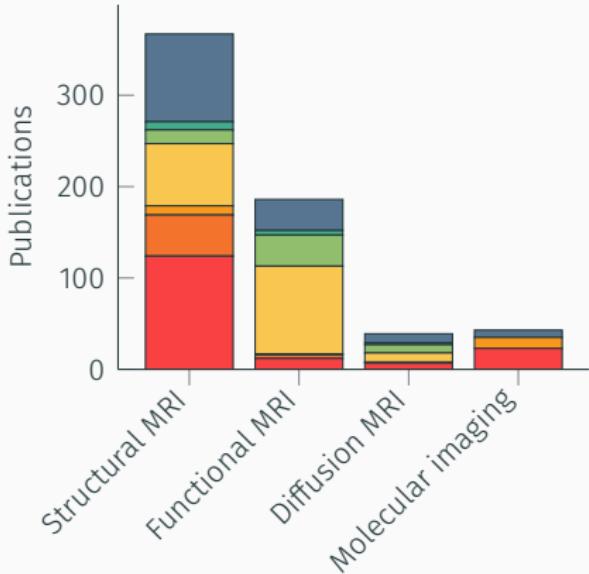


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Bert from FreeSurfer 7.3



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

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



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

Multiple Sclerosis (MS)

Parkinson's Disease (PD)

Bipolar Disorder (BP)
Schizophrenia (SCZ)

Depressive disorders, including
major depressive disorder (MDD)



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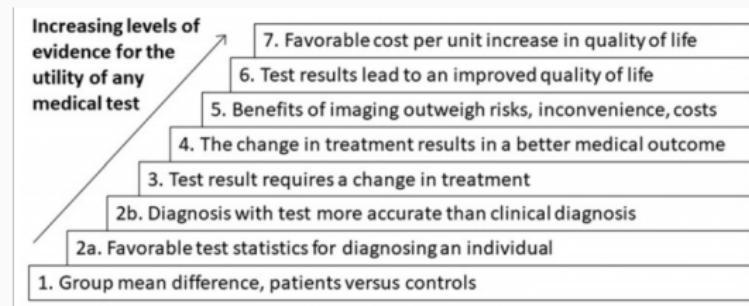


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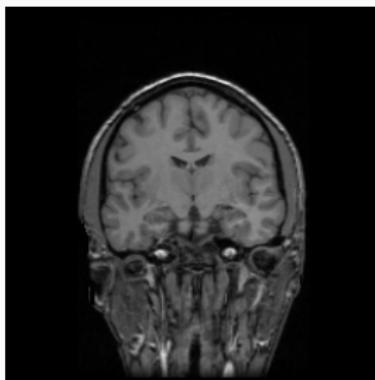


Vogel & Black (2024)



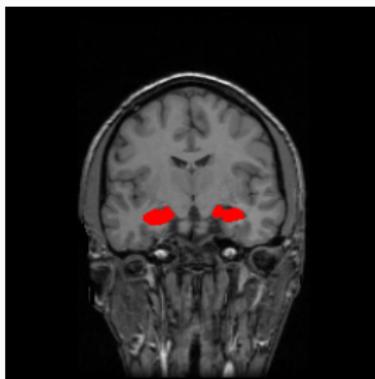
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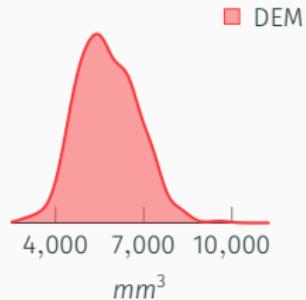
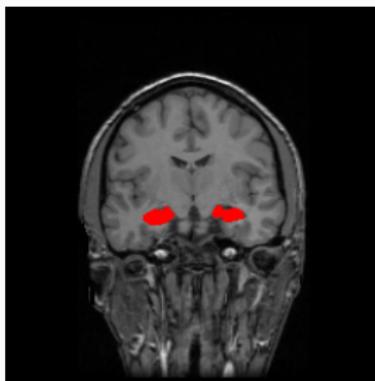
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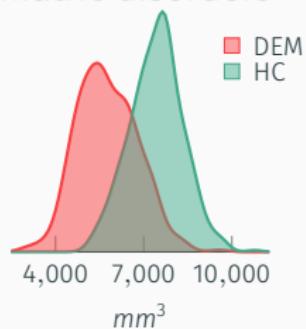
Data from ADNI

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



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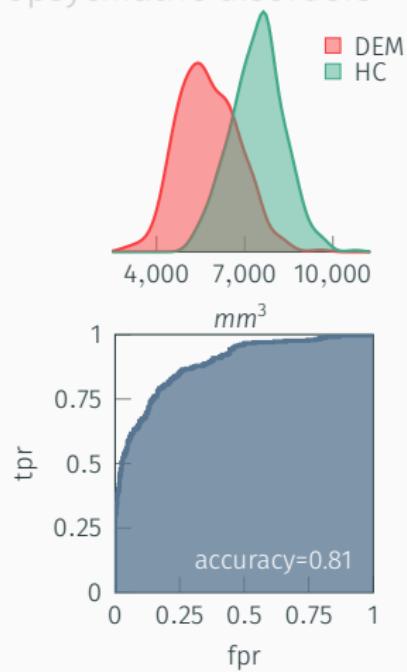
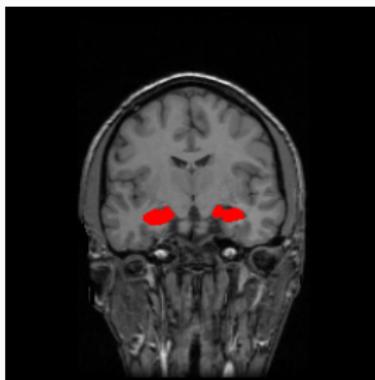
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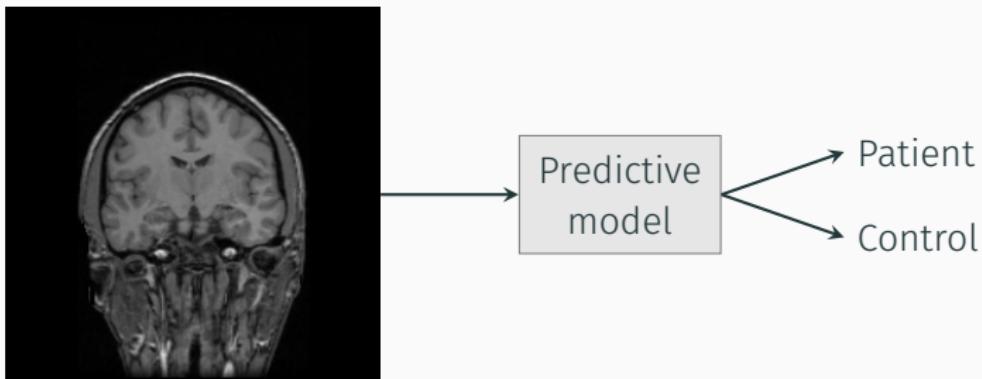
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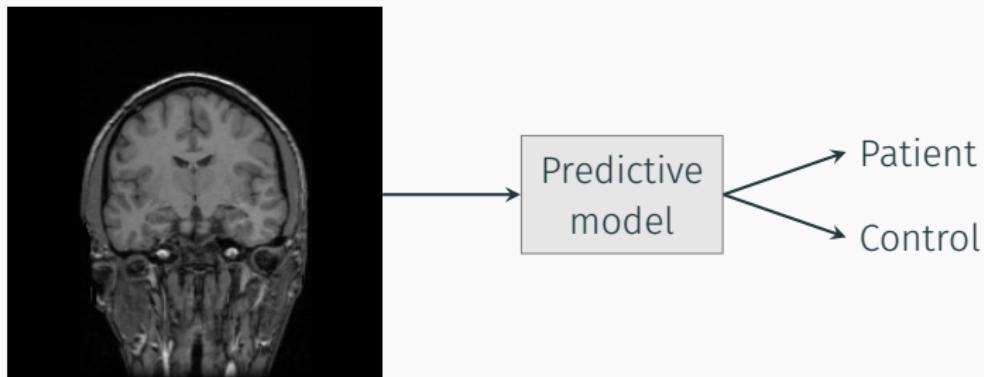
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$$\text{accuracy} = \frac{\text{correct predictions}}{\text{all predictions}}$$



Neuroimaging modalities for diagnostic predictions



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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)						
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Molecular imaging (MOL)						
	DEM	MS	PD	SCZ	MDD	BP

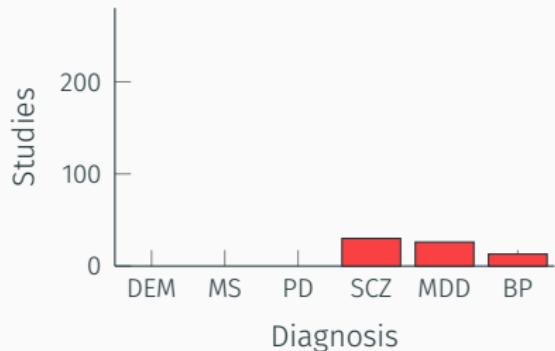


Data



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}



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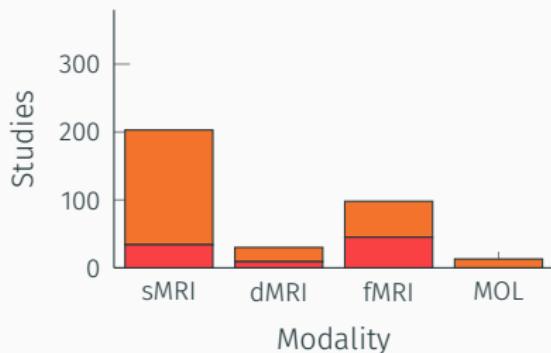
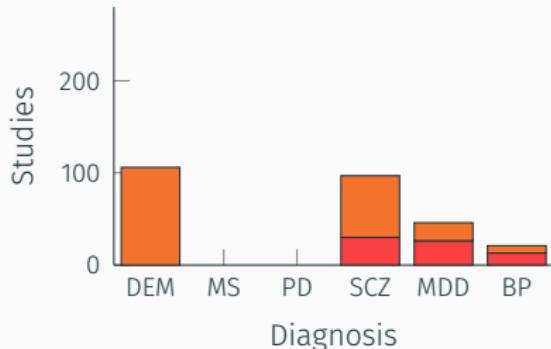


From estimating activation locality to predicting disorder: A review of pattern recognition for neuroimaging-based psychiatric diagnostics

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



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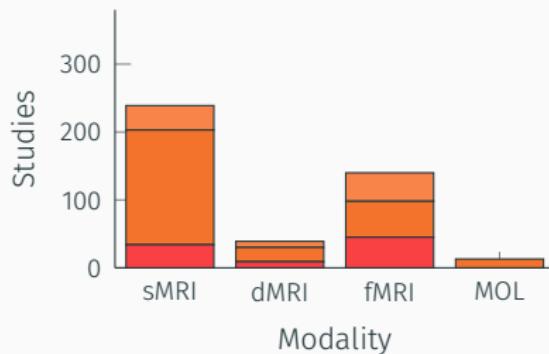
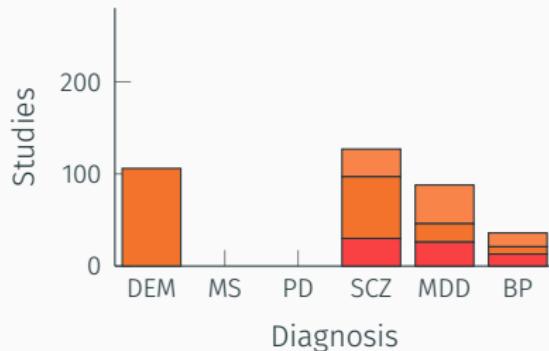
Thomas Wolters ^{a b} , Jan K. Buitelaar ^{c d}, Christian F. Beckmann ^{b c e}, Barbara Franke ^{a f}, Andre F. Marquand ^{a g}

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Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun



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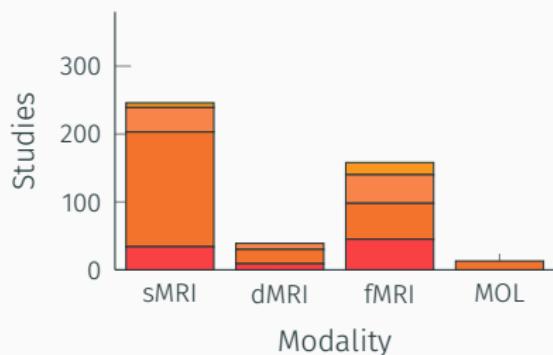
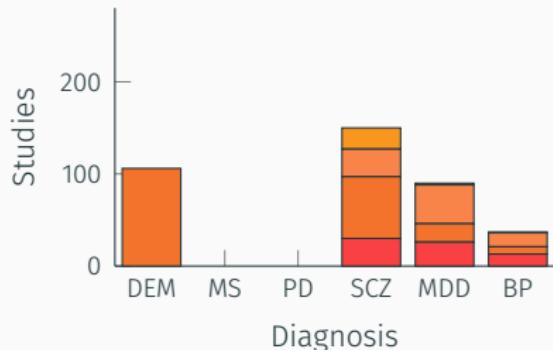
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Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun

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

Mirjam 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

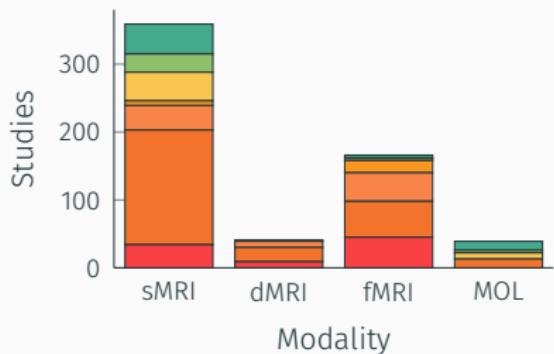
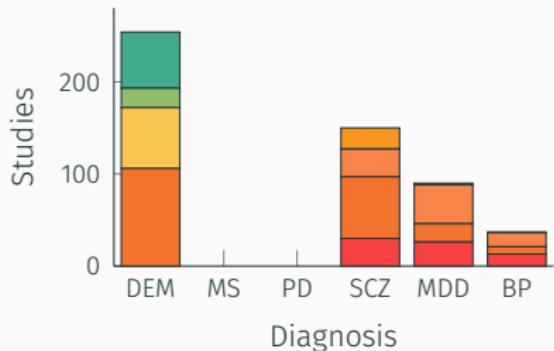
Mr Amir Ebrahimghahnavieh ³, Suhuai Luo ³, Raymond Chiong ²

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

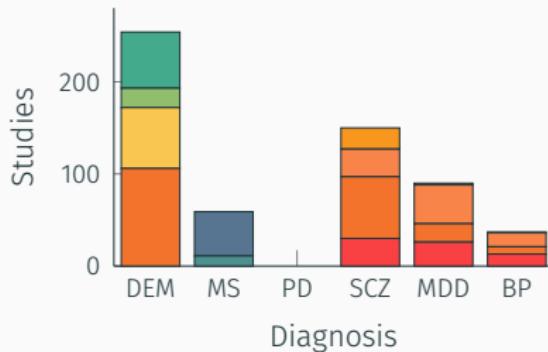


Data



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

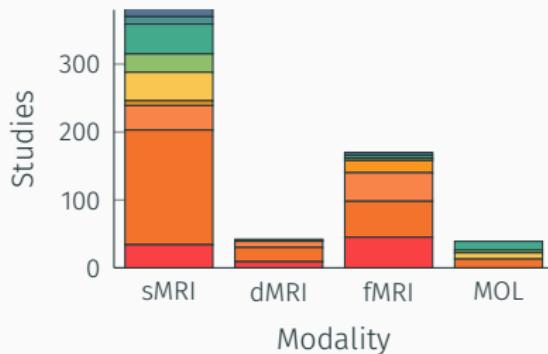
Afshin Shoibii ¹, Marjane Khodatari ², Mahboobeh Jafari ³, Parisa Mordinian ⁴, Mitra Rezaei ⁵, Roohallah Alzadehsani ⁶, Fahime Khozeimeh ⁶, Juan Manuel Gorri ⁷, Jonathan Heras ⁸, Maryam Panahiazar ⁹, Saeid Nahavandi ⁸, U Rajendra Acharya ¹⁰



Diagnosis

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

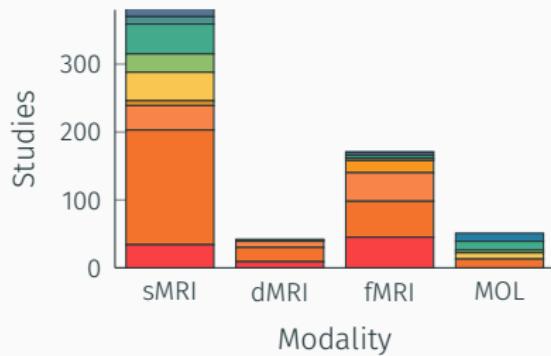
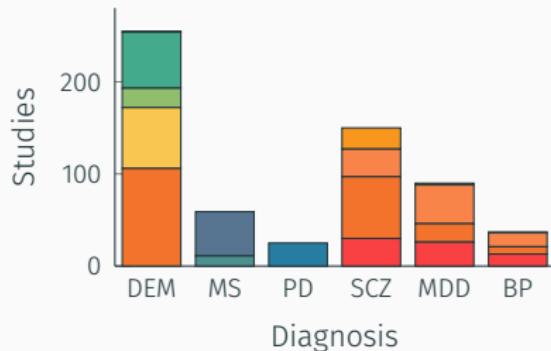
by Nida Aslam ¹ , Irfan Ulah Khan ¹ , Asma Basharat ¹, Fatima A. Alghoot ¹, Meena Aboulhous ¹ , Noorah M. Alsuwayyed ¹, Rawa'a K. Alturash ¹, Samira Brahim ², Sumayth S. Aljanes ¹ and Kholeoud Al Ghendi ³



Modality



Data



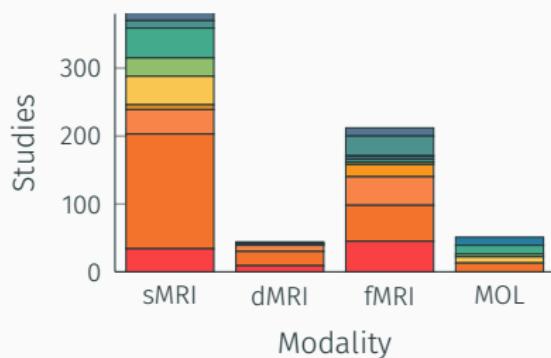
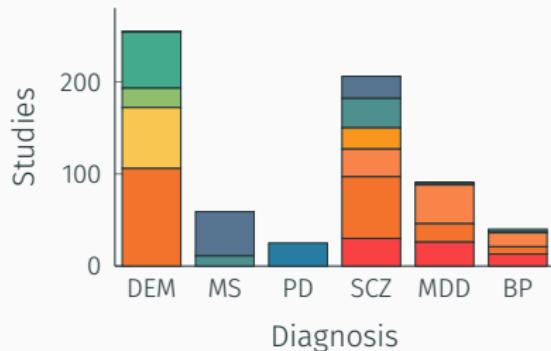
Role of Artificial Intelligence Techniques and Neuroimaging Modalities
in Detection of Parkinson's Disease: A Systematic Review
Nikita Aggarwal¹ • B. S. Saini¹ • Savita Gupta²



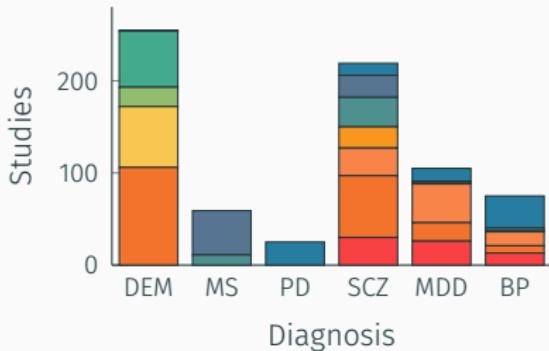
Data



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

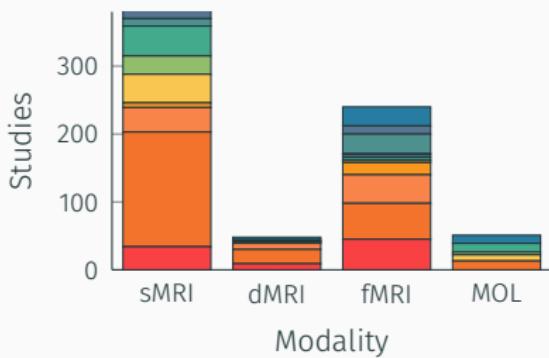


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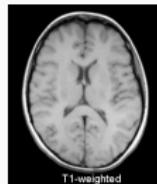


Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

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



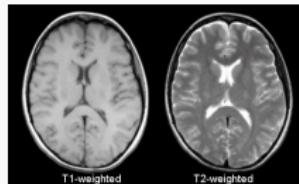
Other structural MRI modalities



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



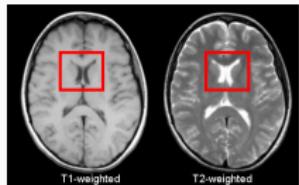
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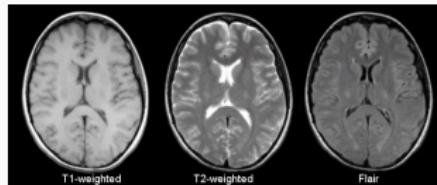
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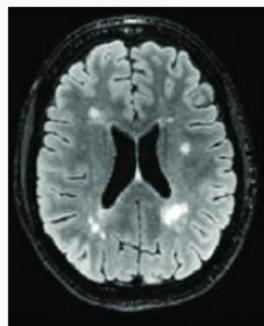
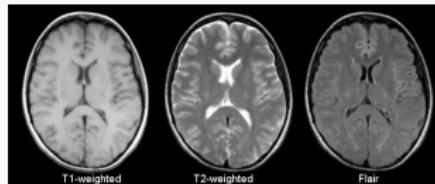
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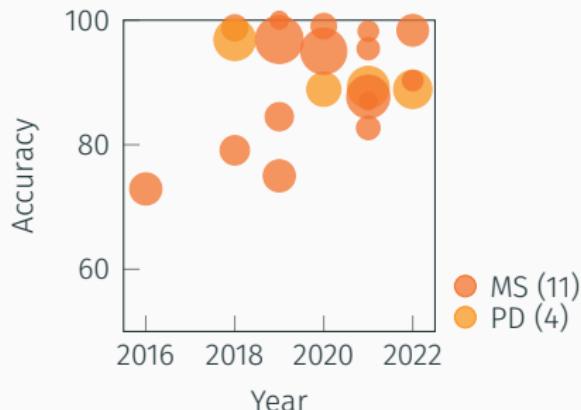
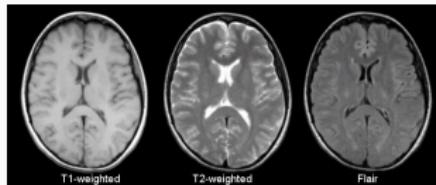
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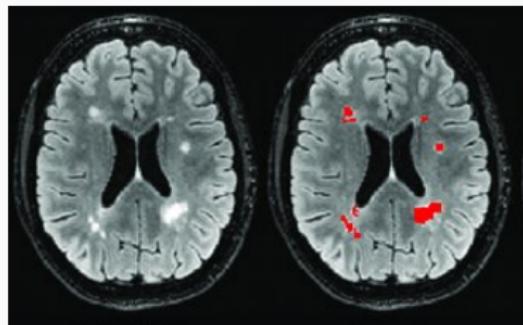
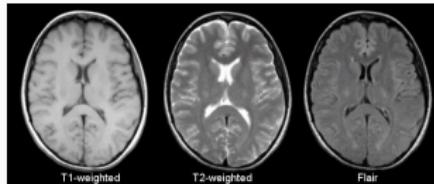
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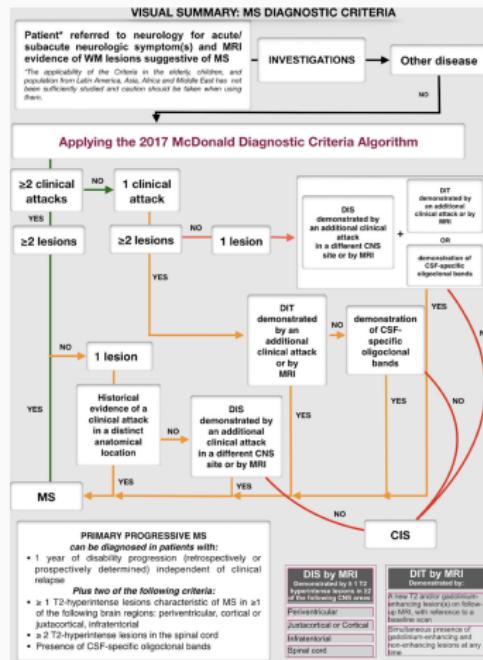
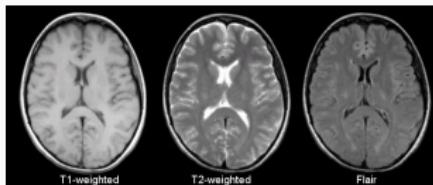
Other structural MRI modalities



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



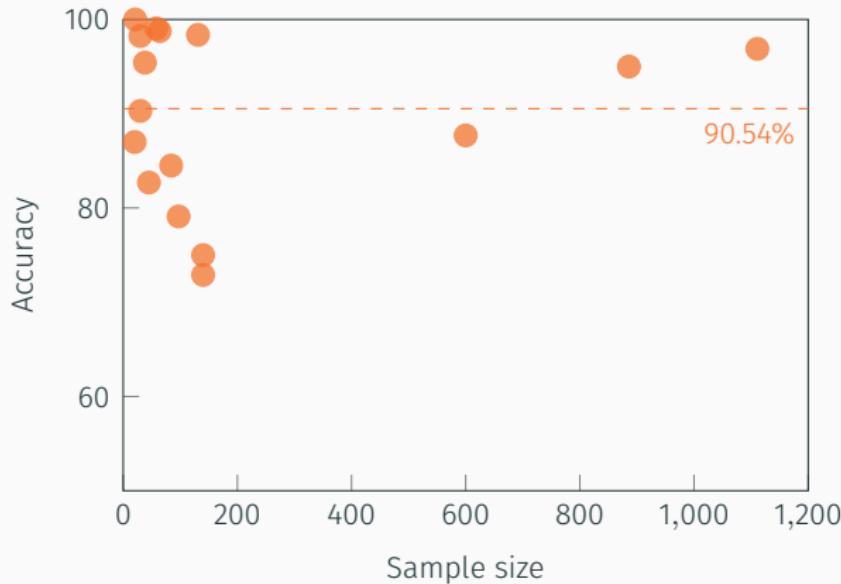
De Angelis, F., Brownlee, W. J., Chard, D. T., & Trip, S. A. (2019). New MS diagnostic criteria in practice. Practical Neurology, 19(1), 64-67



Other structural MRI modalities



MS classification studies using T2/FLAIR



Other structural MRI modalities



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

	Prediction of Clinical Worsening (EDSS Model)	Prediction of Cognitive Worsening (SDMT Model)	Prediction of Clinical and Cognitive Worsening (EDSS + SDMT Model)	P*
CNN deep learning	Accuracy (%)	81.3	67.7	—
	Sensitivity (%)	52.1	60.0	—
	Specificity (%)	90.0	81.8	—
Expert raters consensus	Accuracy (%)	—	—	70.8
	Sensitivity (%)	—	—	74.3
	Specificity (%)	—	—	80.0

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



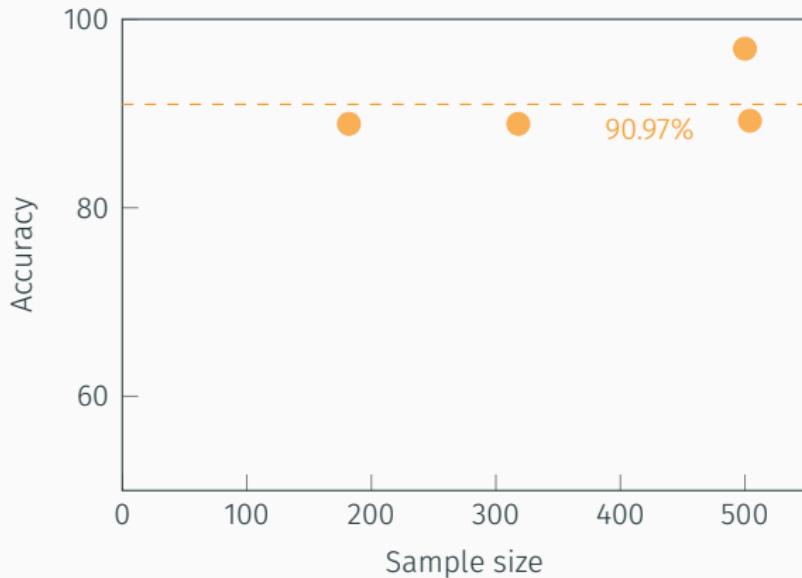
Storelli, L., Azzimonti, M., Gueye, M., Vizzino, C., Preziosa, P., Tedeschi, G., ... & Rocca, M. A. (2022). A deep learning approach to predicting disease progression in multiple sclerosis using magnetic resonance imaging. *Investigative Radiology*, 57(7), 423-432



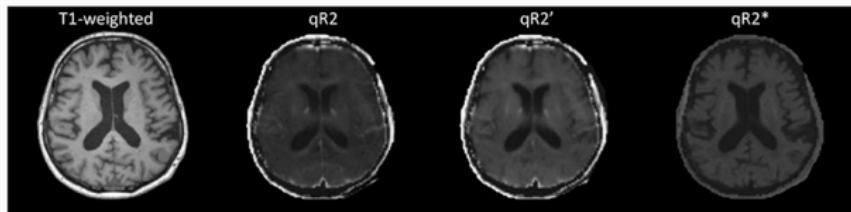
Other structural MRI modalities



PD classification studies using T2/FLAIR



Other structural MRI modalities



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



Other structural MRI modalities



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

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

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



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



Other structural MRI modalities

Non-T1 weighted structural MRI

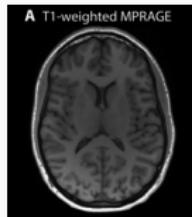
High accuracies for classifying MS and PD (>90%).

T2-weighted images used by Storelli et al. for predicting MS prognosis.

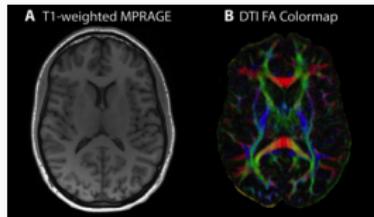
T2-weighted images used by Talai et al. for differential diagnosis of PD and PSP-RS.



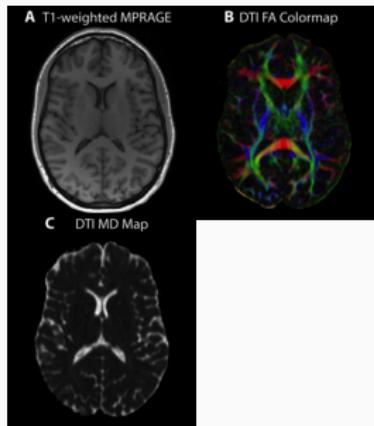
Diffusion MRI



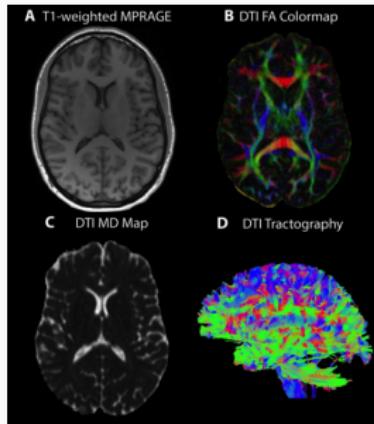
Diffusion MRI



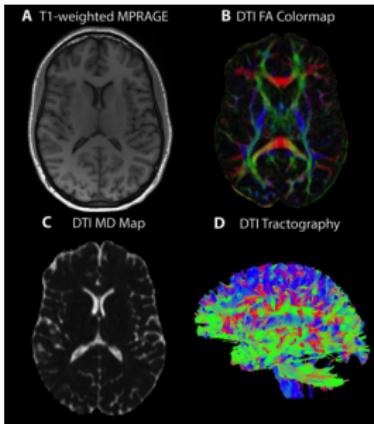
Diffusion MRI



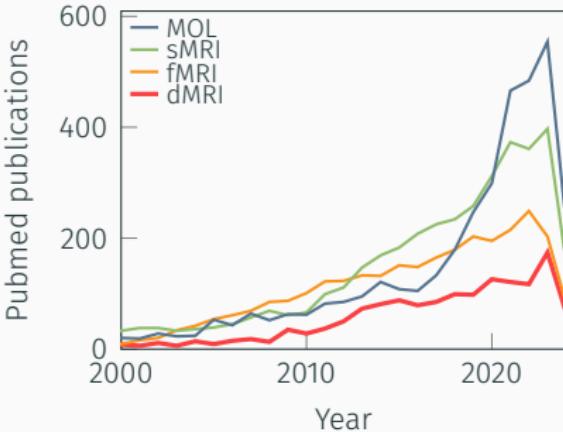
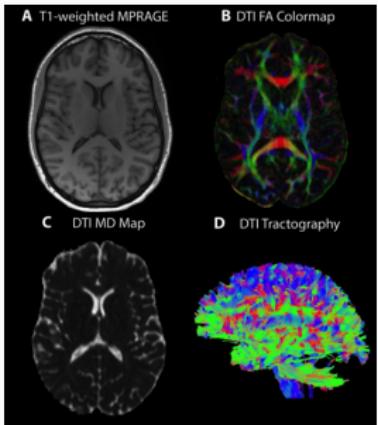
Diffusion MRI



Diffusion MRI



Diffusion MRI

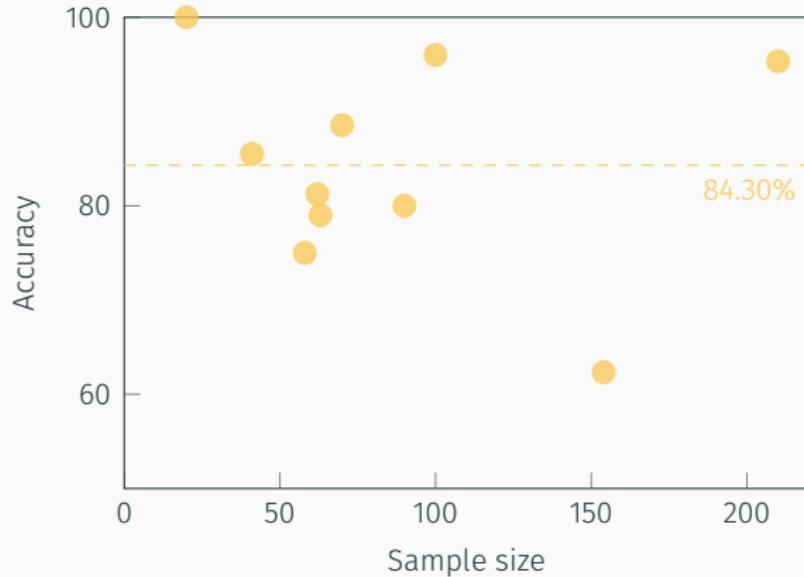


- MOL: ((molecular[Title] AND imaging[Title]) OR PET[Title] OR SPECT[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)"
- sMRI: ((structural[Title] AND MRI[Title]) OR smRI[Title] OR T1[Title] OR T2[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)
- fMRI: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

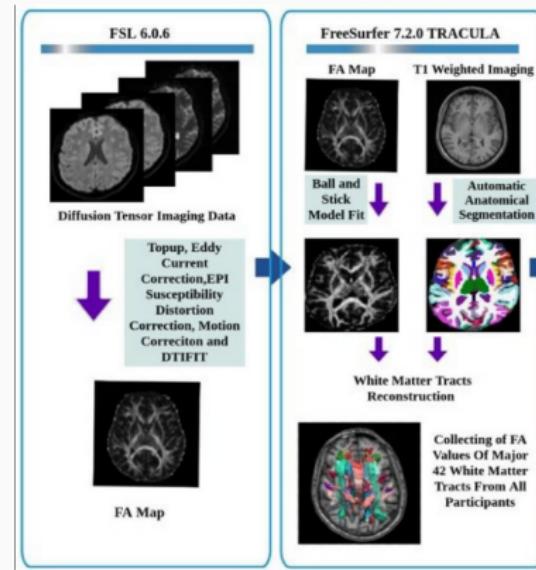




SCZ classification studies using dMRI



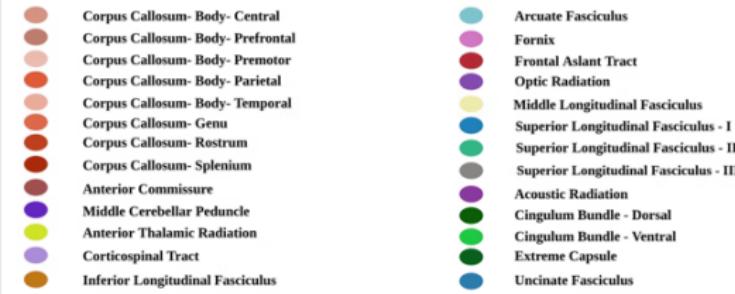
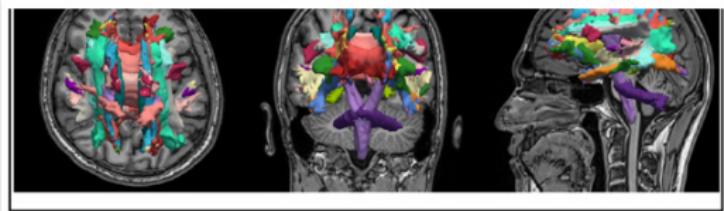
Diffusion MRI



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.



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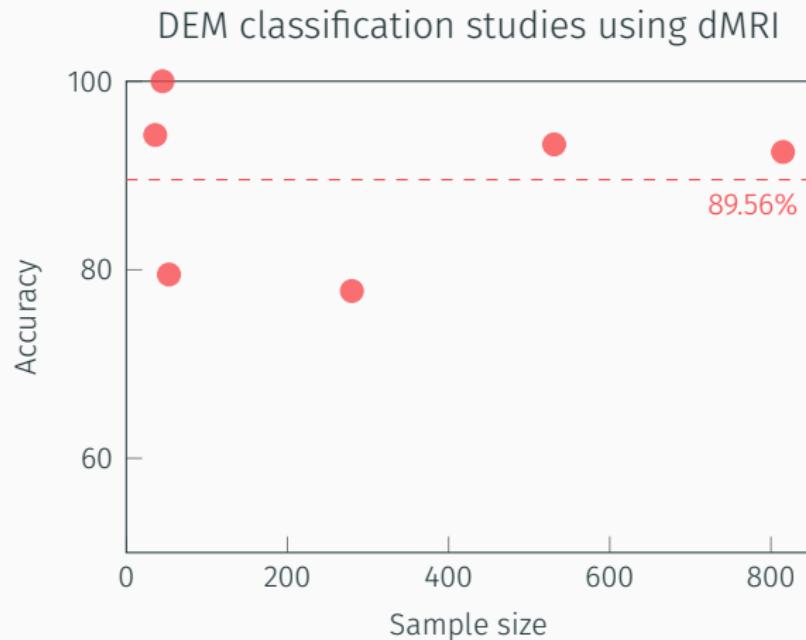
Diffusion MRI



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

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

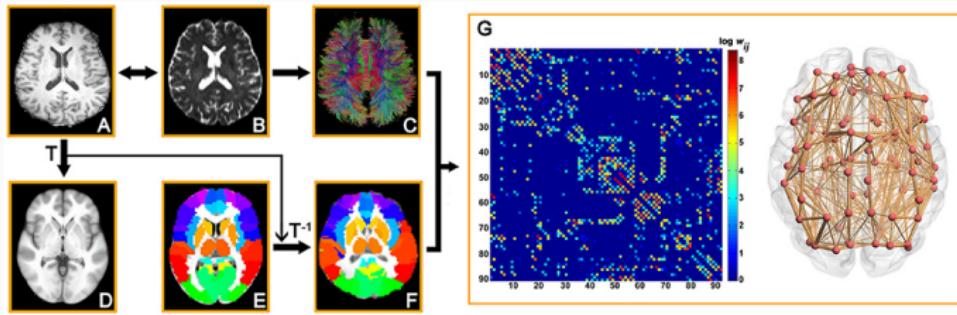




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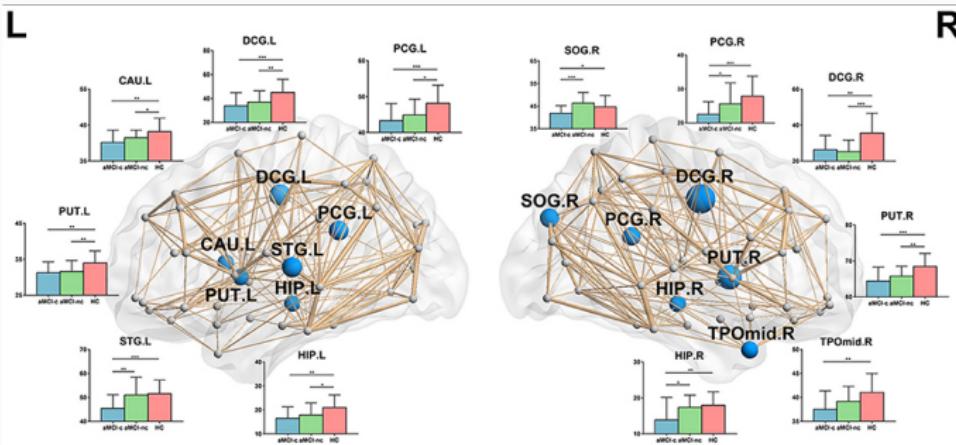
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Sun, Y., Bi, Q., Wang, X., Hu, X., Li, H., Li, X., ... & Han, Y. (2019). Prediction of conversion from amnestic mild cognitive impairment to Alzheimer's disease based on the brain structural connectome. *Frontiers in neurology*, 9, 1178



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Diffusion MRI



Diffusion MRI



Diffusion MRI

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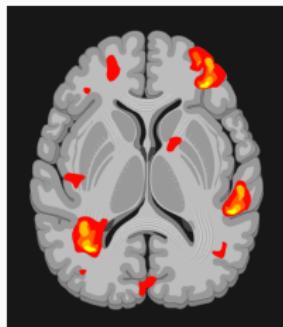
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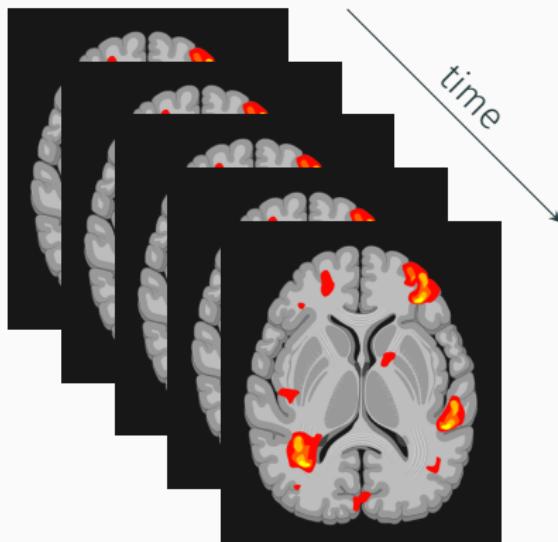
Functional Magnetic Resonance Imaging (fMRI)



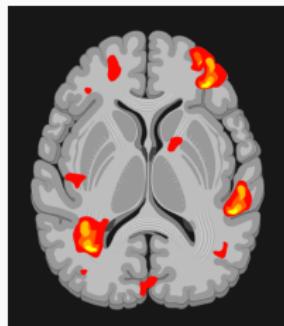
Functional Magnetic Resonance Imaging (fMRI)



Functional Magnetic Resonance Imaging (fMRI)

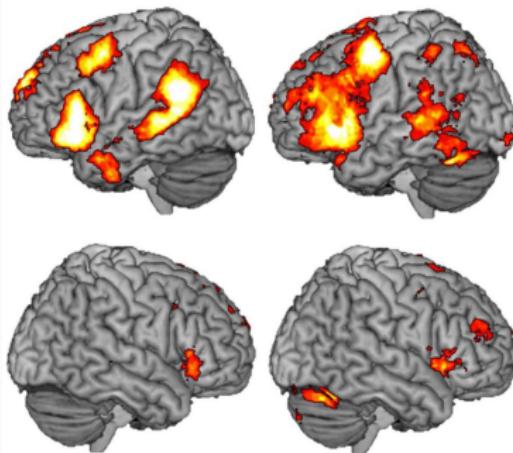


Functional Magnetic Resonance Imaging (fMRI)



rs-fMRI

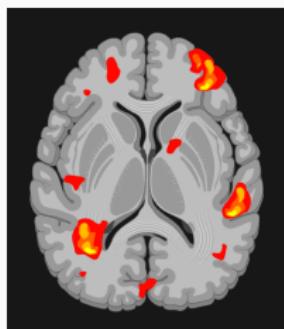
task-fMRI



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



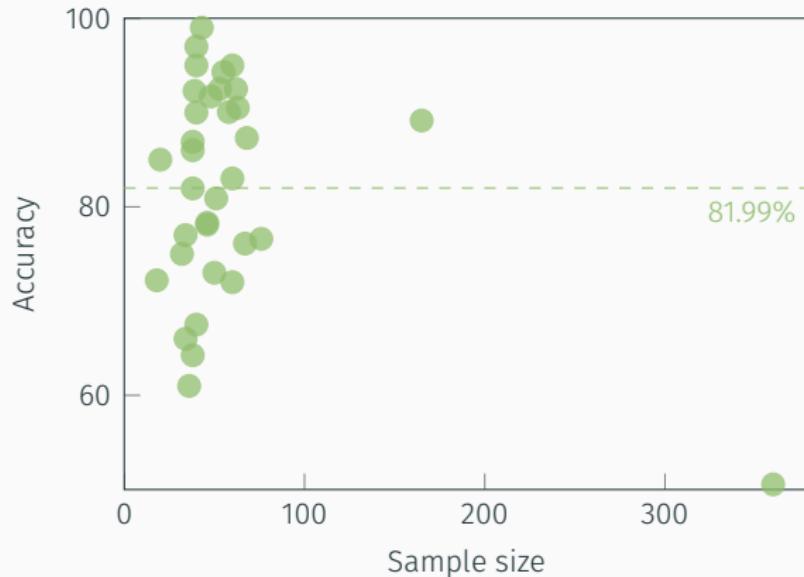
Functional Magnetic Resonance Imaging (fMRI)



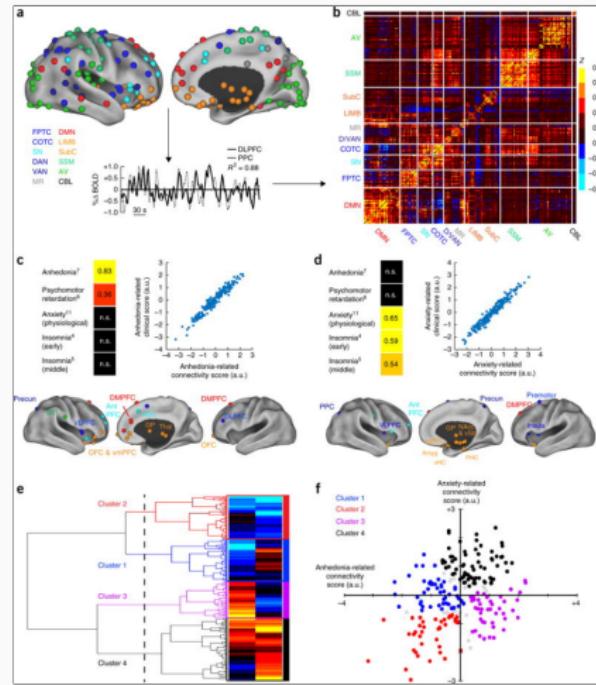
Functional Magnetic Resonance Imaging (fMRI)



MDD classification studies using fMRI



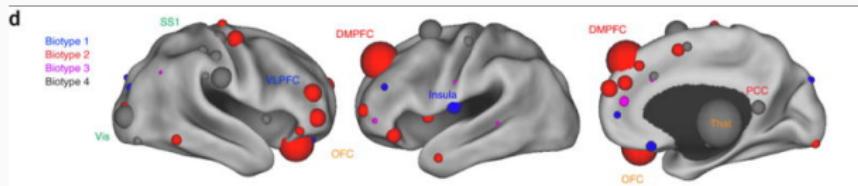
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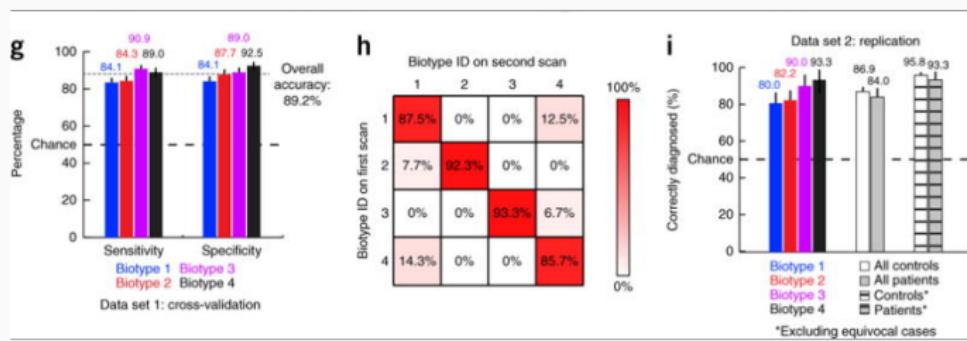
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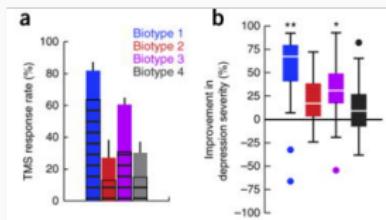
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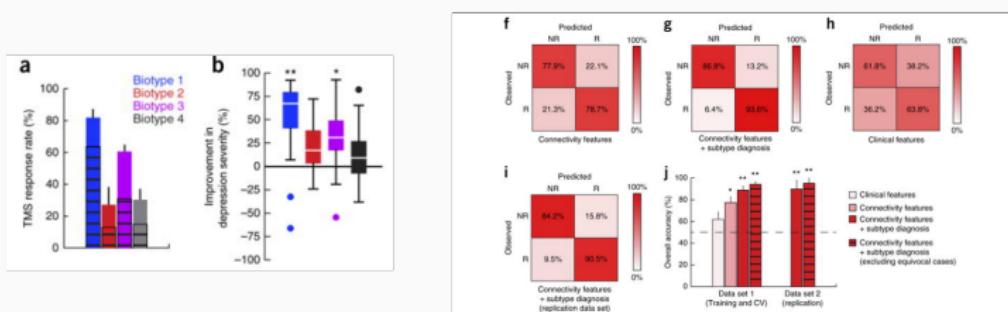
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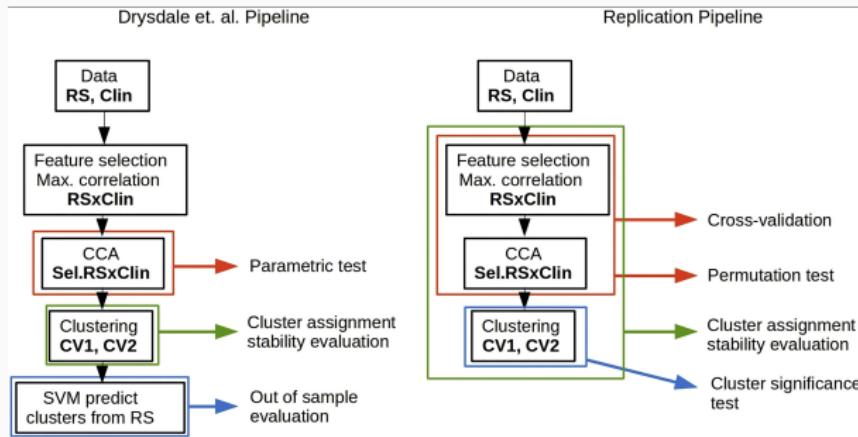
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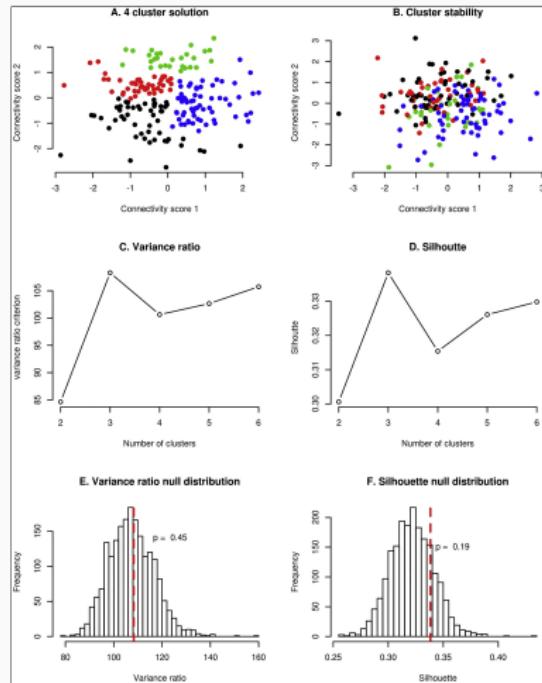
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Dinga, R., Schmaal, L., Penninx, B. W., van Tol, M. J., Veltman, D. J., van Velzen, L., ... & Marquand, A. F. (2019). Evaluating the evidence for biotypes of depression: Methodological replication and extension of. *NeuroImage: Clinical*, 22, 101796



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Functional Magnetic Resonance Imaging (fMRI)

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 - High accuracies for classifying MS and PD (>90%).
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Few prediction studies, mostly for mental disorders with various accuracies (60-100%) and DEM (80-100%)

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 - Used by Sun et al. to predict conversion from MCI to AD with 81% accuracy.

Functional MRI

Widely used for all conditions, most prominently SCZ and MDD with varying accuracies

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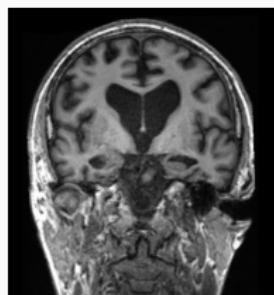
Used by Drysdale et al. to detect biotypes of MDD that reacted differently to

treatment by transcranial magnetic stimulation.

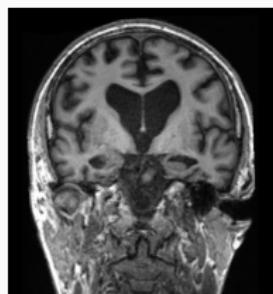
However, Dinga et al. failed to replicate their results **WHY**.



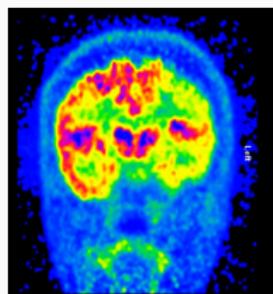
Molecular imaging (PET/SPECT)



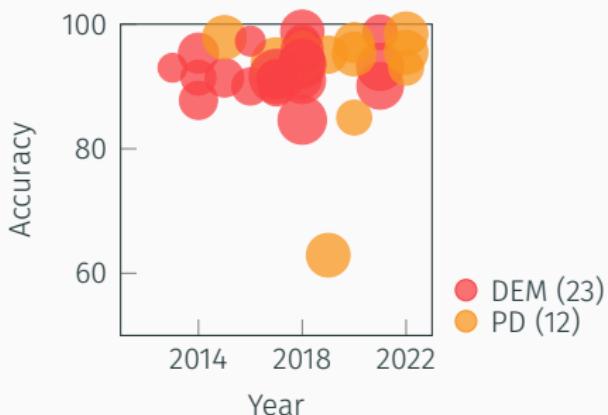
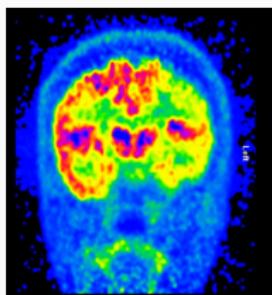
Molecular imaging (PET/SPECT)



Molecular imaging (PET/SPECT)



Molecular imaging (PET/SPECT)



Molecular imaging (PET/SPECT)



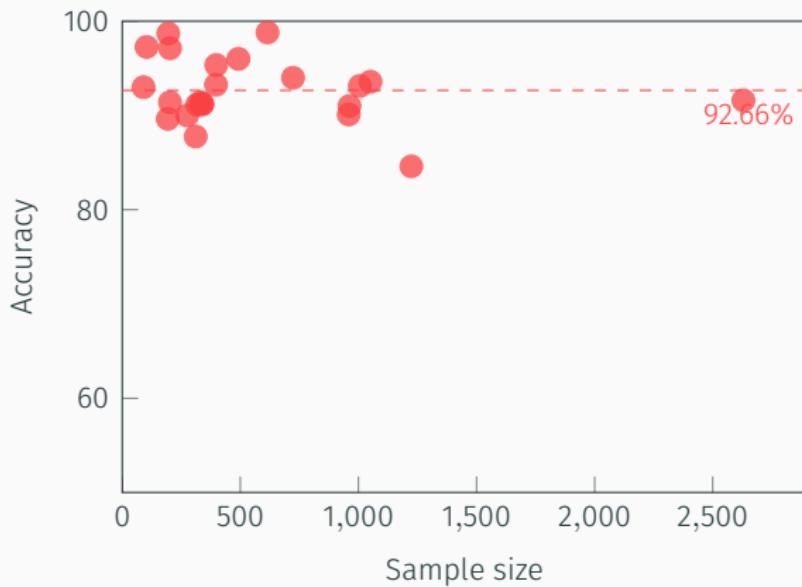
Explanation of PET



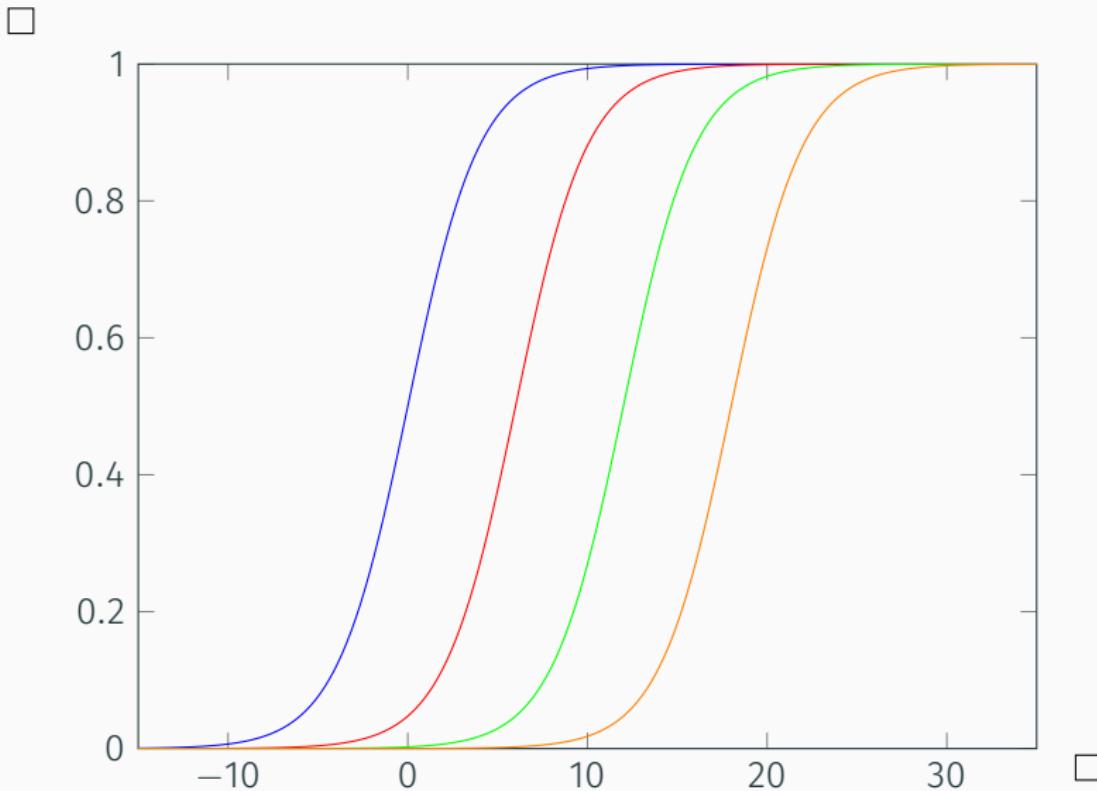
Molecular imaging (PET/SPECT)



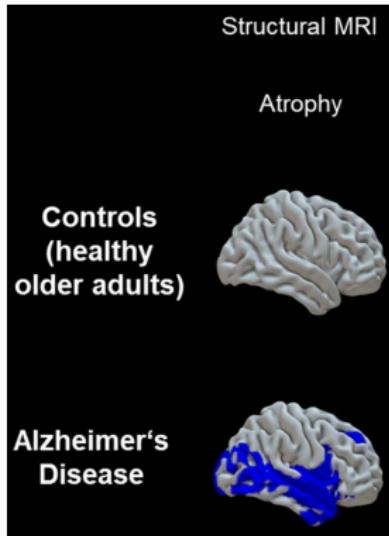
DEM classification studies using PET



Molecular imaging (PET/SPECT)



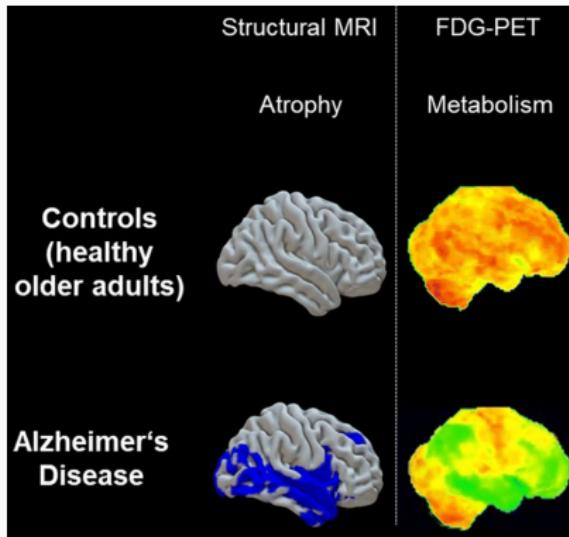
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Chételat, G., Arbizu, J., Barthel, H., Garibotto, V., Lammertsma, A. A., Law, I., ... & Drzezga, A. (2021). Finding our way through the labyrinth of dementia biomarkers. European journal of nuclear medicine and molecular imaging, 48, 2320-2324



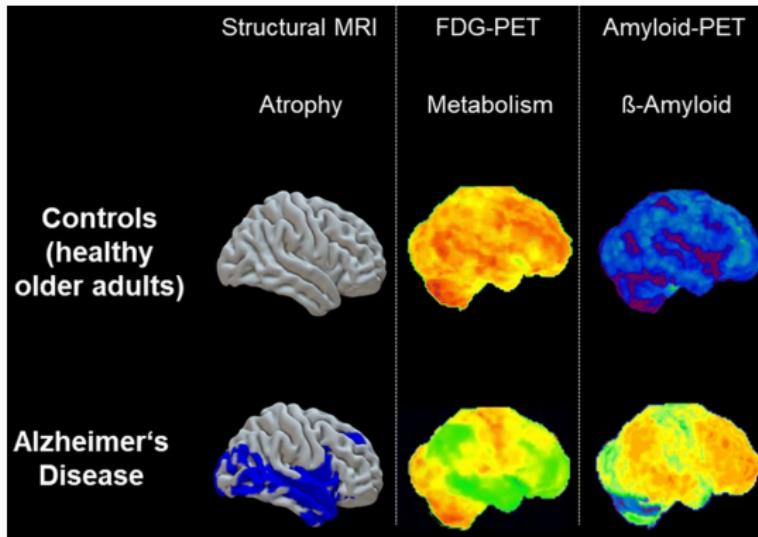
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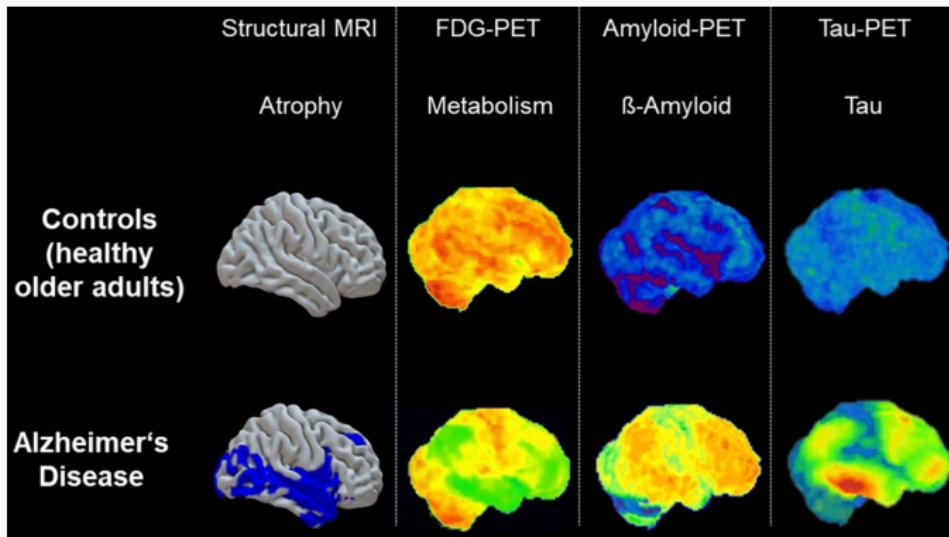
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Molecular imaging (PET/SPECT)



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

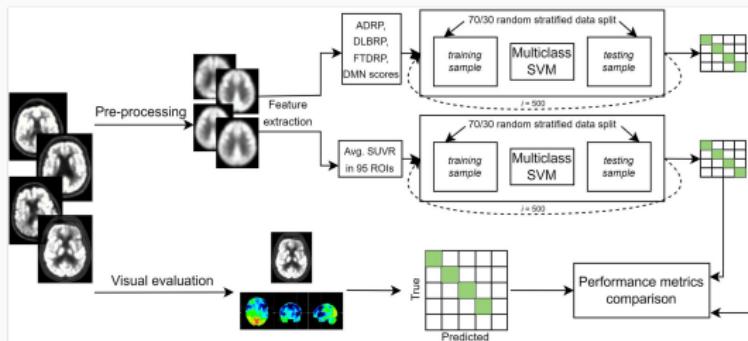
AD exists on a continuum not as discrete clinically defined entities

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)



Perovnik, M., Vo, A., Nguyen, N., Jamšek, J., Rus, T., Tang, C. C., ... & Eidelberg, D. (2022). Automated differential diagnosis of dementia syndromes using FDG PET and machine learning. *Frontiers in Aging Neuroscience*, 14, 1005731



Molecular imaging (PET/SPECT)



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

Model predicted diagnosis (86%)



Perovnik, M., Vo, A., Nguyen, N., Jamšek, J., Rus, T., Tang, C. C., ... & Eidelberg, D. (2022). Automated differential diagnosis of dementia syndromes using FDG PET and machine learning. *Frontiers in Aging Neuroscience*, 14, 1005731



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NC	2			39

Model predicted diagnosis (86%)

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

Human predicted diagnosis (78%)



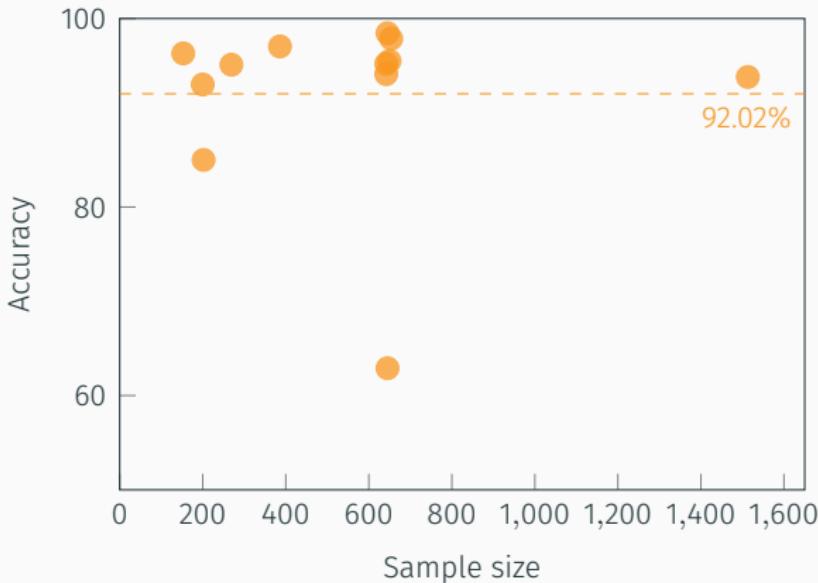
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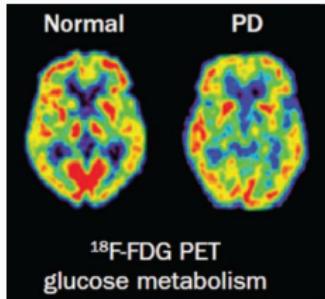
Molecular imaging (PET/SPECT)



PD classification studies using SPECT



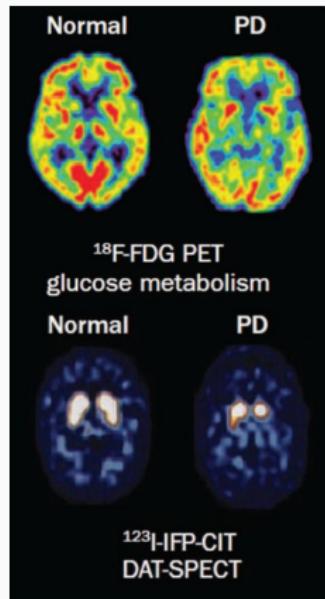
Molecular imaging (PET/SPECT)



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



Molecular imaging (PET/SPECT)



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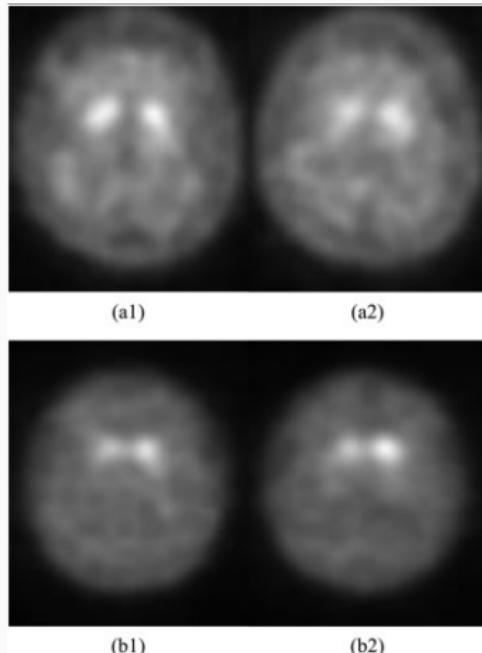
Molecular imaging (PET/SPECT)



Explanation of SPECT



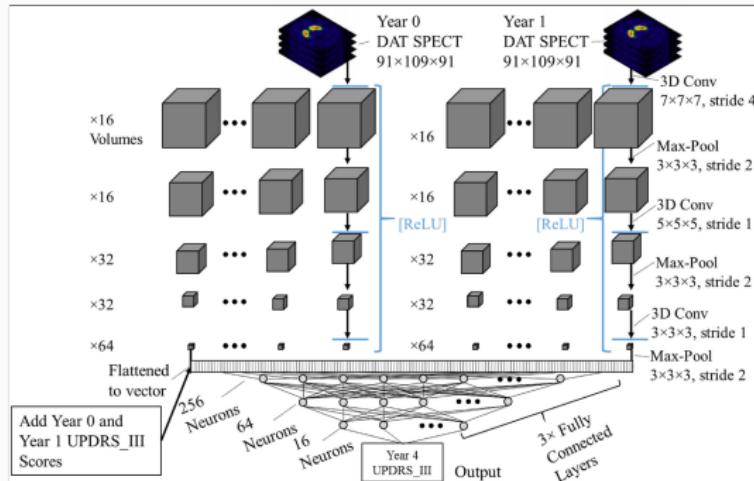
Molecular imaging (PET/SPECT)



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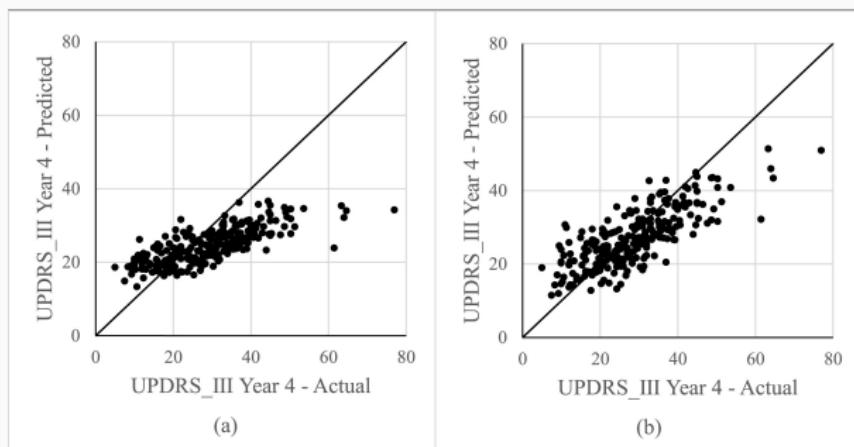
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 - Widely used for all conditions, most prominently SCZ and MDD with varying accuracies (60-100%) and DEM (80-100%).
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 - However, Dinga et al. failed to replicate their results.

Molecular imaging

Used in a moderate amount of studies predicting PD and DEM with good results (mean accuracy=92%).

