

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

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Esten H. Leonardsen

26.10.23



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# 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

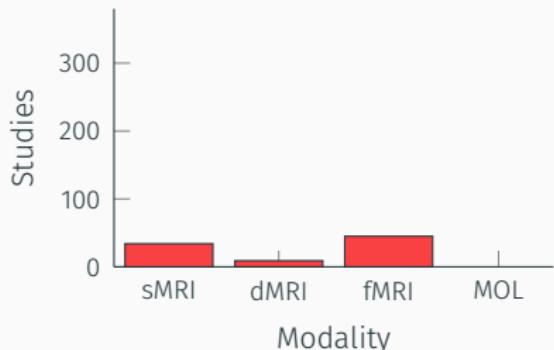
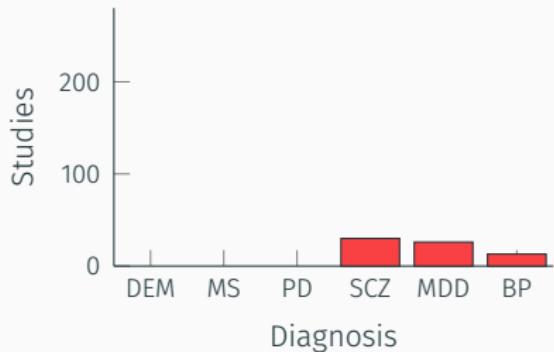
(Non-T1) structural MRI (sMRI)						
Diffusion MRI (dMRI)						
Functional MRI (fMRI)						
Molecular imaging (MOL)						

# Data



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

Thomas Wolters<sup>a,b</sup>, Jon K. Buitelaar<sup>c,d</sup>, Christian F. Beckmann<sup>b,c,e</sup>, Barbara Franke<sup>a,f</sup>, Andre F. Marquand<sup>a,g</sup>



# Data

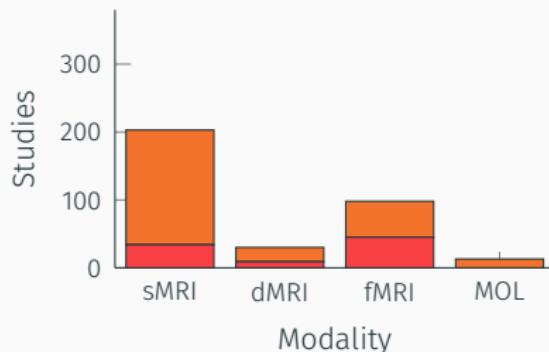
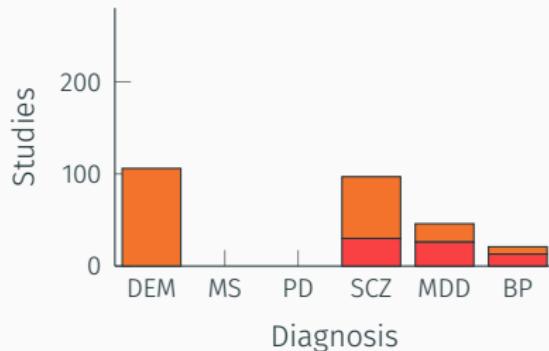


From estimating activation locality to predicting disorder: A review of pattern recognition for neuroimaging-based psychiatric diagnostics

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

Mohammad R. Arbabi Shirani<sup>a,b</sup>, [Sergey Pitis](#)<sup>b</sup>, Jing Sui<sup>a,c</sup>, [Vince D. Calhoun](#)<sup>a,d</sup>



# Data



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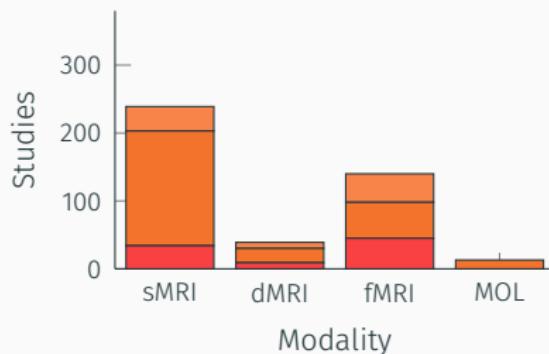
Thomas Wolters <sup>a b</sup> , Jon K. Buitelaar <sup>c d</sup>, Christian F. Beckmann <sup>b c e</sup>, Barbara Franke <sup>a f</sup>, Andre F. Marquand <sup>a g</sup>

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Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun



# Data



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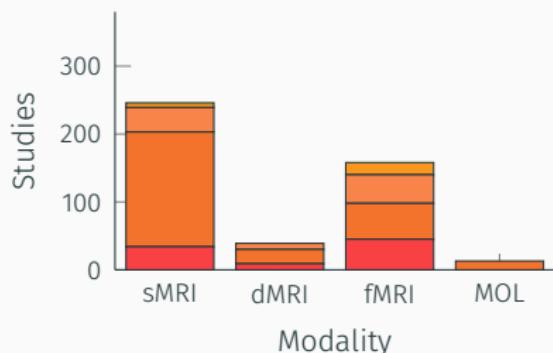
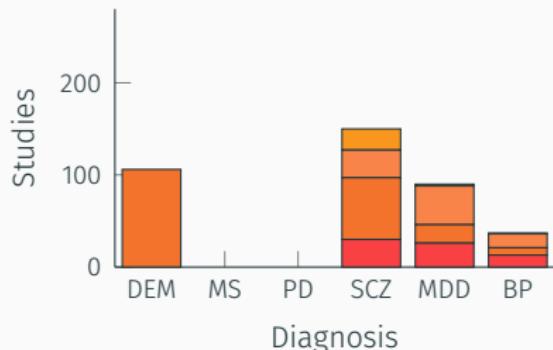
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Towards a brain-based predictome of mental illness

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

Mirjam Quaak<sup>3</sup>, Laurens van de Mortel<sup>3</sup>, Rajat Mani Thomas<sup>3</sup>, Guido van Wingen<sup>2</sup>



# Data



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

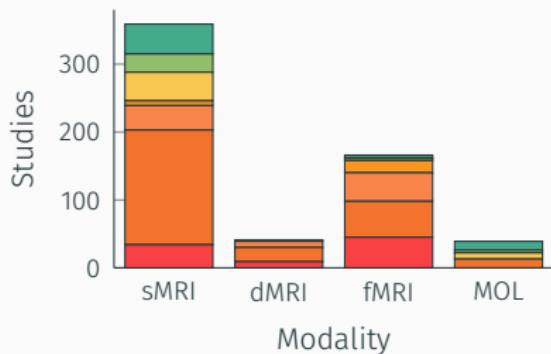
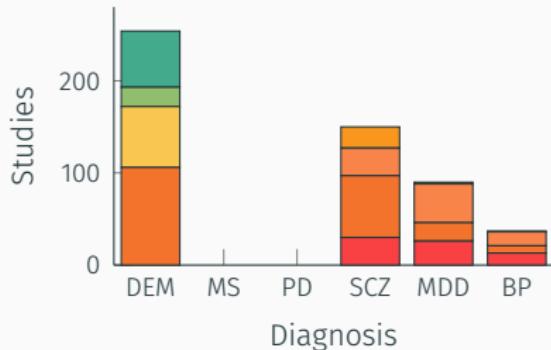
Mr Amir Ebrahimghahnavieh <sup>3</sup>, Suhuai Luo <sup>3</sup>, Raymond Chiong <sup>2</sup>

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

Golrokh Mirzaei <sup>2</sup>, R., Hajjari Adeli <sup>3</sup>

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

Sina Fathi <sup>1</sup>, Maryam Ahmadi <sup>2</sup>, Afshaneh Dehnad <sup>3</sup>

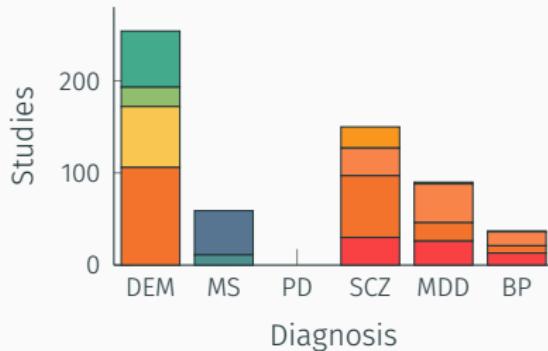


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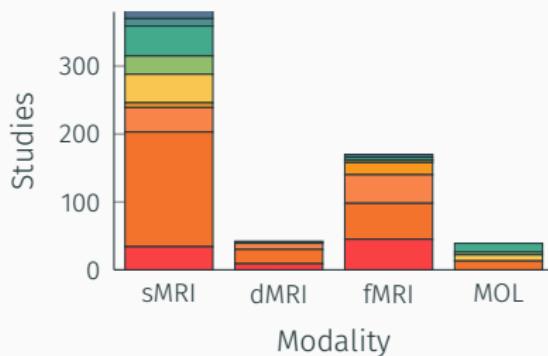
## Applications of deep learning techniques for automated multiple sclerosis detection using magnetic resonance imaging: A review

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

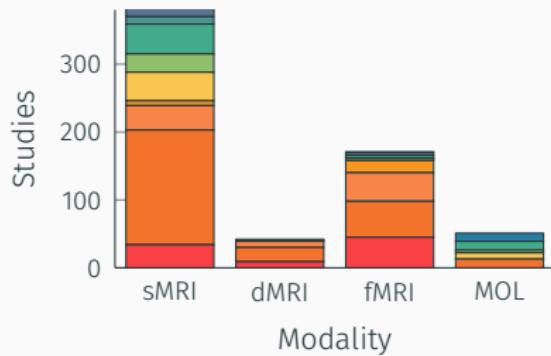
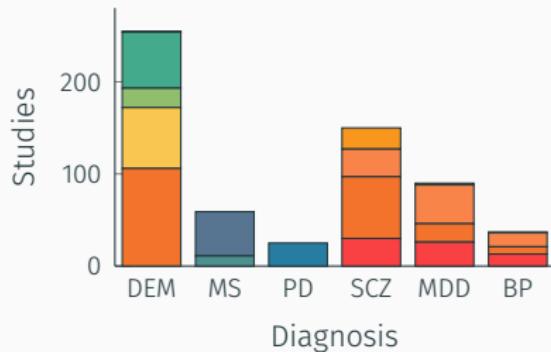


## Multiple Sclerosis Diagnosis Using Machine Learning and Deep Learning: Challenges and Opportunities

by Nida Aslam <sup>1</sup> , Irfan Ultil Khan <sup>1</sup> , Asma Basharat <sup>1</sup>, Fatima A. Alghoot <sup>1</sup>, Meena Aboulhous <sup>1</sup> , Noorah M. Alsuwayyed <sup>1</sup>, Rawa'a K. Alturais <sup>1</sup>, Samira Brahim <sup>2</sup>, Sumayyah S. Aljanees <sup>1</sup> and Kholeoud Al Ghendi <sup>3</sup>



# Data



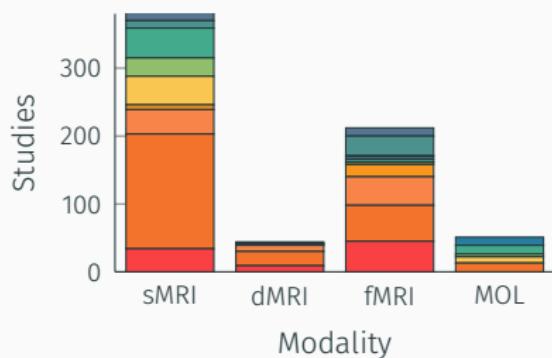
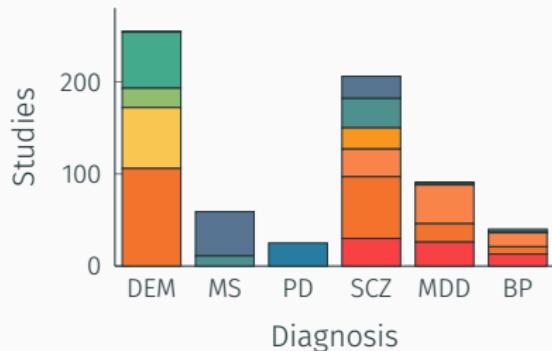
Role of Artificial Intelligence Techniques and Neuroimaging Modalities in Detection of Parkinson's Disease: A Systematic Review  
Nikita Aggarwal<sup>1</sup> • B. S. Saini<sup>1</sup> • Savita Gupta<sup>2</sup>



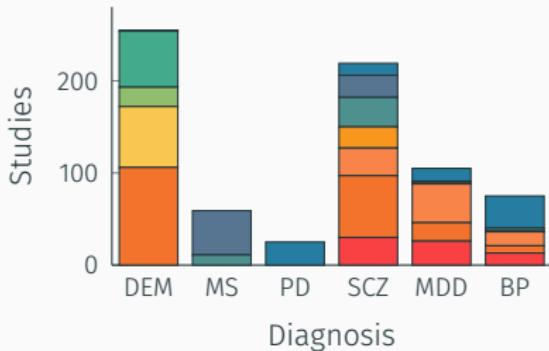
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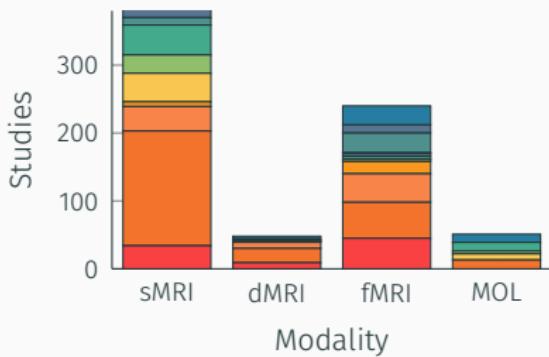
Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review  
Renato de Faria,<sup>1\*</sup> Elvira Anna Carbone,<sup>1†</sup> Raffaele Gastone,<sup>1</sup> Antonella Brusa,<sup>1</sup> Valentina Pugliese,<sup>1</sup> Cristina Segura-García,<sup>2</sup> and Pasquale De Fazio<sup>1</sup>



# Data



Diagnosis

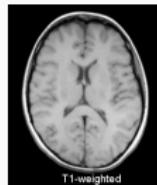


Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

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



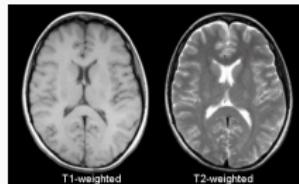
# Other structural MRI modalities



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



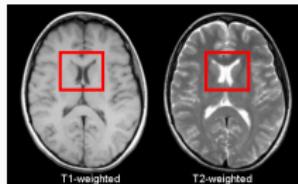
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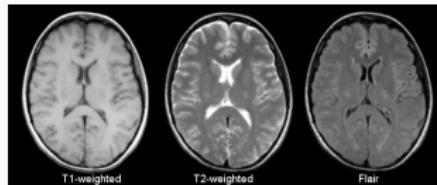
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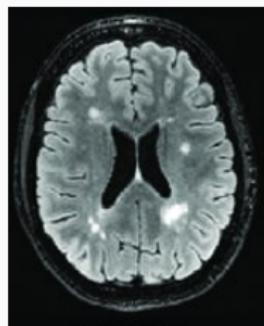
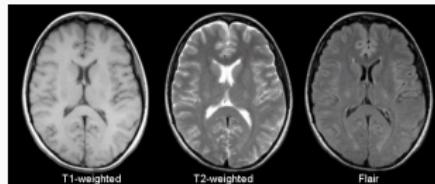
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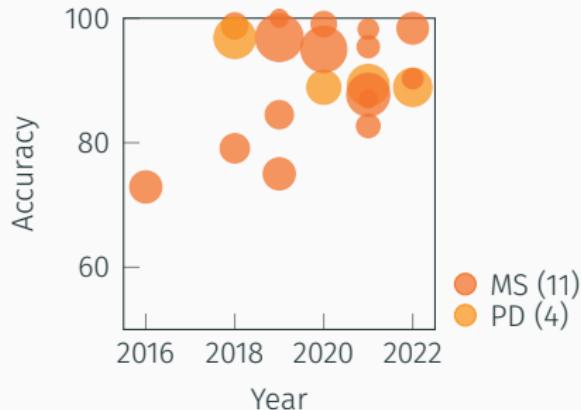
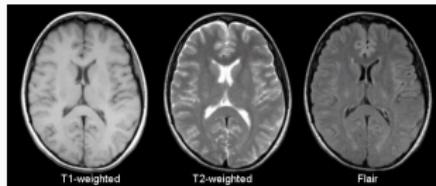
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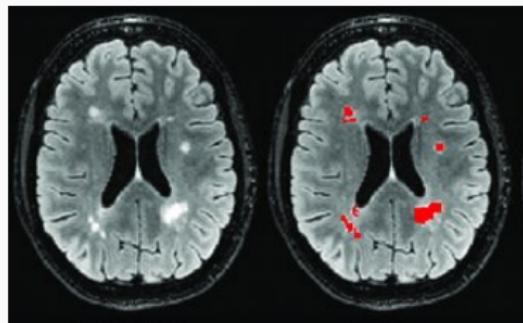
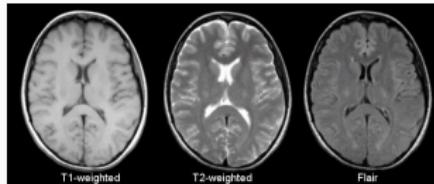
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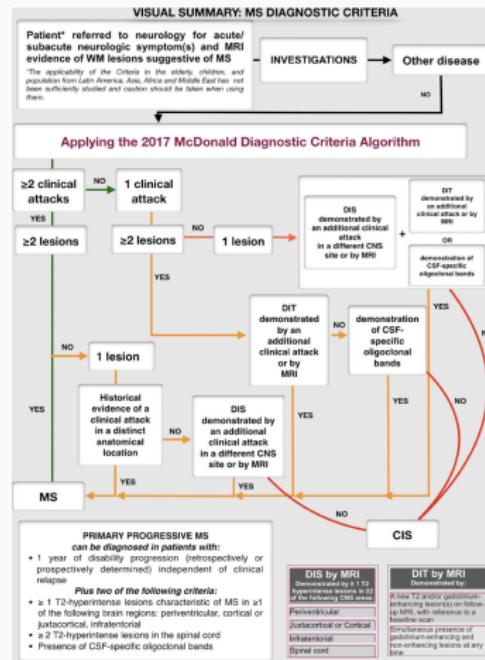
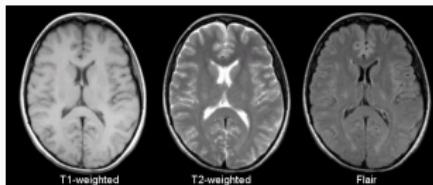
# Other structural MRI modalities



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



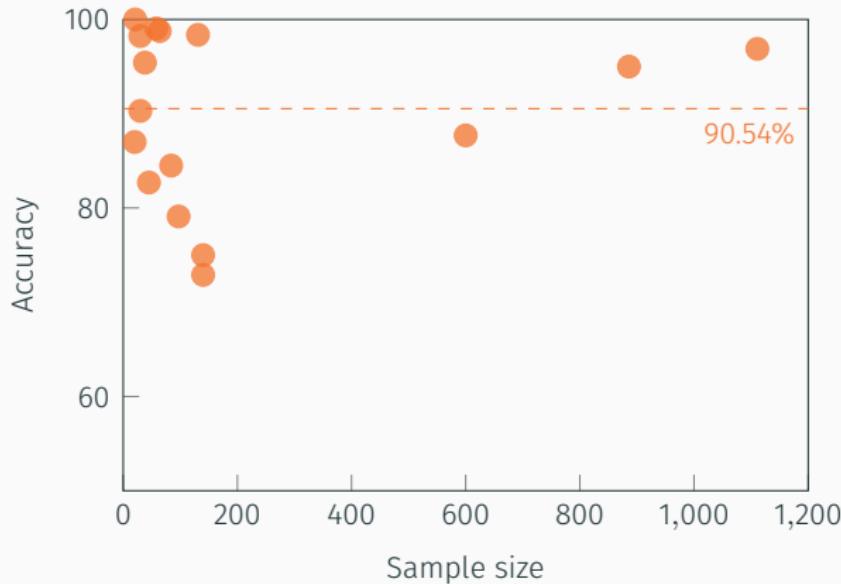
De Angelis, F., Brownlee, W. J., Chard, D. T., & Trip, S. A. (2019). New MS diagnostic criteria in practice. *Practical Neurology*, 19(1), 64-67



# Other structural MRI modalities



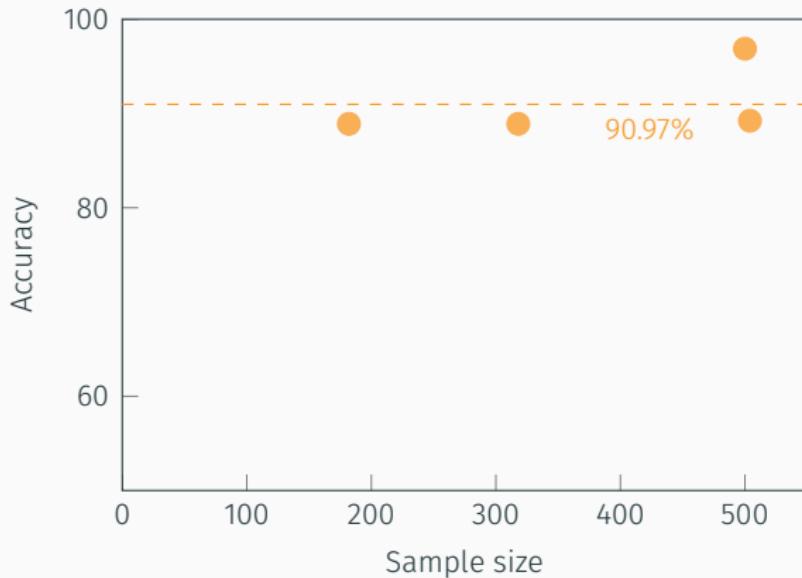
## MS classification studies using T2/FLAIR



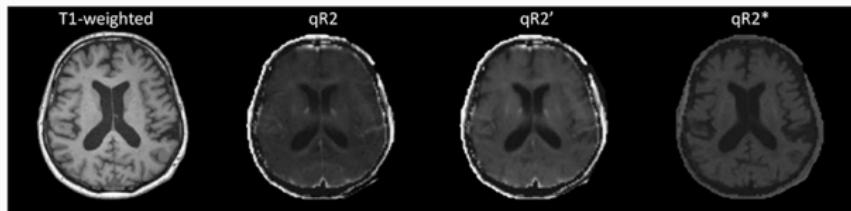
## Other structural MRI modalities



### 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

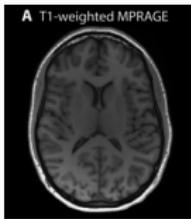
High accuracies for classifying MS and PD (>90%).

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

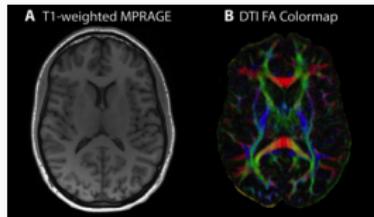
T2-weighted images used by Talai et al. for differential diagnosis of PD and PSP-RS.



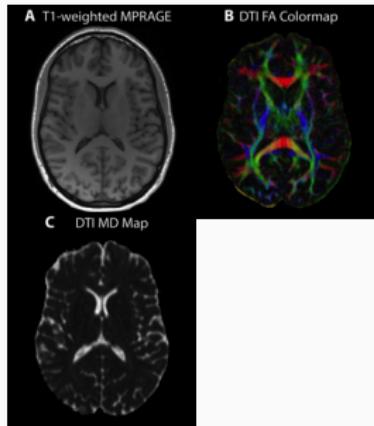
# Diffusion MRI



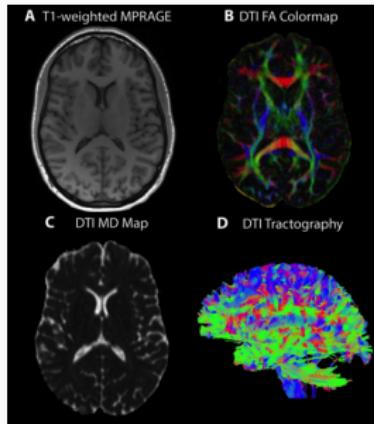
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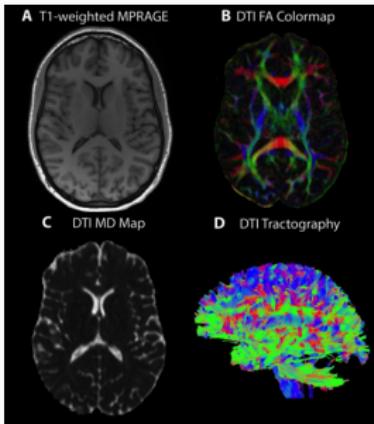
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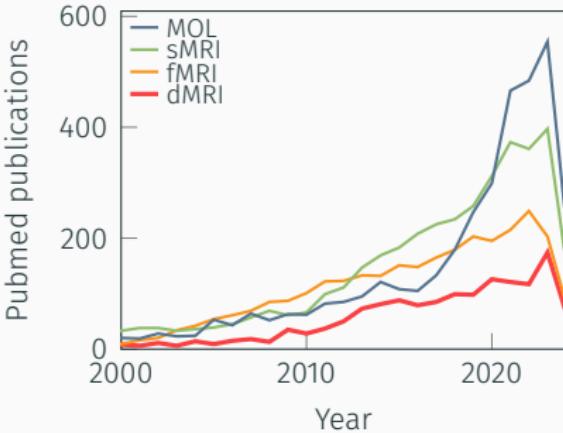
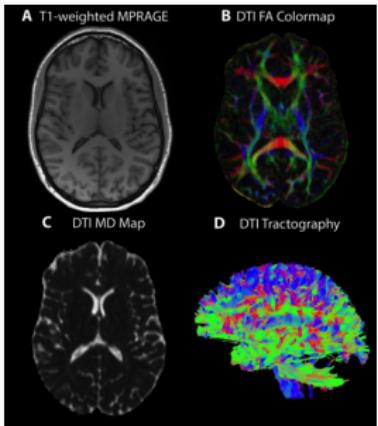
# Diffusion MRI



# 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)

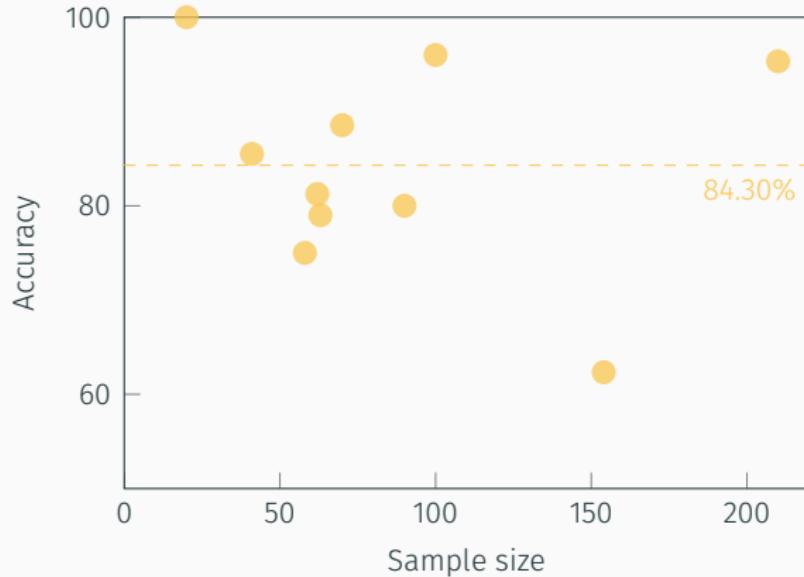
fMRI: ((functional[Title] AND MRI[Title]) OR fMRI[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)

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

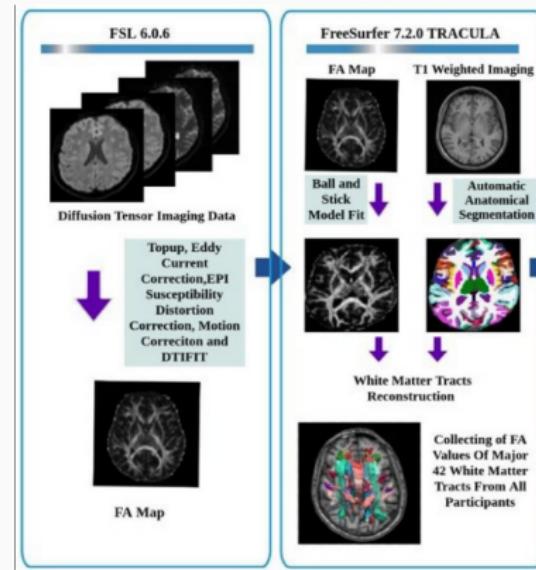




## SCZ classification studies using dMRI



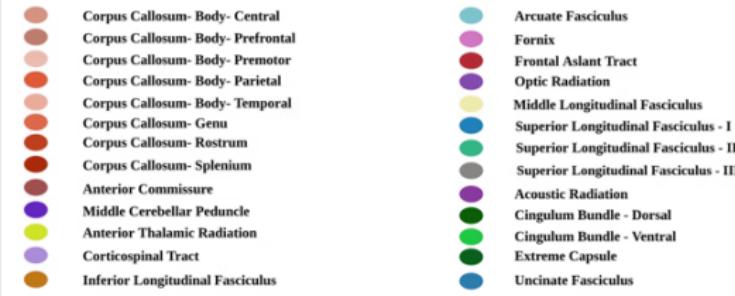
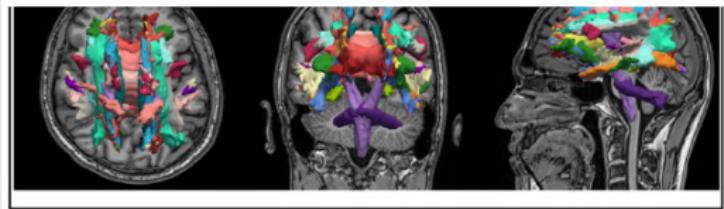
# Diffusion MRI



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



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# Diffusion MRI



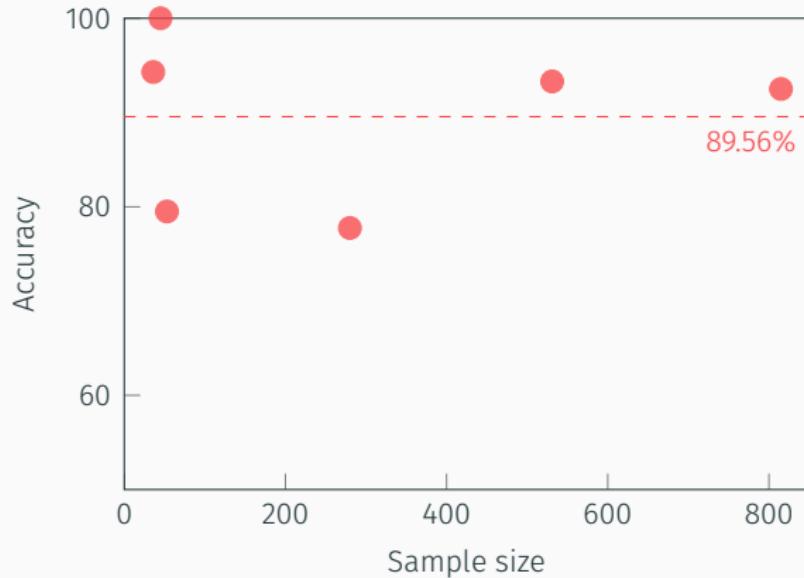
Classifier	AUC	Accuracy	Sensitivity	Specificity	Precision	F1 score	MCC
SVM-linear	0.85	0.80	0.75	0.86	0.79	0.77	0.74
Random forest	0.82	0.79	0.72	0.81	0.76	0.74	0.70
SVM-Gaussian	0.83	0.78	0.71	0.80	0.75	0.73	0.70
LR	0.78	0.76	0.70	0.79	0.73	0.71	0.68
Naive Bayes	0.75	0.72	0.65	0.74	0.68	0.66	0.62

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

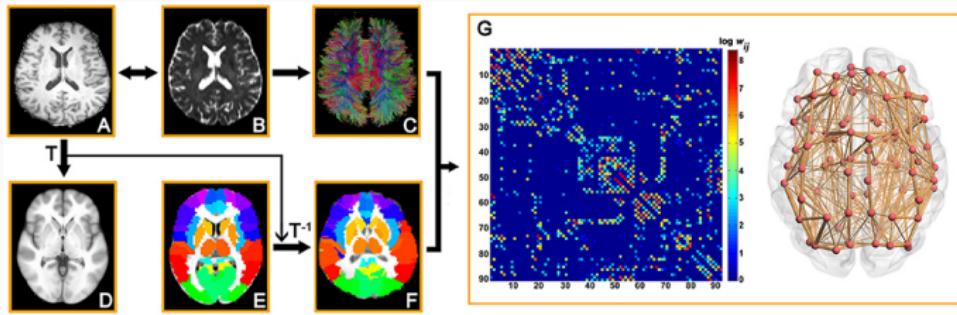




## DEM classification studies using dMRI



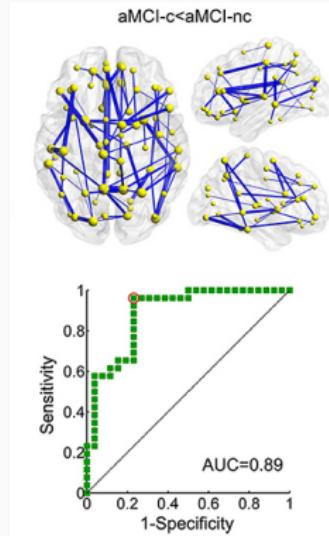
# Diffusion MRI



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



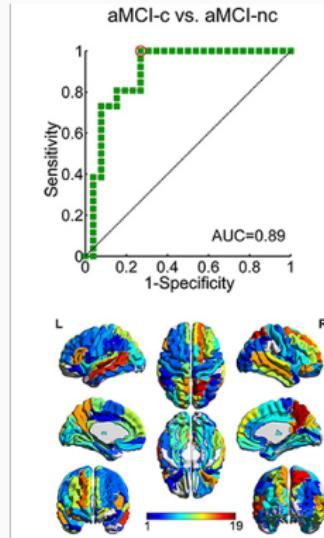
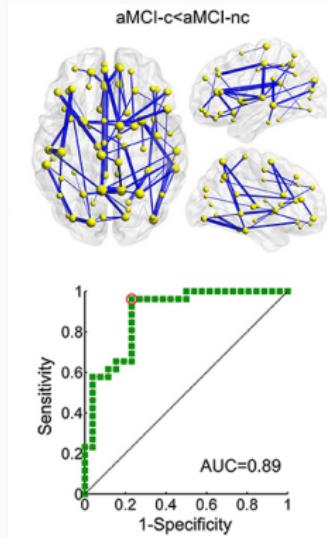
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# Diffusion MRI

- 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

Few prediction studies, mostly for mental disorders with various accuracies (60-100%) and DEM (80-100%)

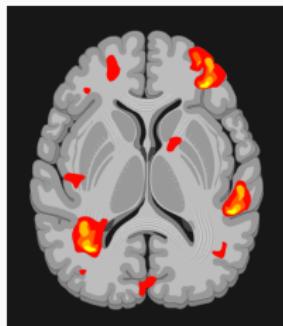
Used by Saglam et al. to differentially diagnose SCZ and BP with 80% accuracy.  
Used by Sun et al. to predict conversion from MCI to AD with 81% accuracy.



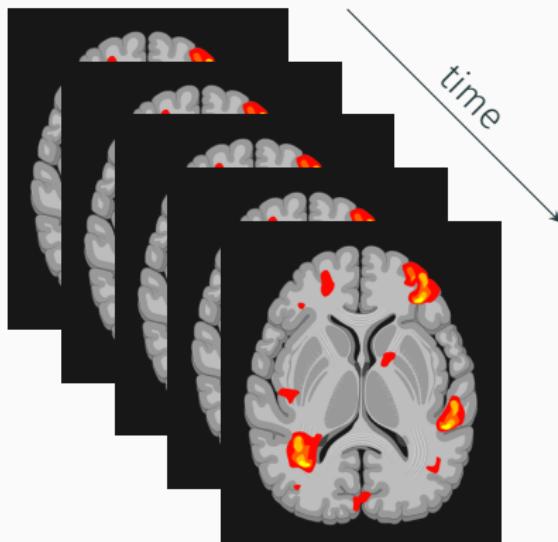
# Functional Magnetic Resonance Imaging (fMRI)



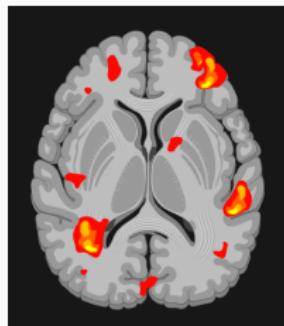
# Functional Magnetic Resonance Imaging (fMRI)



# Functional Magnetic Resonance Imaging (fMRI)

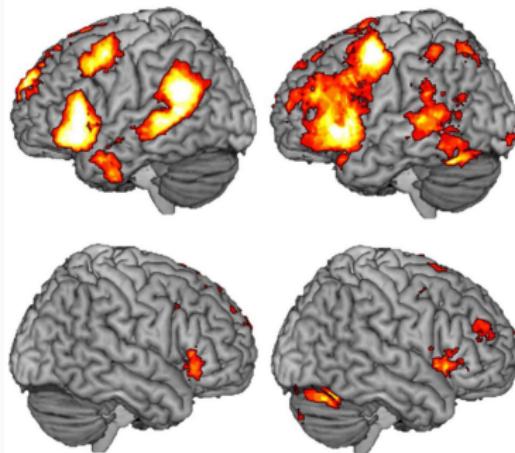


# Functional Magnetic Resonance Imaging (fMRI)



rs-fMRI

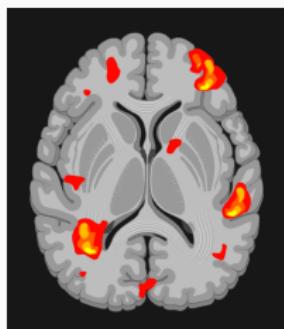
task-fMRI



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



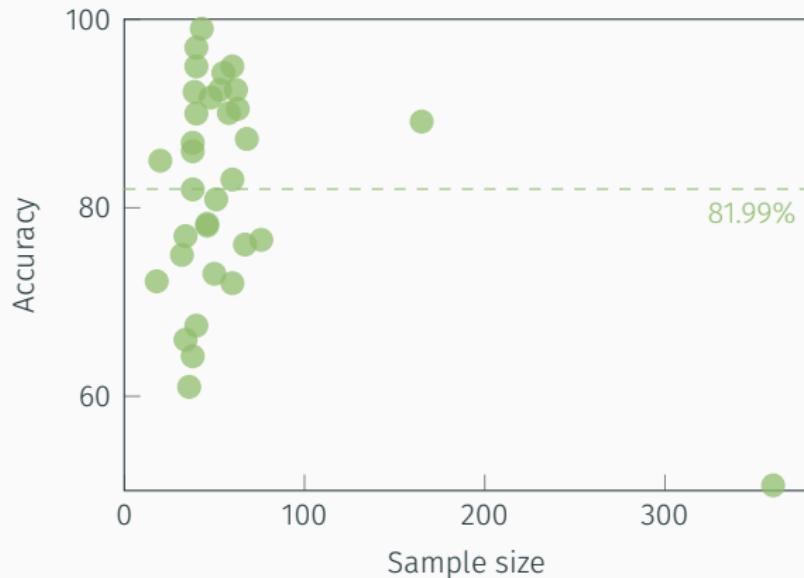
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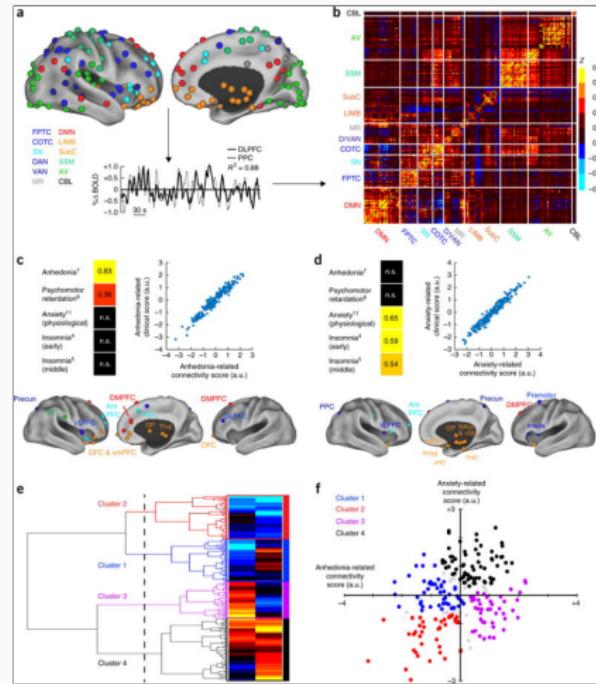
# Functional Magnetic Resonance Imaging (fMRI)



MDD classification studies using fMRI



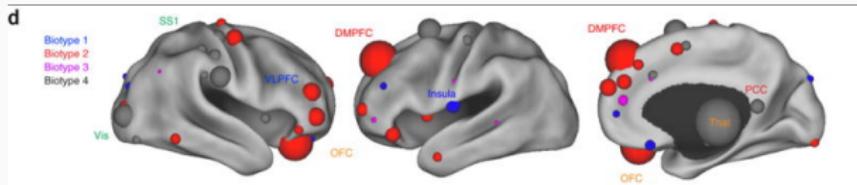
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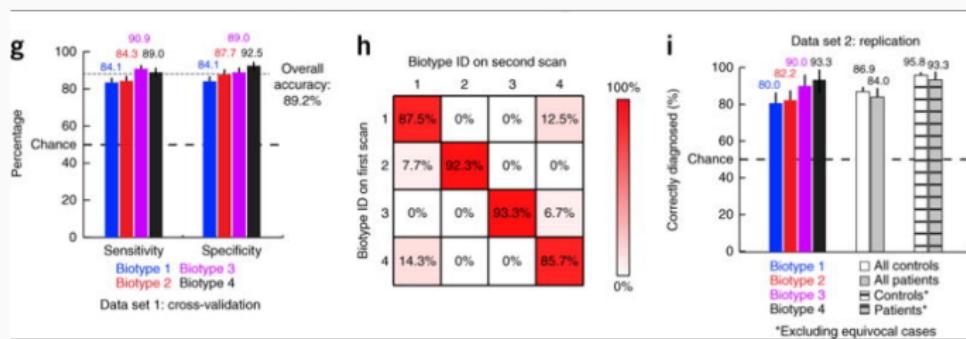
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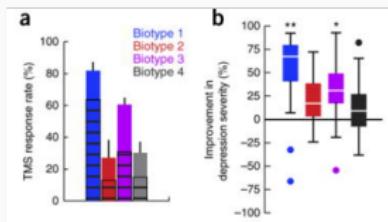
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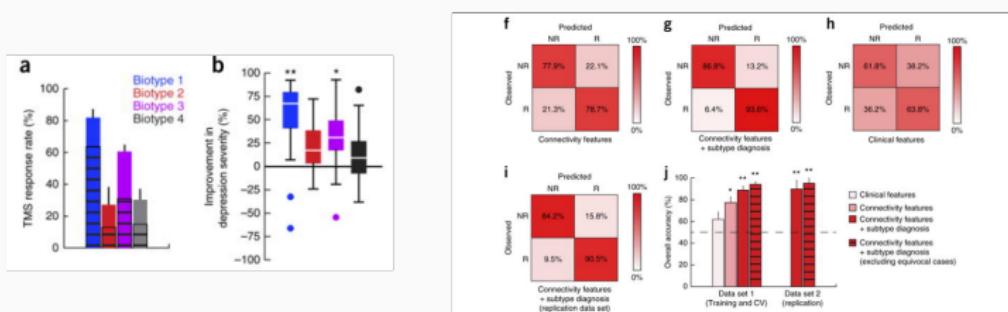
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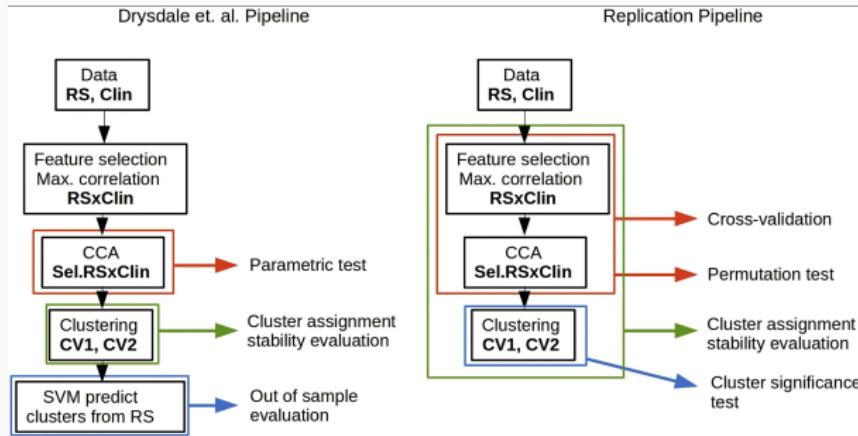
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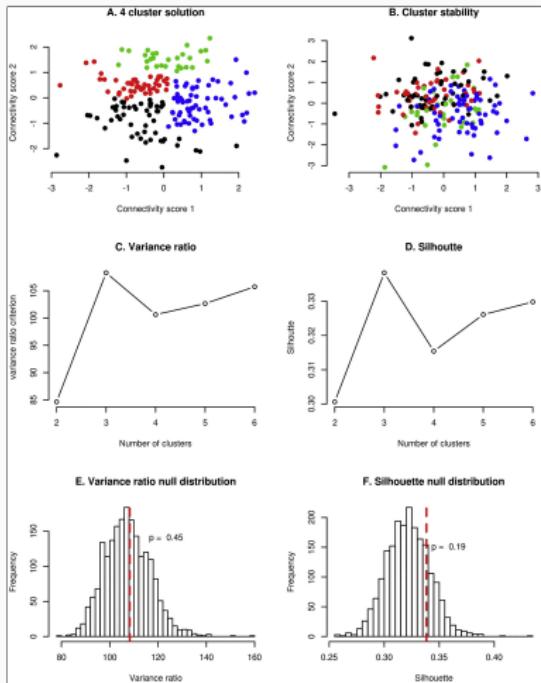
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Dinga, R., Schmaal, L., Penninx, B. W., van Tol, M. J., Veltman, D. J., van Velzen, L., ... & Marquand, A. F. (2019). Evaluating the evidence for biotypes of depression: Methodological replication and extension of. *NeuroImage: Clinical*, 22, 101796



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# Functional Magnetic Resonance Imaging (fMRI)

- 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

Few prediction studies, mostly for mental disorders with various 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 AD with 81% accuracy.

## Functional MRI

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

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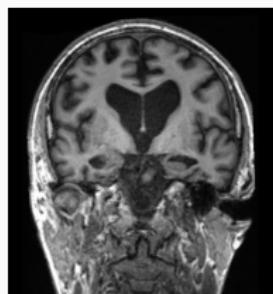
Used by Drysdale et al. to detect biotypes of MDD that reacted differently to

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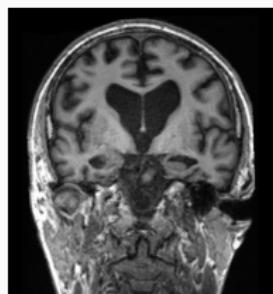
However, Dinga et al. failed to replicate their results **WHY**.



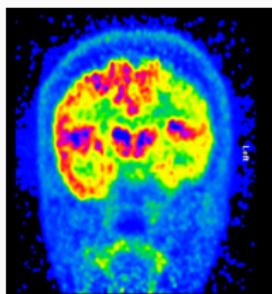
# Molecular imaging (PET/SPECT)



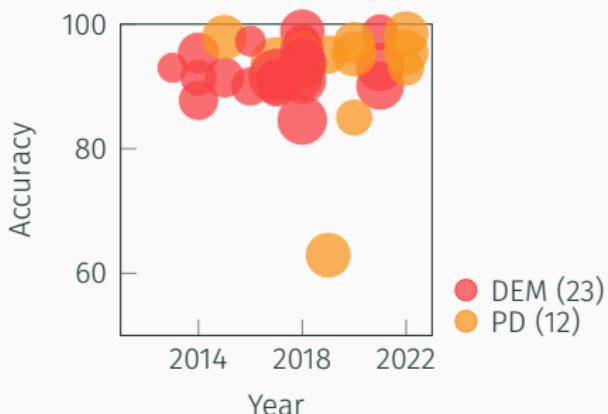
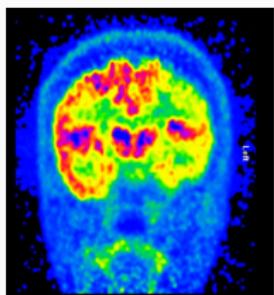
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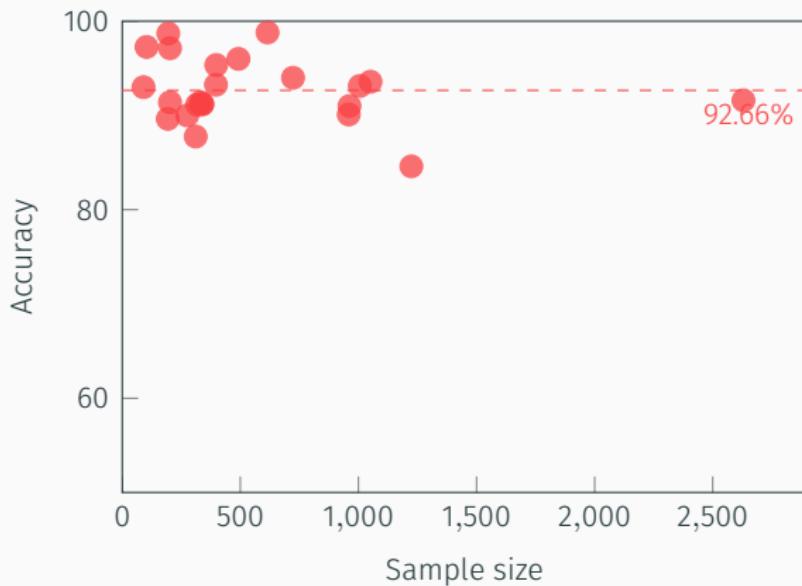
Explanation of PET



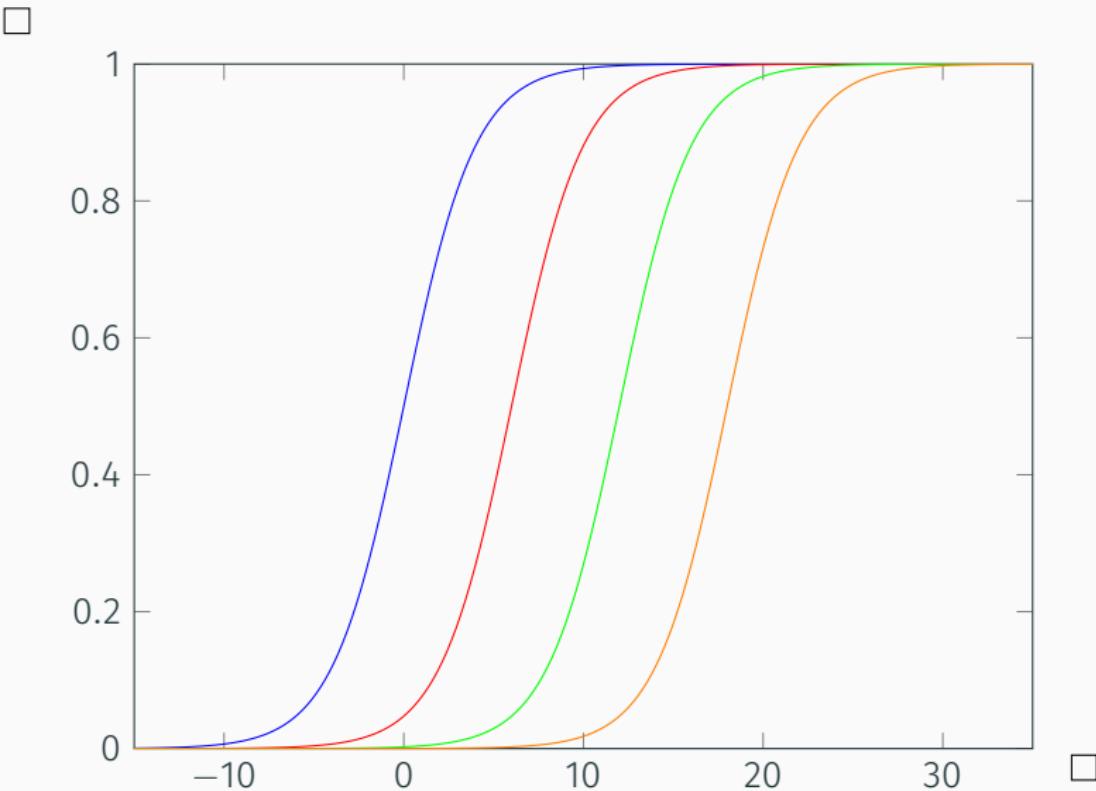
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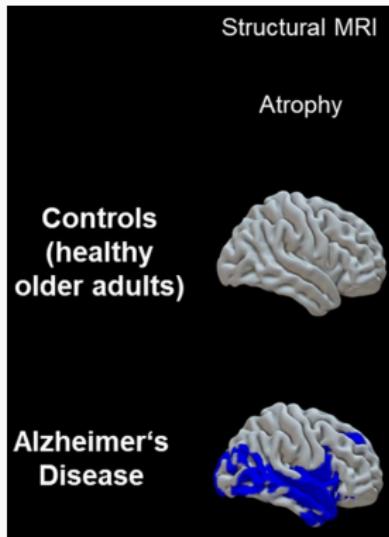
DEM classification studies using PET



## Molecular imaging (PET/SPECT)



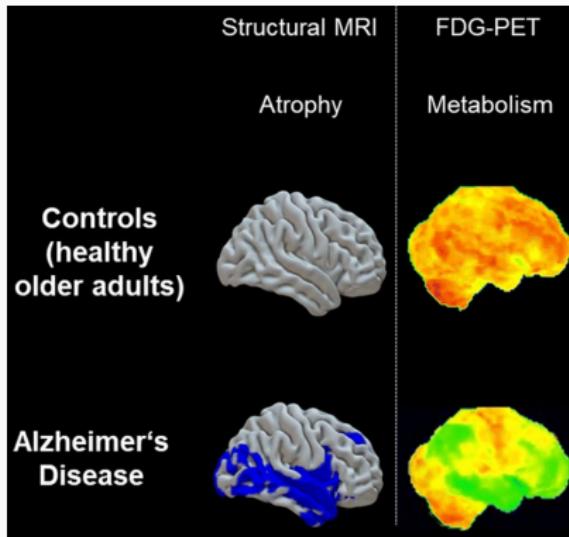
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Chételat, G., Arbizu, J., Barthel, H., Garibotto, V., Lammertsma, A. A., Law, I., ... & Drzezga, A. (2021). Finding our way through the labyrinth of dementia biomarkers. European journal of nuclear medicine and molecular imaging, 48, 2320-2324



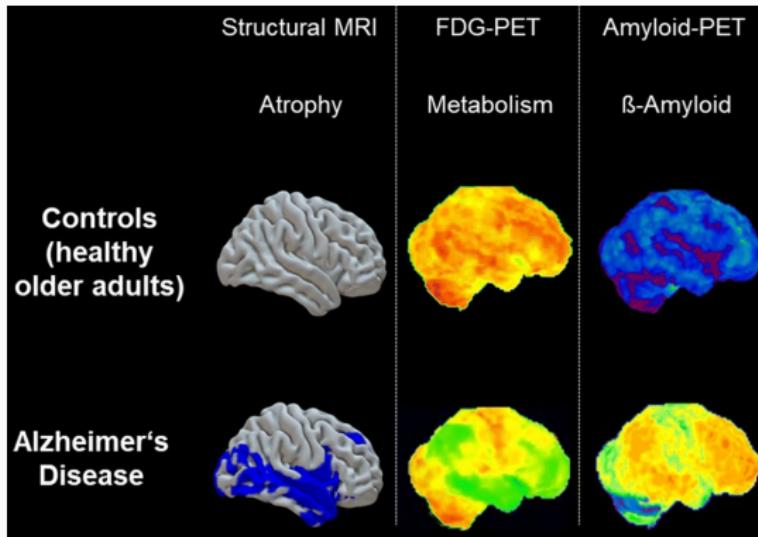
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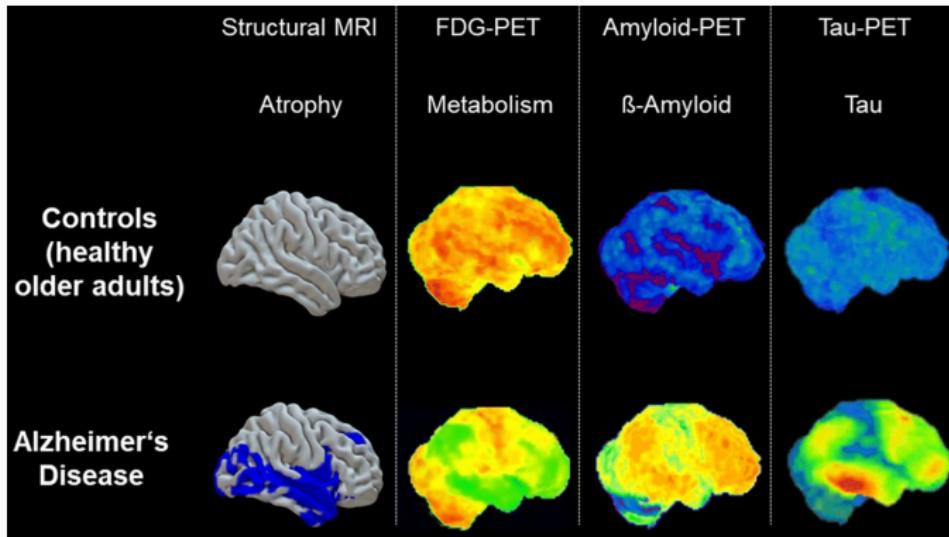
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# Molecular imaging (PET/SPECT)



# 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*

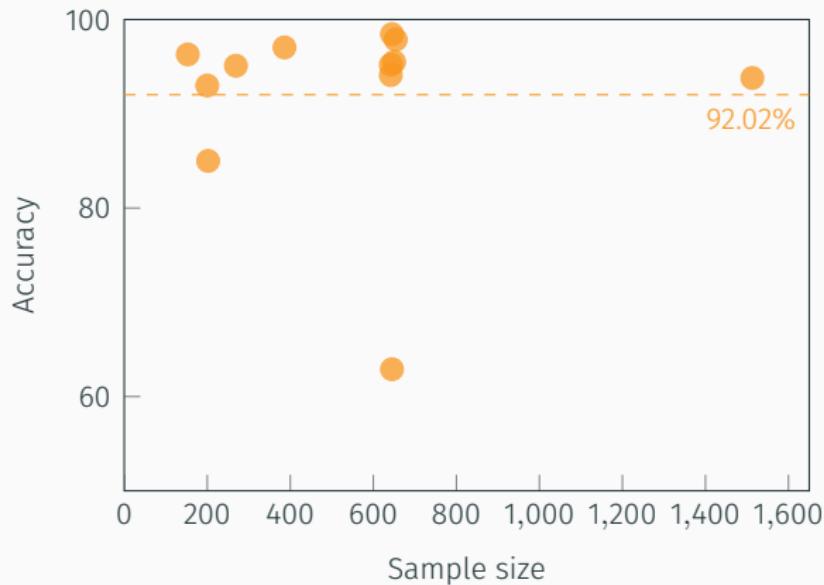
*The same AD biology may result in different phenotypic presentations"*



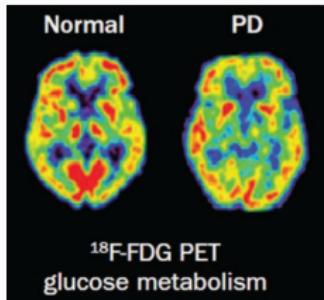
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## PD classification studies using SPECT



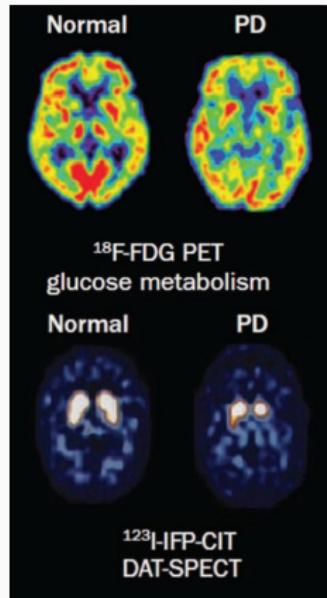
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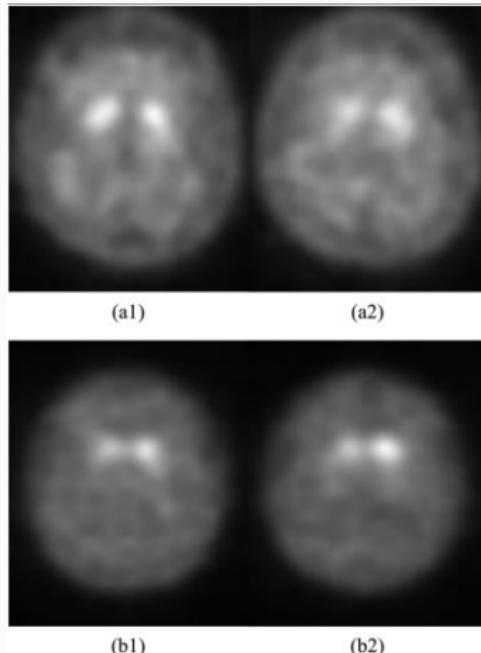
# Molecular imaging (PET/SPECT)



## Explanation of SPECT



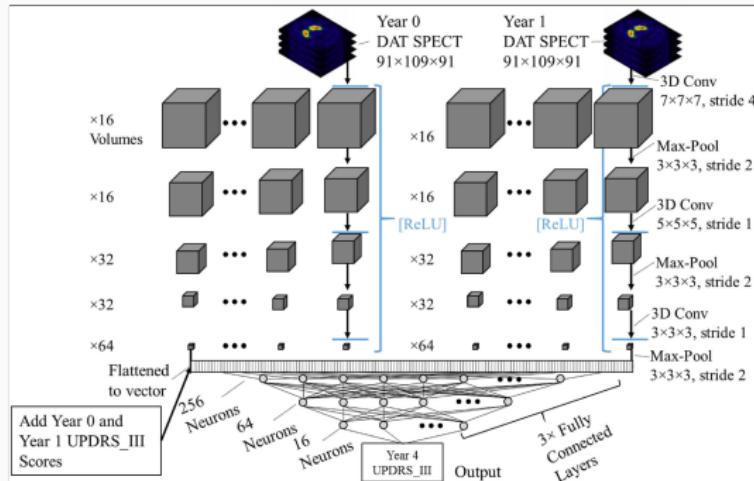
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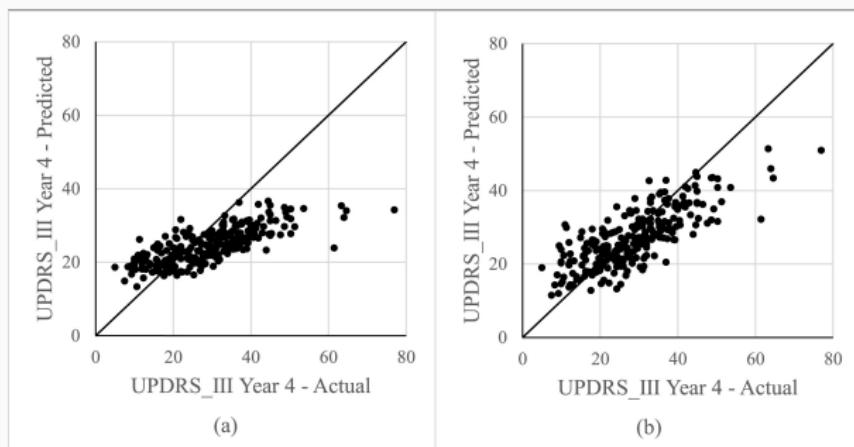
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## Molecular imaging

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

