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.

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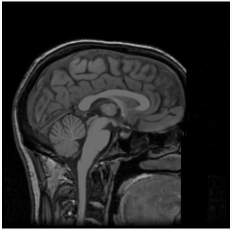

Bert from FreeSurfer 7.3

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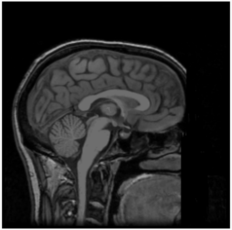

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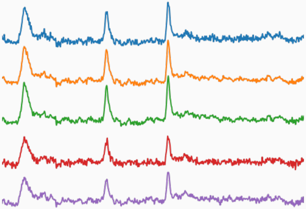

Sample from the MNE library

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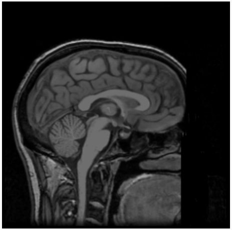

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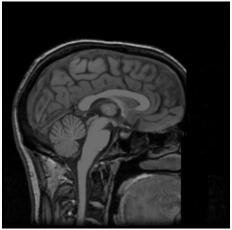

Bert from FreeSurfer 7.3

3D

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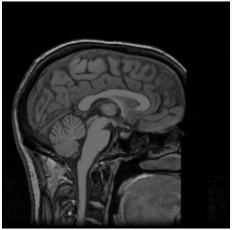

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Saggital, axial

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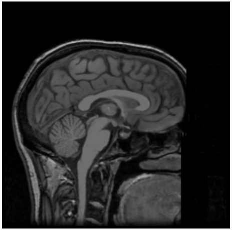

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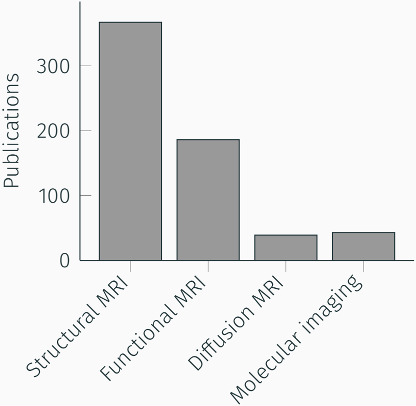

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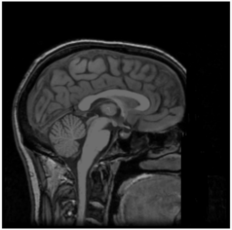

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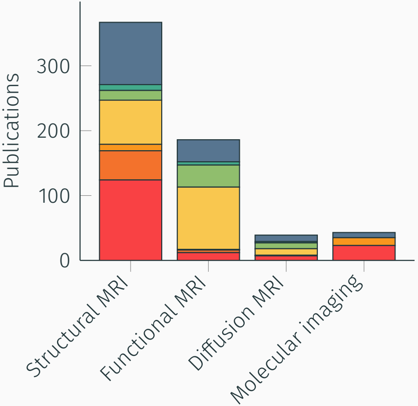

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Alzheimer's disease (AD) and other causes of dementia (DEM)

Multiple Sclerosis (MS)

Parkinson's Disease (PD)

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

Multiple Sclerosis (MS)

Parkinson's Disease (PD)

Bipolar Disorder (BP)

Schizophrenia (SCZ)

Depressive disorders, including major depressive disorder (MDD)

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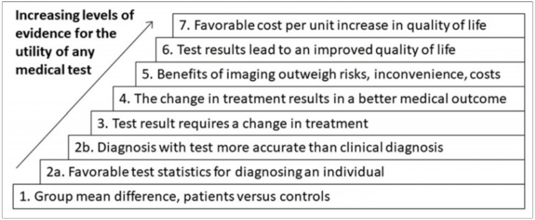

Vogel & Black (2024)

Vogel, A. C., & Black, K. J. (2024). Brain Imaging in Routine Psychiatric Practice. Missouri Medicine, 121(1), 37

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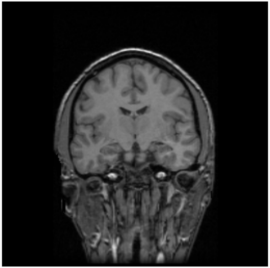

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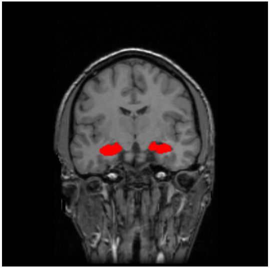

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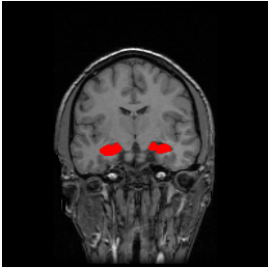

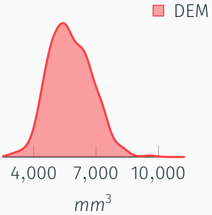

Data from ADNI

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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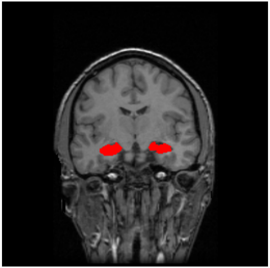

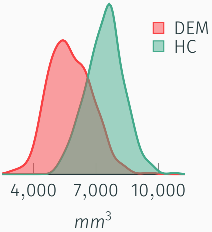

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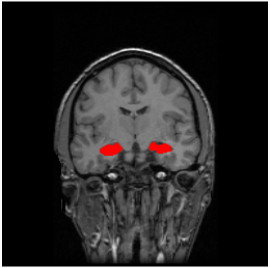

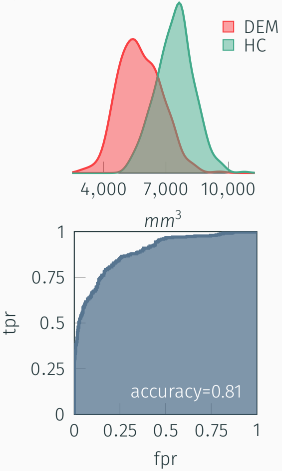

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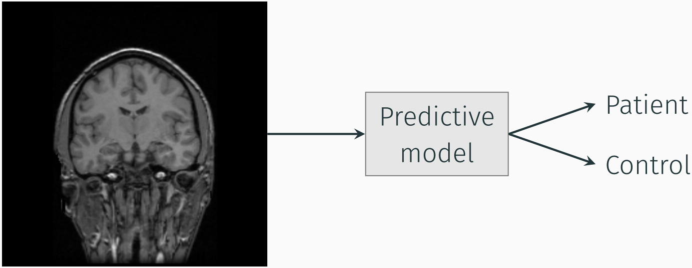

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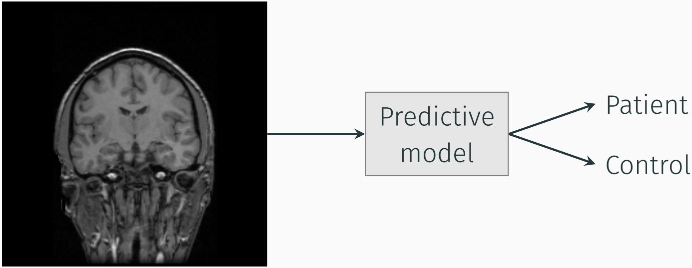

$$\text{accuracy} = \frac{\text{correct predictions}}{\text{all predictions}}$$

Neuroimaging modalities for diagnostic predictions

Approach

(Non-T1) structural MRI (sMRI)

Diffusion MRI (dMRI)

Functional MRI (fMRI)

Molecular imaging (MOL)

Approach

	DEM	MS	PD	SCZ	MDD	BP
(Non-T1) structural MRI (sMRI)						
Diffusion MRI (dMRI)						
Functional MRI (fMRI)						
Molecular imaging (MOL)						

Approach

	DEM	MS	PD	SCZ	MDD	BP
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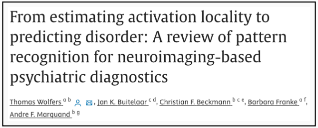
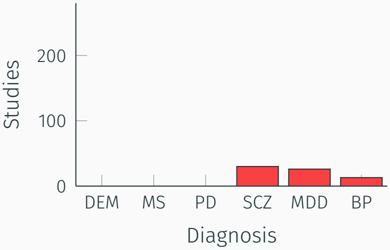
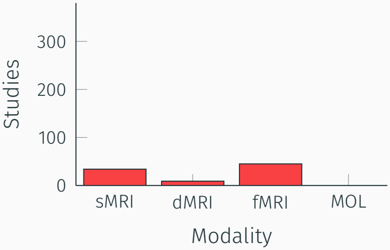

From estimating activation locality to predicting disorder: A review of pattern recognition for neuroimaging-based psychiatric diagnostics

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





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

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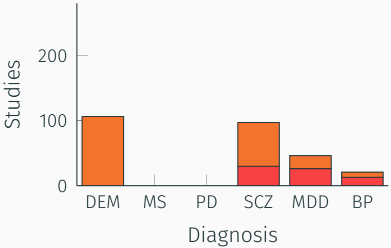
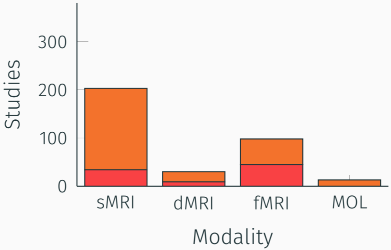
Single subject prediction of brain disorders in neuroimaging: Promises and pitfalls

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





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Towards a brain-based predictome of mental illness

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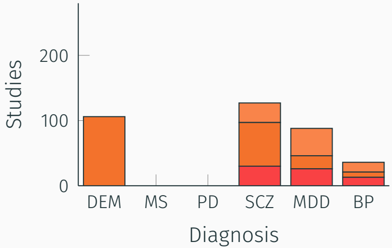

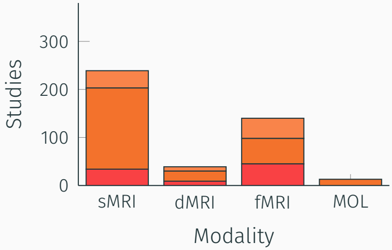

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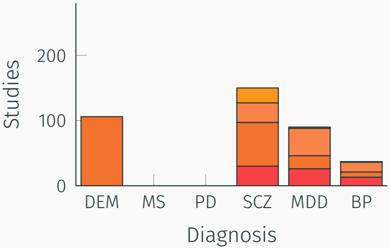
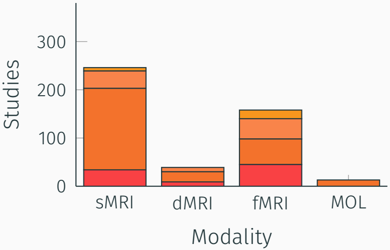
Barnaly Rashid, Vince Calhoun

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

Mirjam Quaak [1], Laurens van de Mortel [1], Rajat Mani Thomas [1], Guido van Wingen [2]





Data

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

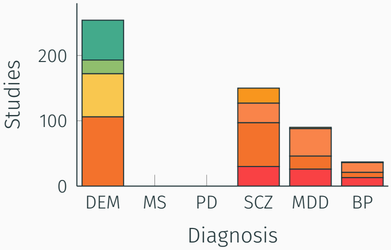
Mr Amir Ebrahimighahnavieh [1], Suhuai Luo [1], Raymond Chiong [2]

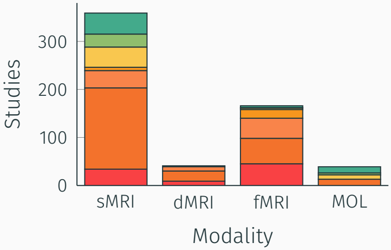
Machine learning techniques for diagnosis of alzheimer disease, mild cognitive disorder, and other types of dementia

Golrokh Mirzaei [a], Hojjat Adeli [b]

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

Sina Fathi [1], Maryam Ahmadi [2], Afsaneh Dehnad [3]





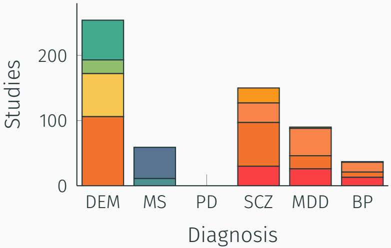
Data

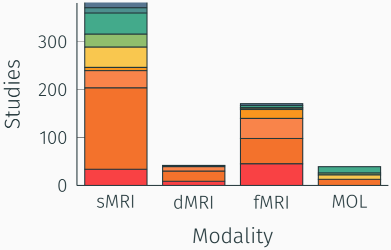
Applications of deep learning techniques for automated multiple sclerosis detection using magnetic resonance imaging: A review

Afshin Shoeibi [1], Marjane Khodatars [2], Mahboobeh Jafari [3], Parisa Moridian [4], Mitra Rezaei [5], Roohallah Alizadehsani [6], Fahime Khozeimeh [6], Juan Manuel Gorriz [7], Jónathan Heras [8], Maryam Panahiazar [9], Saeid Nahavandi [6], U Rajendra Acharya [10]

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

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





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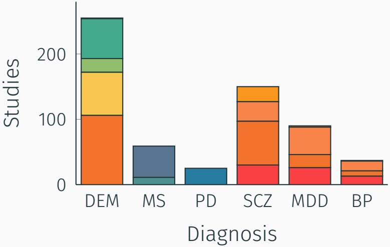
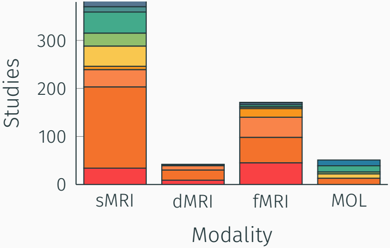
Role of Artificial Intelligence Techniques and Neuroimaging Modalities in Detection of Parkinson's Disease: A Systematic Review

Nikita Aggarwal[1] · B. S. Saini[1] · Savita Gupta[2]





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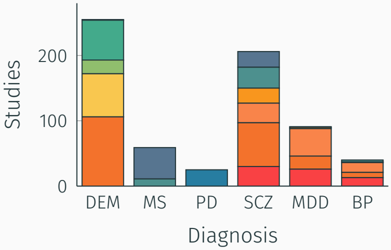
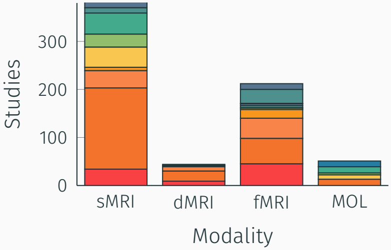
Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review

Renato de Filippis,[#1] Elvira Anna Carbone,[#1] Raffaele Gaetano,[1] Antonella Bruni,[1] Valentina Pugliese,[1] Cristina Segura-Garcia,[2] and Pasquale De Fazio[1]

Machine learning techniques for the Schizophrenia diagnosis: a comprehensive review and future research directions

Shradha Verma[1] · Tripti Goel[1] · M. Tanveer[2] · Weiping Ding[3] · Rahul Sharma[1] · R. Murugan[1]





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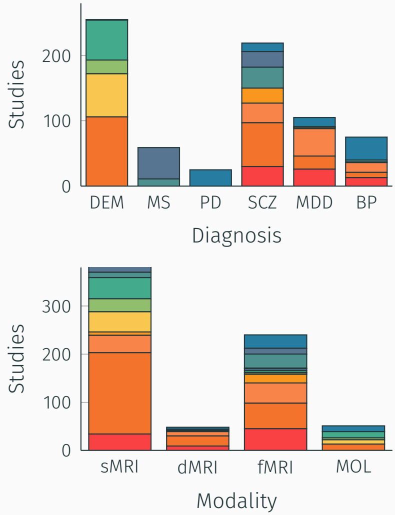
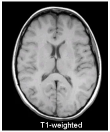
Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

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



Other structural MRI modalities



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

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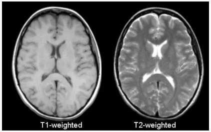

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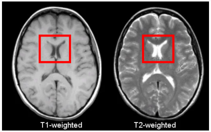

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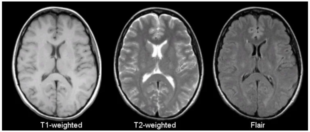

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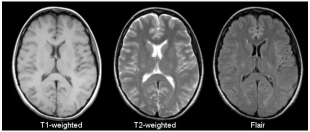

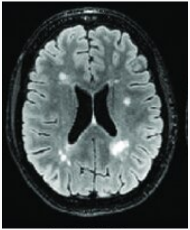

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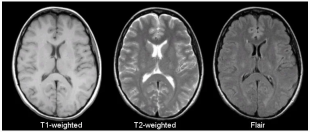

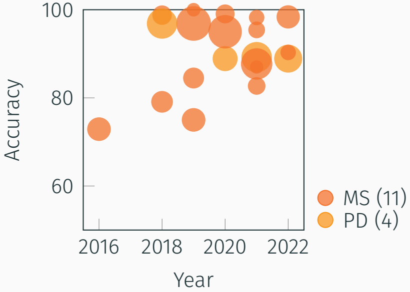

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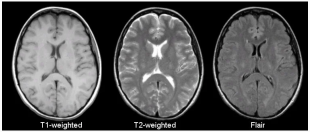

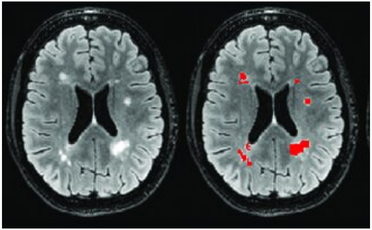

Weeda, M. M., Brouwer, I., de Vos, M. L., de Vries, M. S., Barkhof, F., Pouwels, P. J. W., & Vrenken, H. (2019). Comparing lesion segmentation methods in multiple sclerosis: Input from one manually delineated subject is sufficient for accurate lesion segmentation. NeuroImage: Clinical, 24, 102074

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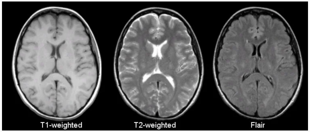

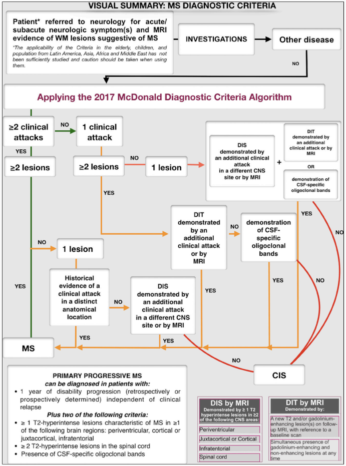

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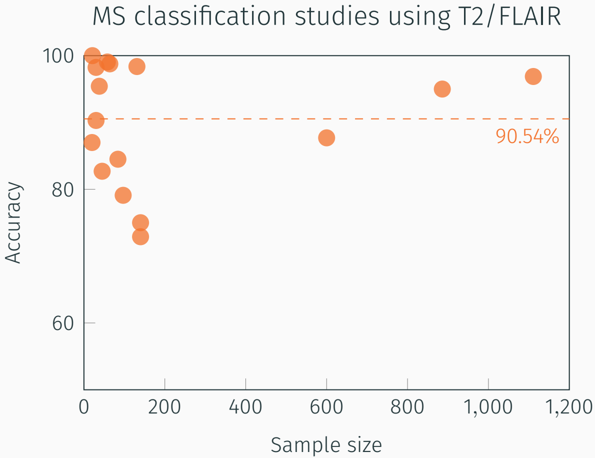
Other structural MRI modalities



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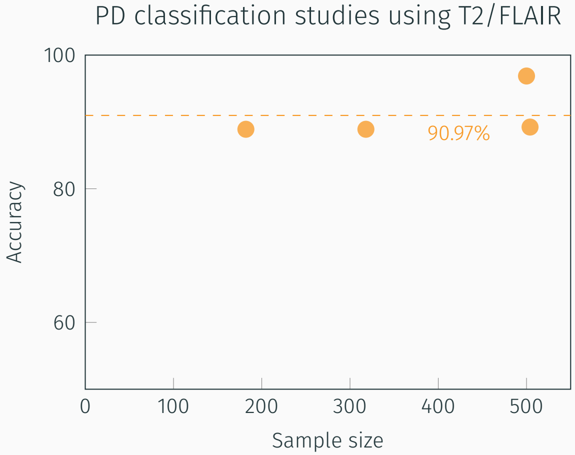

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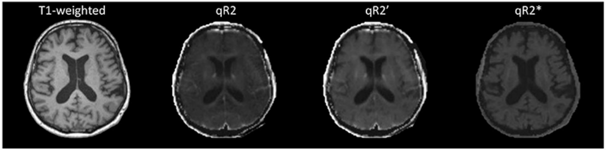

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								HC	PD	PSP-RS	
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PSP-RS	0.750	0.072	0.714	0.750	0.732	0.665	0.948	0	5	15	

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.

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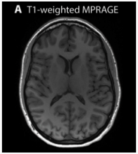

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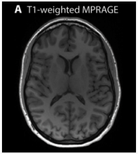

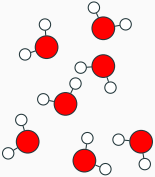

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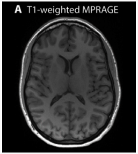

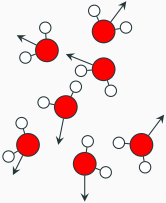

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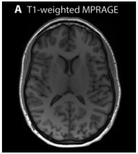

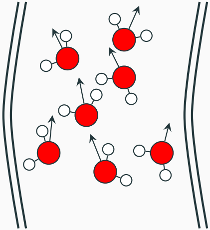

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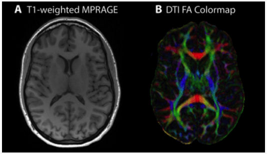

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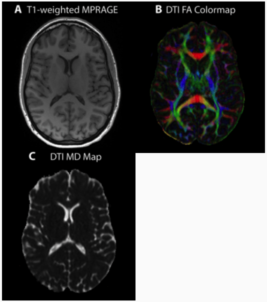

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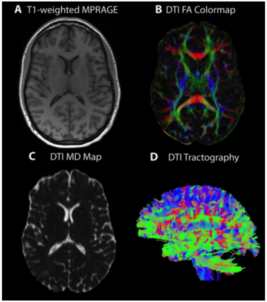

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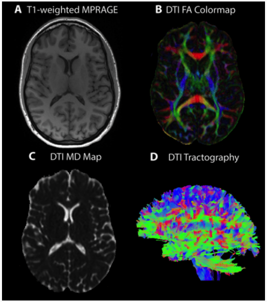

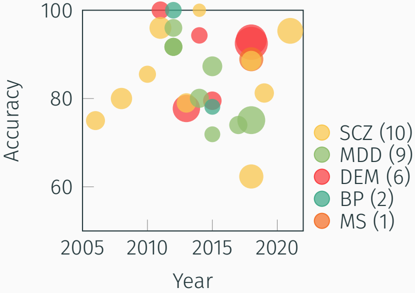

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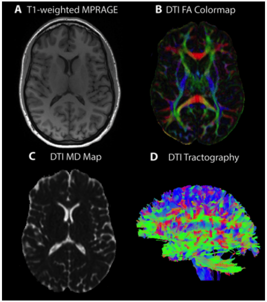

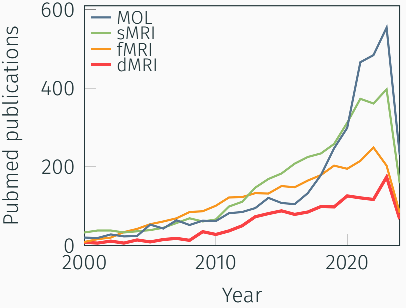

MOL:	((molecular[Title] AND imaging[Title]) OR PET[Title] OR SPECT[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)”
sMRI:	((structural[Title] AND MRI[Title]) OR sMRI[Title] OR T1[Title] OR T2[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)
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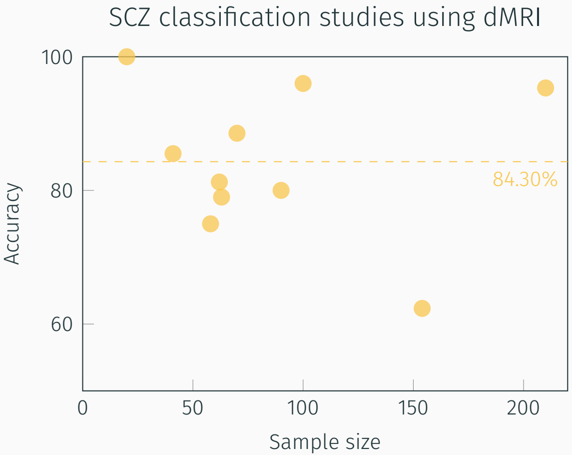

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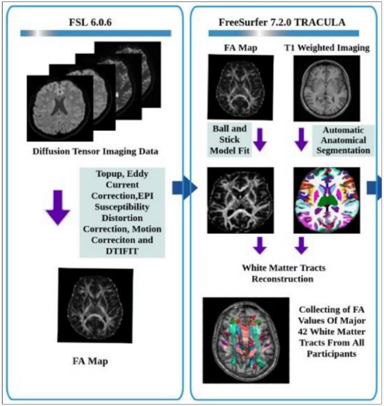

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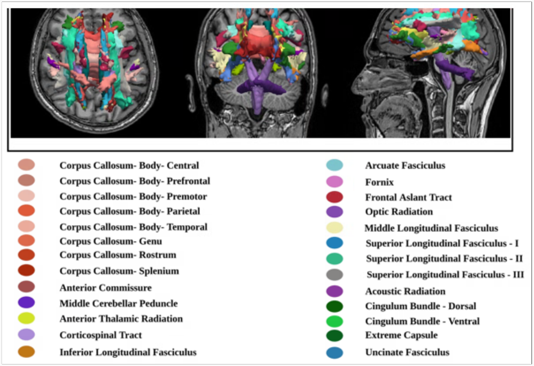

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Diffusion MRI

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

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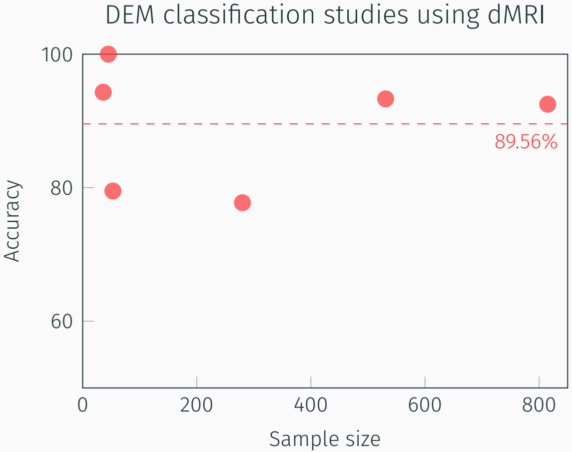

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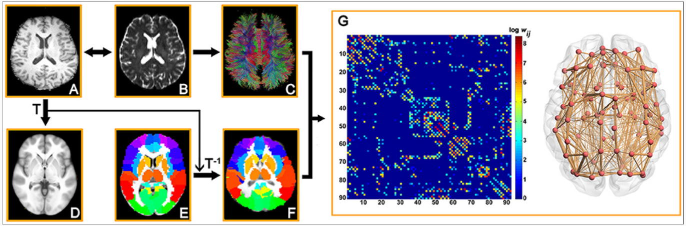

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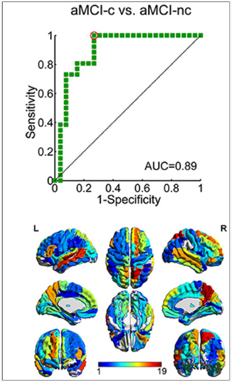

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Diffusion Tensor Imaging Features (MD, FA, RD, AD Features)											
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HC	1.000	0.000	1.000	1.000	1.000	1.000	1.000	38	0	0	95.1%
PD	0.933	0.034	0.955	0.933	0.944	0.901	0.975	0	42	3	
PSP-RS	0.900	0.036	0.857	0.900	0.878	0.848	0.968	0	2	18	

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Functional Magnetic Resonance Imaging (fMRI)

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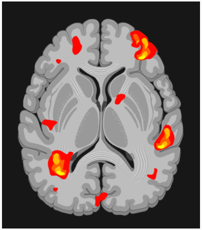

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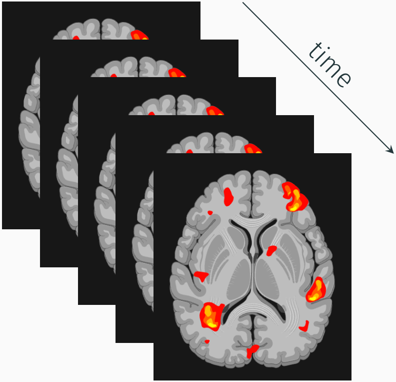

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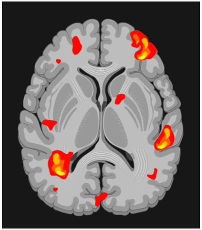

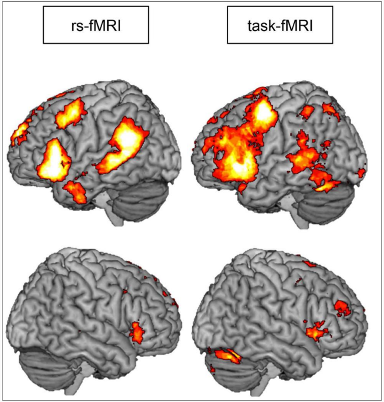

Branco, P., Seixas, D., Deprez, S., Kovacs, S., Peeters, R., Castro, S. L., & Sunaert, S. (2016). Resting-state functional magnetic resonance imaging for language preoperative planning. Frontiers in human neuroscience, 10, 11

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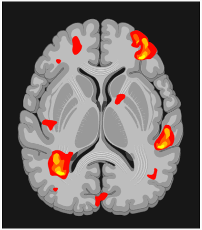

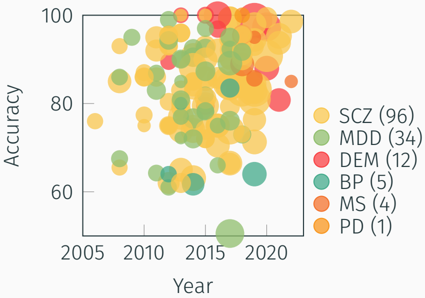

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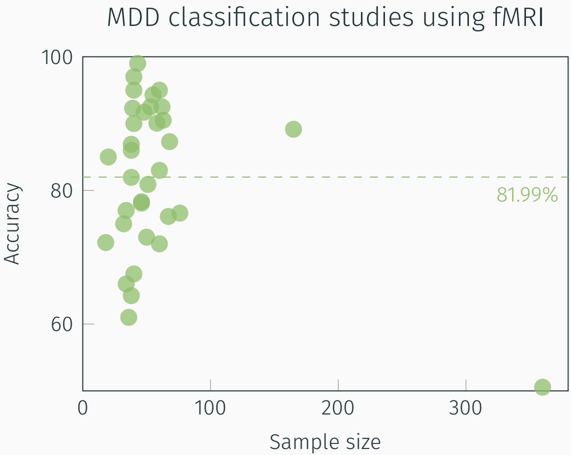

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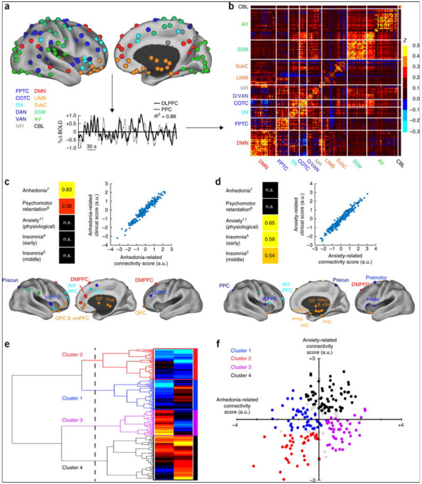

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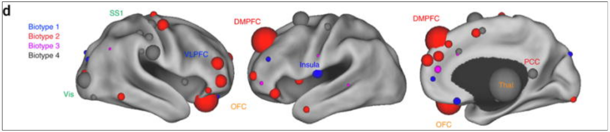

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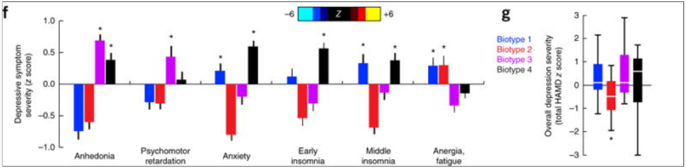

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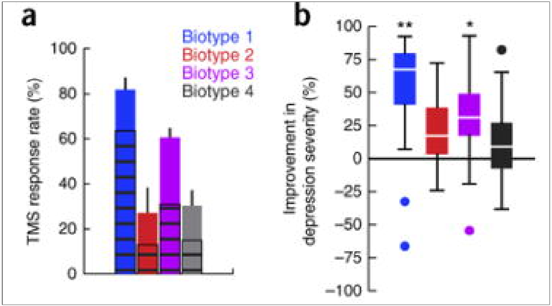

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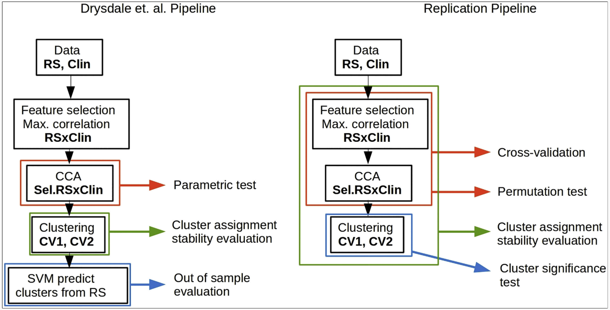

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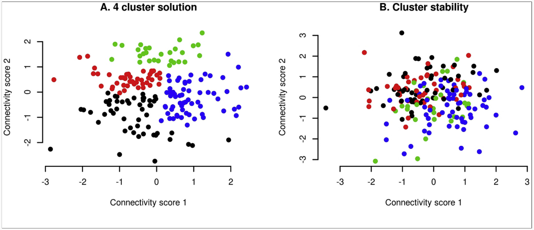

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  - Used by Saglam et al. to differentially diagnose SCZ and BP with 80% accuracy.
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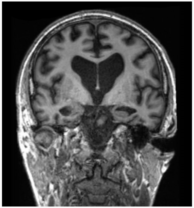
- Functional MRI
  - Widely used for all conditions, most prominently SCZ and MDD with varying accuracies (60-100%) and DEM (80-100%).
  - Used by Drysdale et al. to characterize MDD biotypes responding differently to MTS.
  - However, Dinga et al. failed to replicate their results.

Molecular imaging (PET/SPECT)



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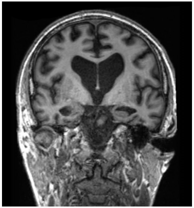

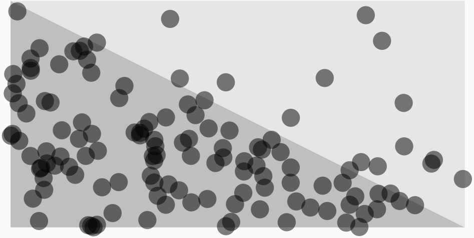

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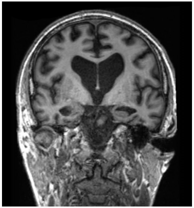

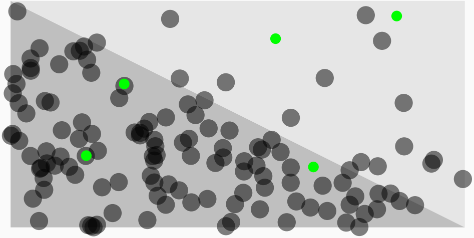

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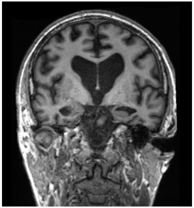

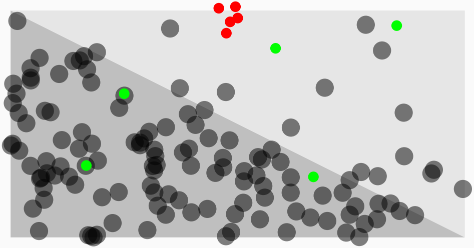

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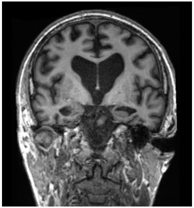

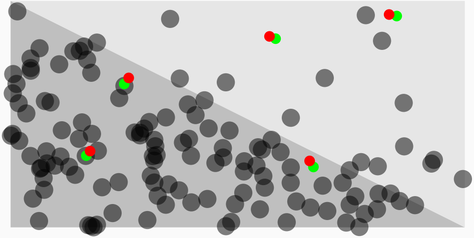

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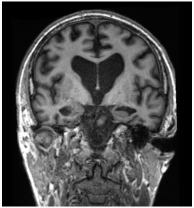

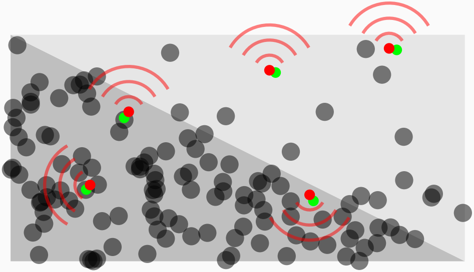

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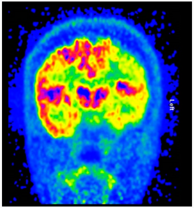

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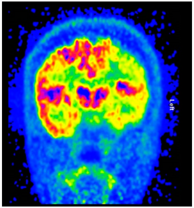
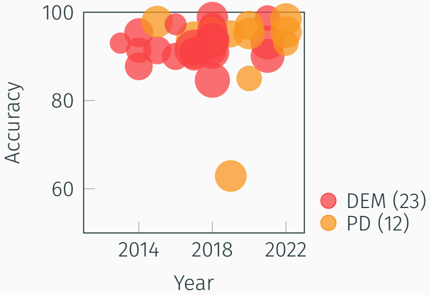
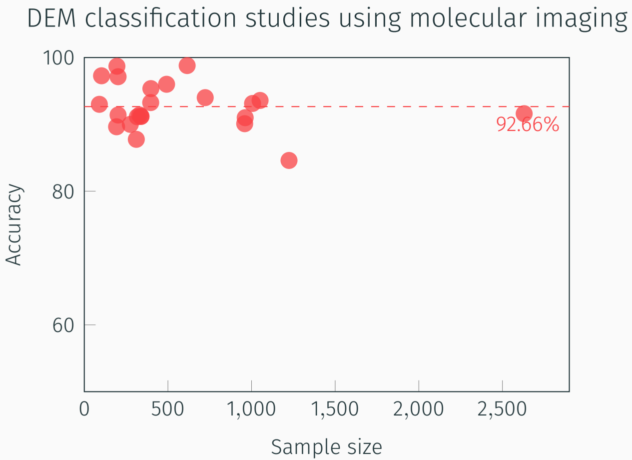
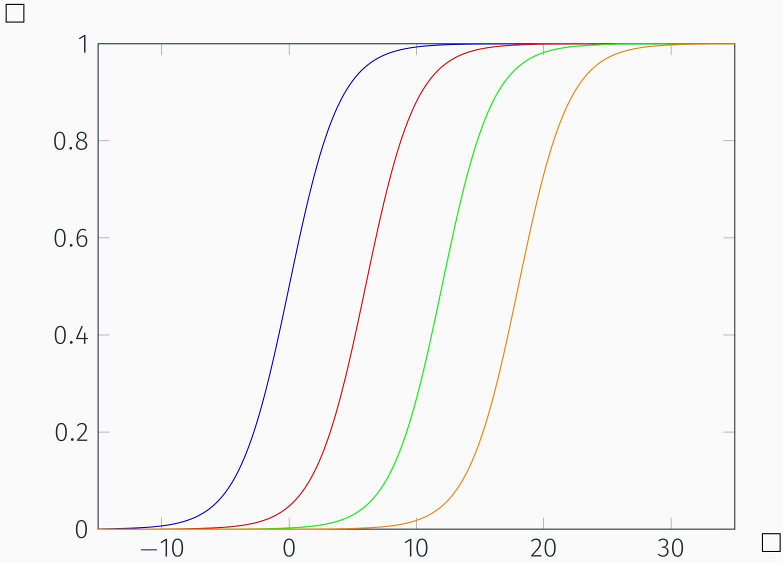





DEM classification studies using molecular imaging
100
80
60
Accuracy
92.66%
0
500
1,000
1,500
2,000
2,500
Sample size

Molecular imaging (PET/SPECT)



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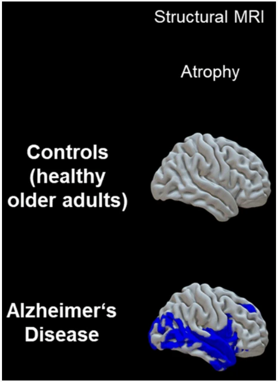

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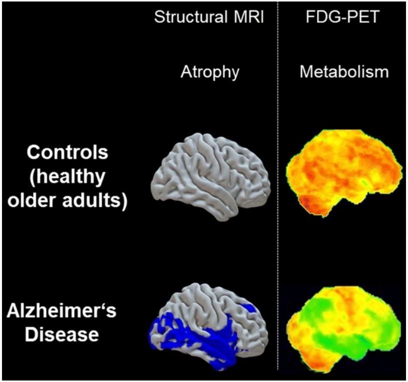

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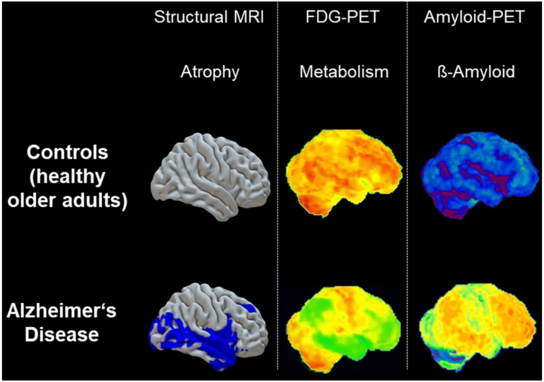

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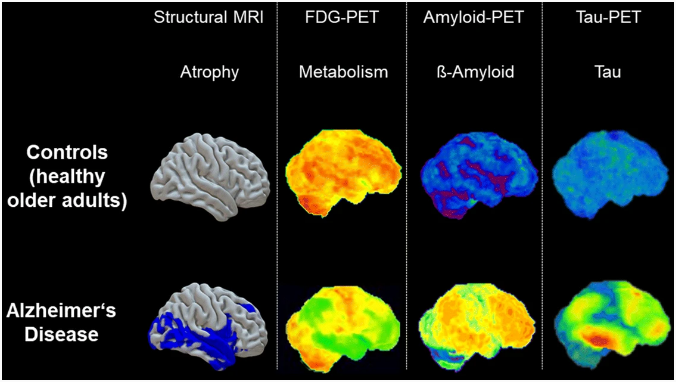

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Molecular imaging (PET/SPECT)

"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

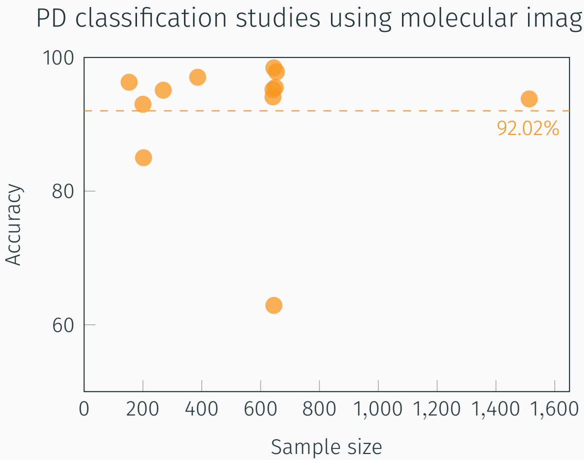
AD exists on a continuum not as discrete clinically defined entities

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"

Revised Criteria for Diagnosis and Staging of Alzheimer's Disease: Alzheimer's Association Workgroup, http://alz.org/diagnosticcriteria

Molecular imaging (PET/SPECT)



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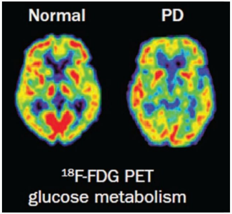

Pagano, G., Niccolini, F., & Politis, M. (2016). Imaging in Parkinson's disease. Clinical Medicine, 16(4), 371

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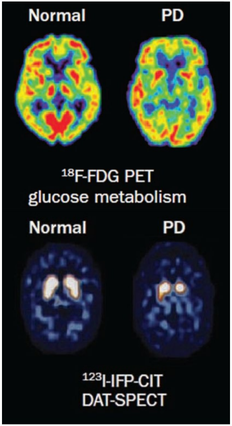

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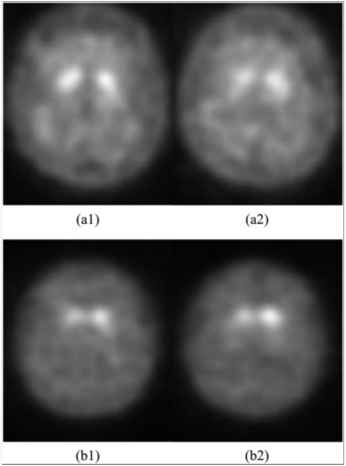

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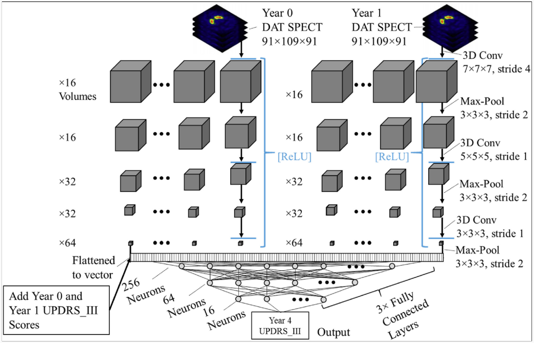

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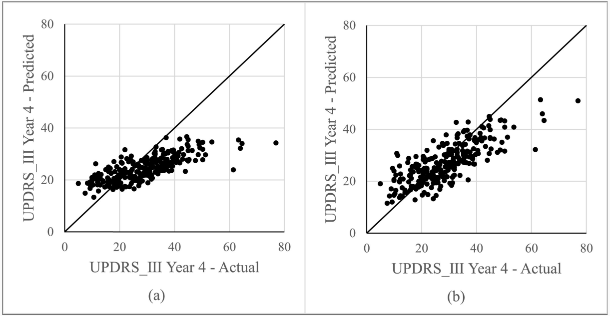

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Molecular imaging (PET/SPECT)

- (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 Aβ plaues and TAU tangles.
  - SPECT useful to characterize degeneration of dopamine-producing cells in PD, and, as shown by Adams et al., is plausibly useful to predict prognosis.

The future of neuroimaging-based prediction

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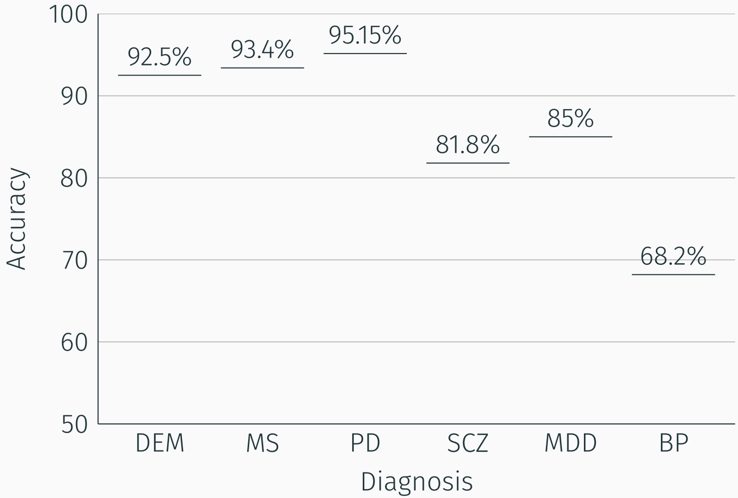
Challenges: Predictiveness



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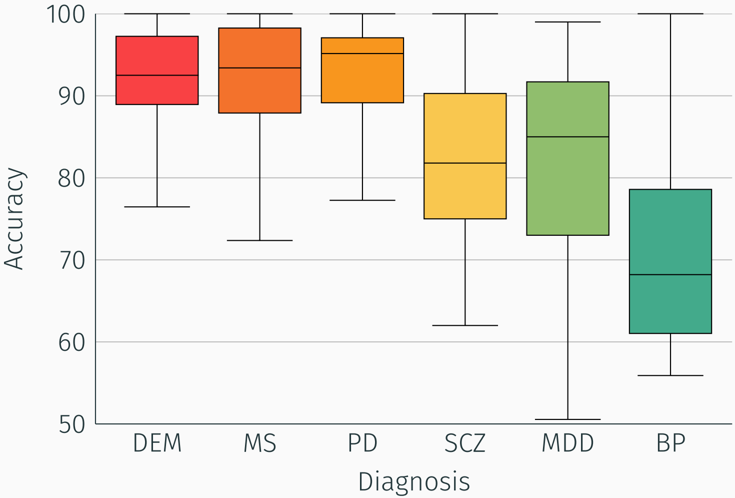

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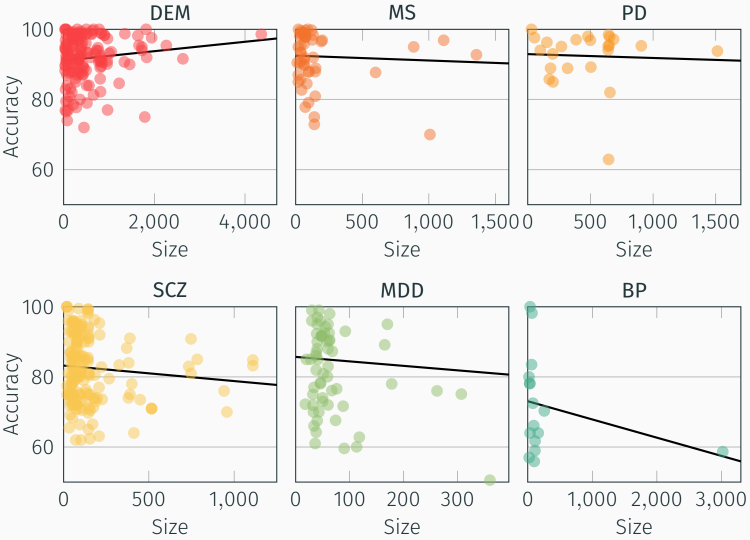

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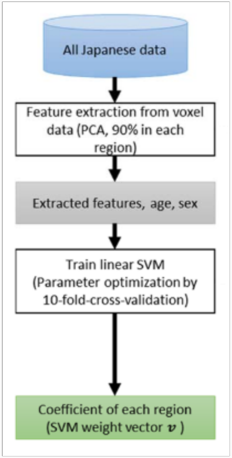

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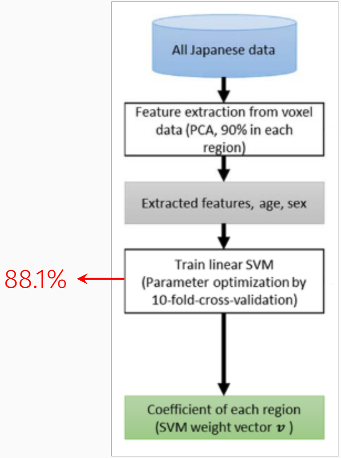

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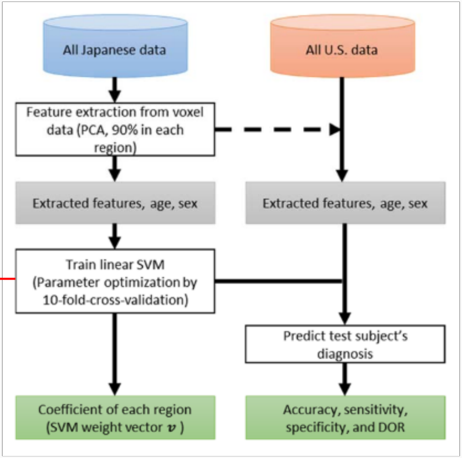

88.1%

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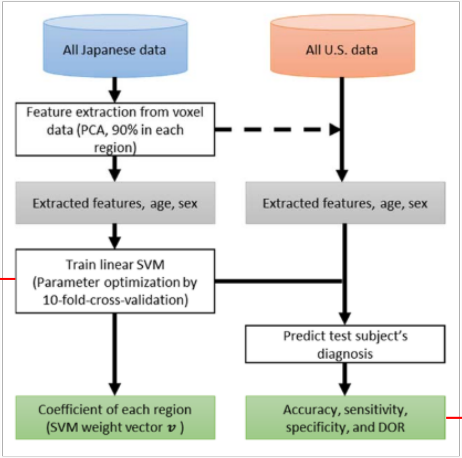

58.3%

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Challenges: Preprocessing and degrees of freedom

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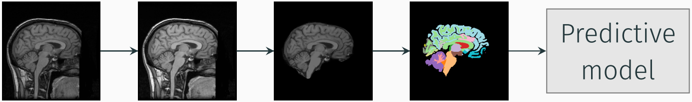

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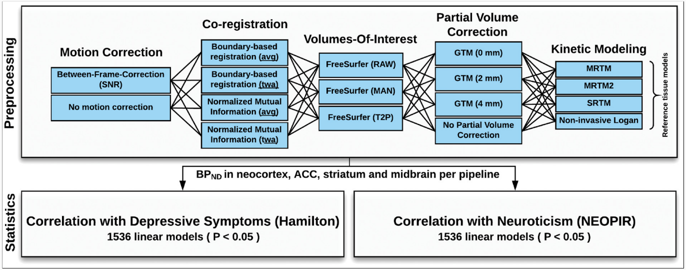

Nørgaard et al., 2020

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

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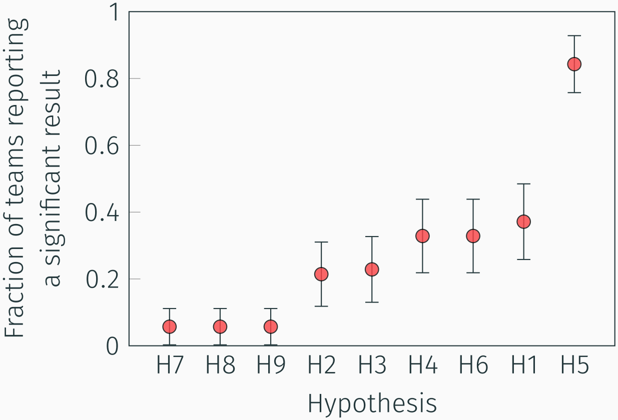
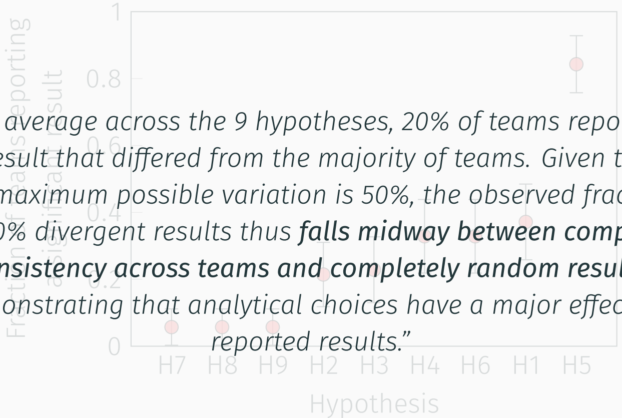


Adapted from Botvinik-Nezer et al., 2020

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



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

Adapted from Botvinik-Nezer et al., 2020

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

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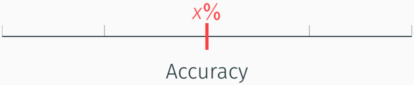

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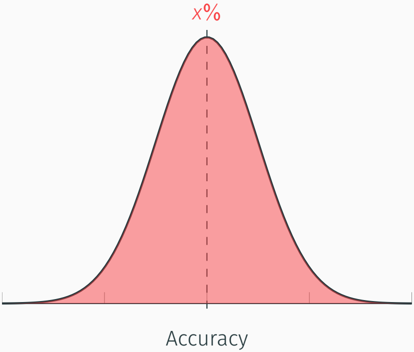

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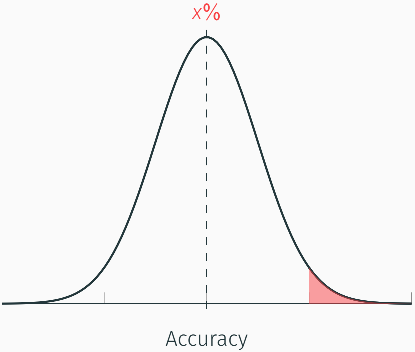
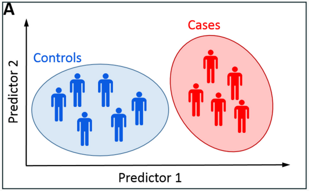


Challenges: Predictive targets



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

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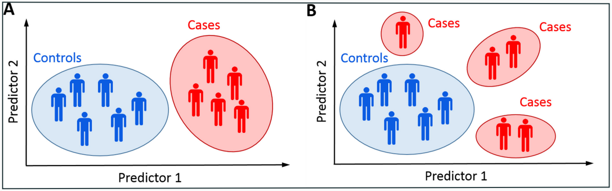

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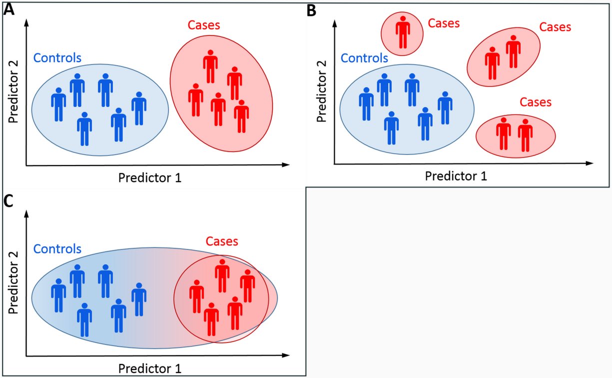

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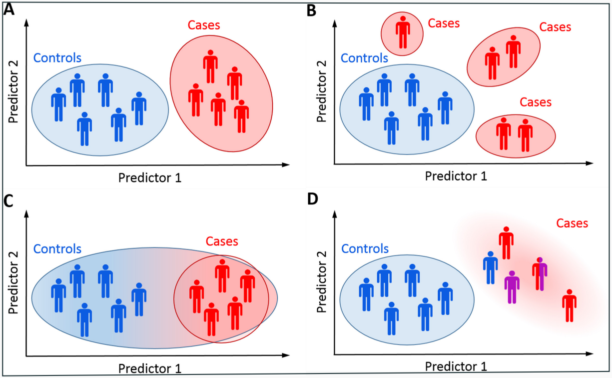

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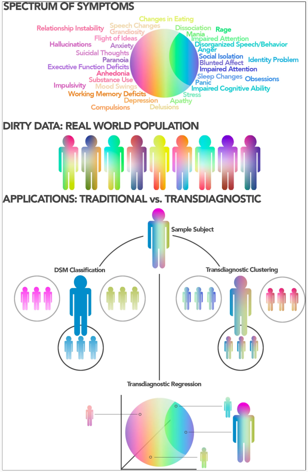
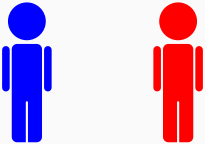


Vogel & Black (2024)

Vogel, A. C., & Black, K. J. (2024). Brain Imaging in Routine Psychiatric Practice. Missouri Medicine, 121(1), 37

Challenges: Predictive targets



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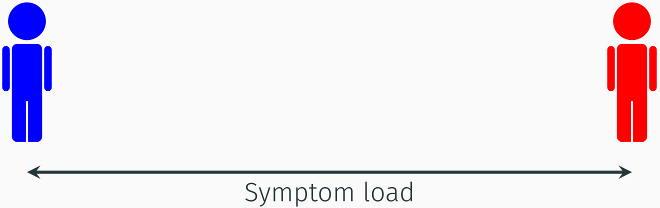

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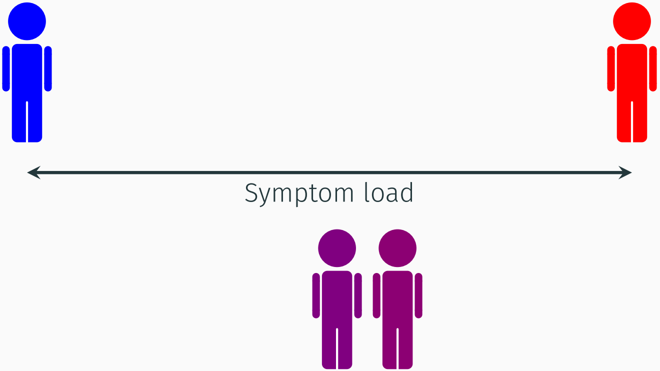

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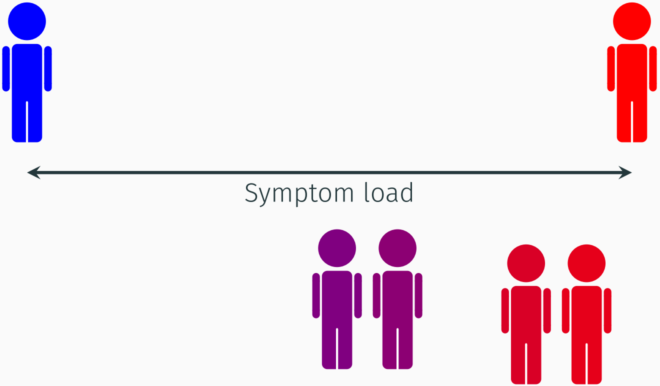
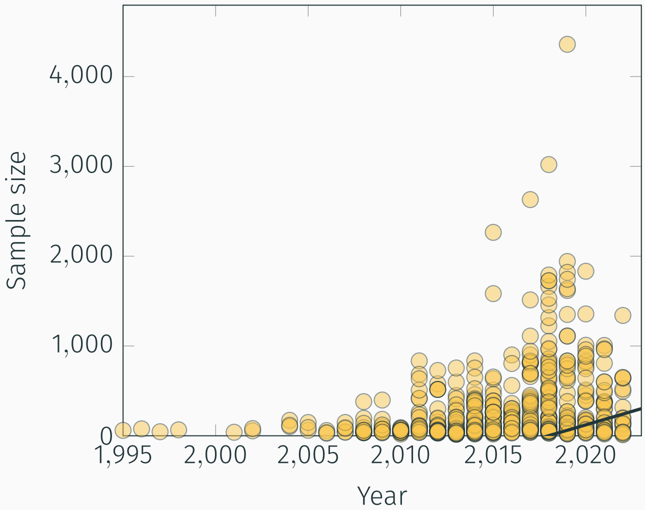
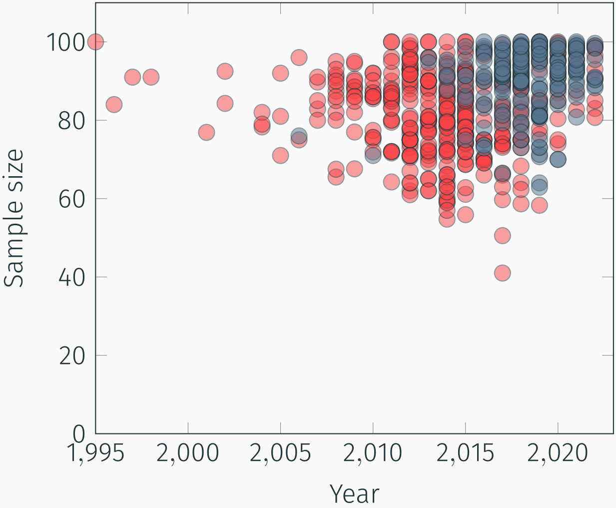


Opportunities: Larger datasets



Opportunities: Better methods



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