Diagnostisk prediksjon av nevrologiske sykdommer med kunstig intelligens og MR-data

Esten H. Leonardsen

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UNIVERSITETET
I OSLO

Oversikt

1. Innledning: Bakgrunn og kontekst
2. State-of-the-art: Hvordan brukes MR-data for prediksjon av nevrologiske sykdommer i forskningen i dag?
3. Oppsummering: Utfordringer og muligheter for fremtiden

Innledning

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Alzheimers sykdom (AD) og andre
årsaker til demens (DEM)

Multippel sklerose (MS)

Parkinsons sykdom (PD)

Bipolar lidelse (BP)

Schizofreni (SCZ)

Depressive lidelser, inkludert
alvorlig depresjon (MDD)

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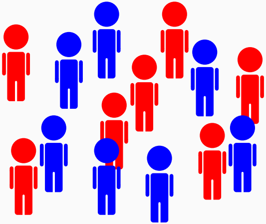

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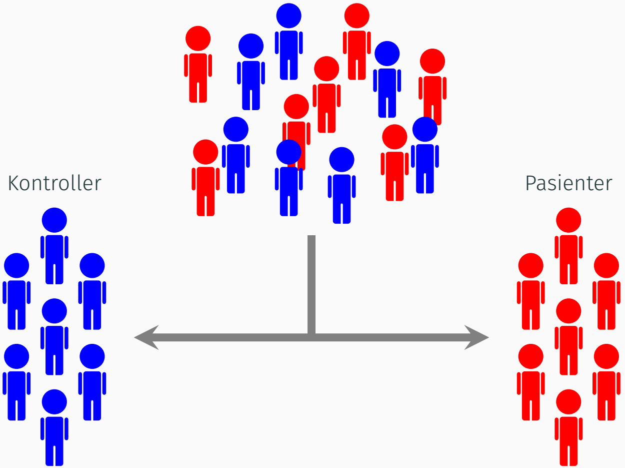

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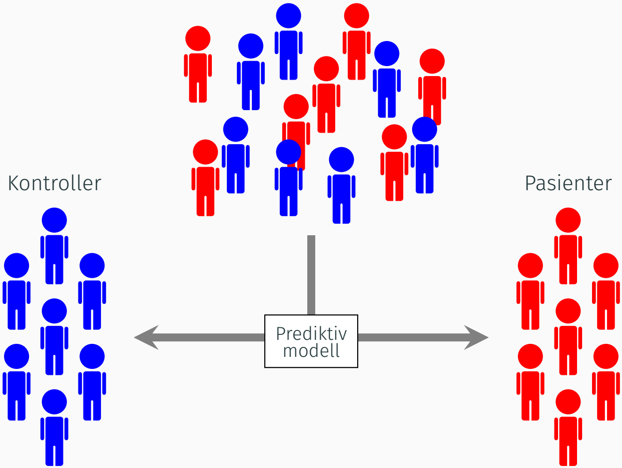

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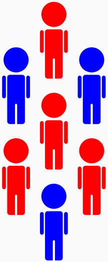
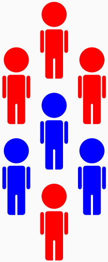
Diagnostisk prediksjon av nevrologiske sykdommer med kunstig intelligens og MR-data

Kontroller



Treffsikkerhet
50%

Pasienter



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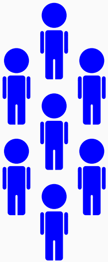

Treffsikkerhet
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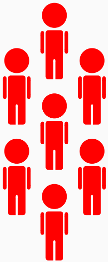
Pasienter



Diagnostiske prediksjoner i forskningslitteraturen

Datagrunnlag

Demens (DEM)
Multippel sklerose (MS)
Parkinsons sykdom (PD)
Schizofreni (SCZ)
Bipolar lidelse (BP)
Alvorlig depresjon (MDD)

DEM MS PD SCZ MDD BP

Diagnose

Datagrunnlag

Demens (DEM)
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Parkinsons sykdom (PD)
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Bipolar lidelse (BP)
Alvorlig depresjon (MDD)

DEM MS PD SCZ MDD BP
Diagnose

Strukturell MR (sMRI)
Diffusjons MR (dMRI)
Funksjonell MR (fMRI)
Molekylær avbildning (MOL)

sMRI dMRI fMRI MOL
Modality

Datagrunnlag

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]

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

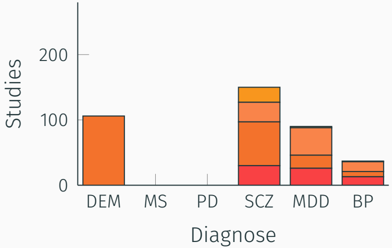
Mohammad R. Arbabshirani[a b], Sergey Plis[a], Jing Sui[a c], Vince D. Calhoun[a d]

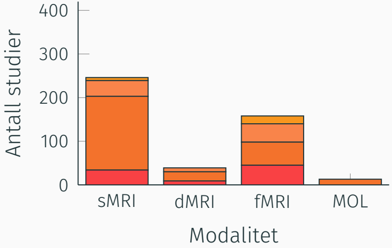
Towards a brain-based predictome of mental illness

Barnaly Rashid, Vince Calhoun

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

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





Datagrunnlag

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

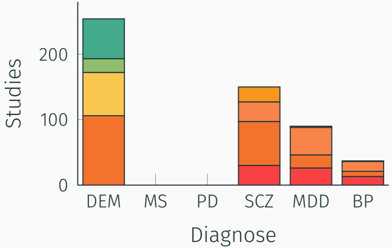
Mr Amir Ebrahimighahnavieh [1], Suhuai Luo [1], Raymond Chiong [2]

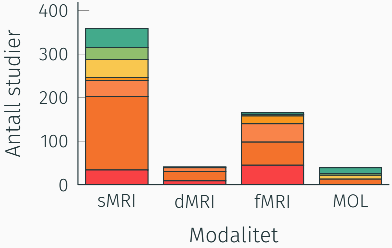
Machine learning techniques for diagnosis of alzheimer disease, mild cognitive disorder, and other types of dementia

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]





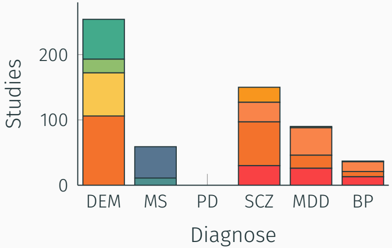
Datagrunnlag

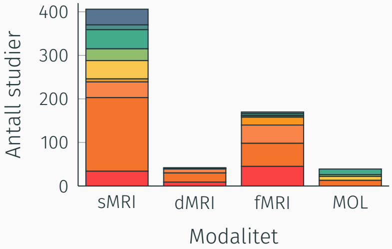
Applications of deep learning techniques for automated multiple sclerosis detection using magnetic resonance imaging: A review

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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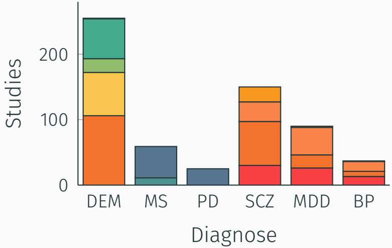
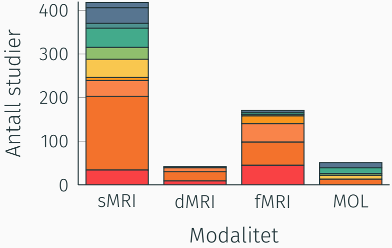


Role of Artificial Intelligence Techniques and Neuroimaging Modalities in Detection of Parkinson's Disease: A Systematic Review

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



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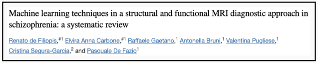
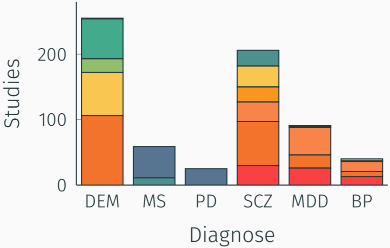
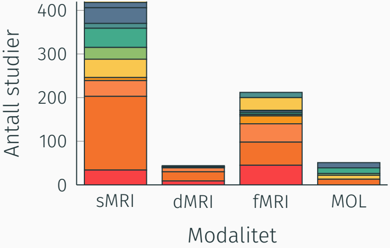

Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review

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]





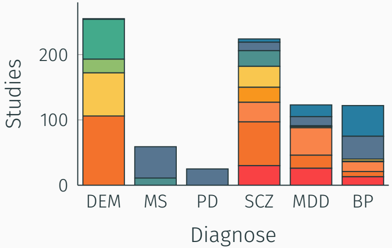
Datagrunnlag

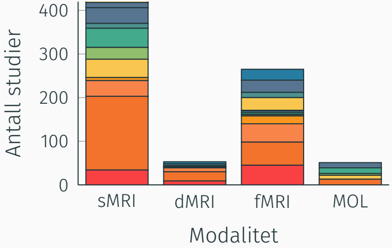
Will machine learning applied to neuroimaging in bipolar disorder help the clinician? A critical review and methodological suggestions

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

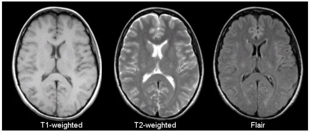
Machine learning approaches for prediction of bipolar disorder based on biological, clinical and neuropsychological markers: A systematic review and meta-analysis

Federica Colombo [1], Federico Calesella [2], Mario Gennaro Mazza [3], Elisa Maria Teresa Melloni [3], Marco J Morelli [4], Giulia Maria Scotti [4], Francesco Benedetti [3], Irene Bollettini [5], Benedetta Vai [6]



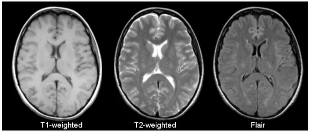


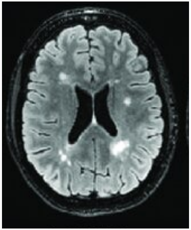
Strukturelle MR modaliteter (sMRI)



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

Strukturelle MR modaliteter (sMRI)





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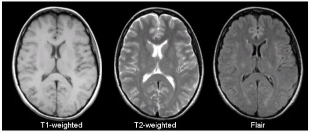

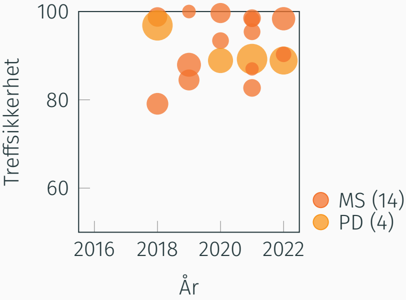

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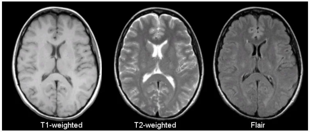

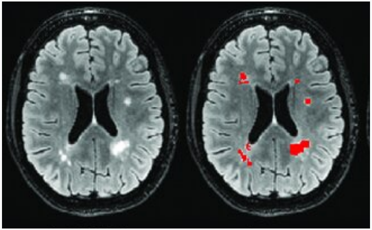

Weeda, M. M., Brouwer, I., de Vos, M. L., de Vries, M. S., Barkhof, F., Pouwels, P. J. W., & Vrenken, H. (2019). Comparing lesion segmentation methods in multiple sclerosis: Input from one manually delineated subject is sufficient for accurate lesion segmentation. NeuroImage: Clinical, 24, 102074

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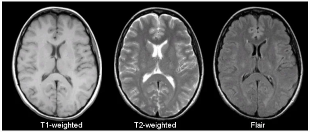

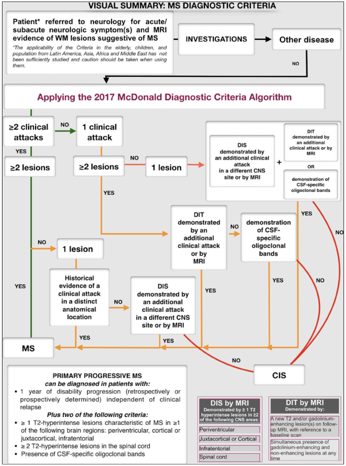

De Angelis, F., Brownlee, W. J., Chard, D. T., & Trip, S. A. (2019). New MS diagnostic criteria in practice. Practical Neurology, 19(1), 64-67

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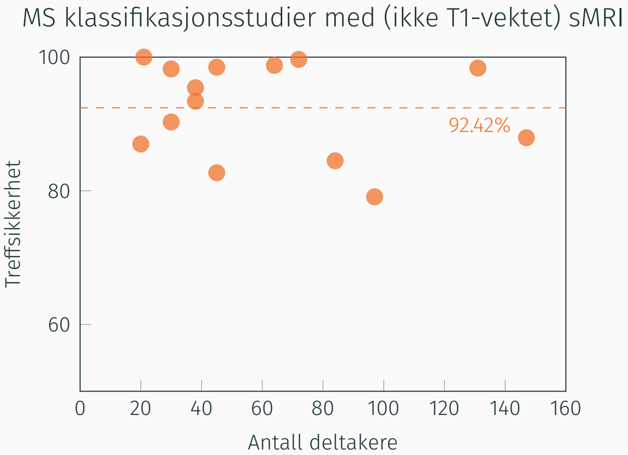

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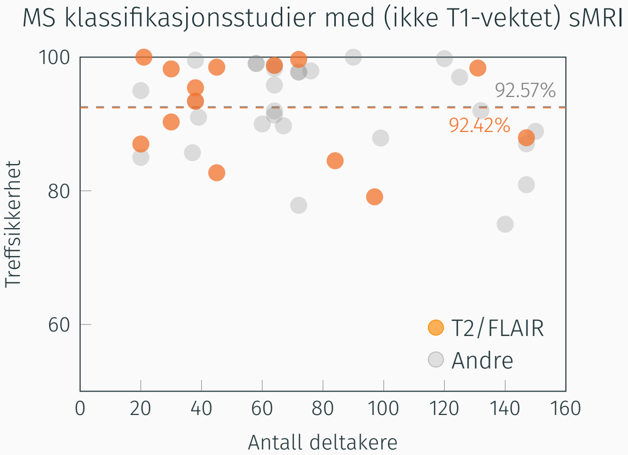

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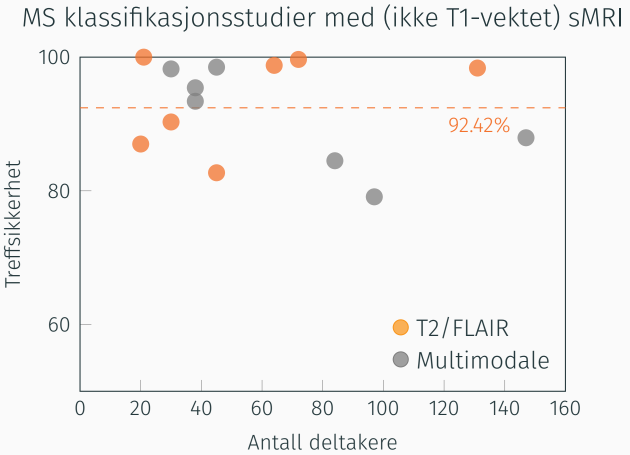

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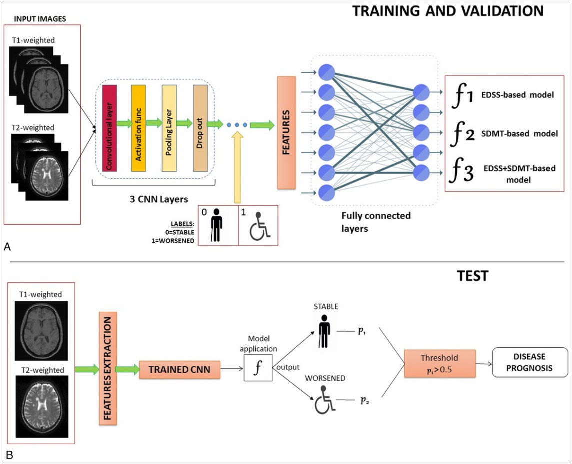


Storelli, L., Azzimonti, M., Gueye, M., Vizzino, C., Preziosa, P., Tedeschi, G., ... & Rocca, M. A. (2022). A deep learning approach to predicting disease progression in multiple sclerosis using magnetic resonance imaging. Investigative Radiology, 57(7), 423-432

Strukturelle MR modaliteter (sMRI)

		Prediction of Clinical Worsening (EDSS Model)	Prediction of Cognitive Worsening (SDMT Model)	Prediction of Clinical and Cognitive Worsening (EDSS + SDMT Model)	*P**
CNN deep learning	Accuracy (%)	83.3	67.7	85.7	—
	Sensitivity (%)	57.1	60.0	75.0	—
	Specificity (%)	90.0	81.8	87.5	—
Expert raters consensus	Accuracy (%)	—	—	70.0	<0.001
	Sensitivity (%)	—	—	14.3	<0.0001
	Specificity (%)	—	—	80.0	<0.01

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

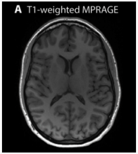
Storelli, L., Azzimonti, M., Gueye, M., Vizzino, C., Preziosa, P., Tedeschi, G., ... & Rocca, M. A. (2022). A deep learning approach to predicting disease progression in multiple sclerosis using magnetic resonance imaging. Investigative Radiology, 57(7), 423-432

Strukturelle MR modaliteter (sMRI)

Strukturelle (ikke T1-vektede) MR-bilder: Avbilder stabile egenskaper ved hjernevev.

- Mest brukt i studier som klassifiserer MS og PD, med høy treffsikkerhet (gjennomsnittlig $\sim$90%).
- T2 relatert til MS grunnet modalitetens evne til å fange opp karakteristiske lesjoner.
- Maskinlæringsmodeller trent på T1 og T2-vektede bilder kan predikere prognose bedre enn menneskelige eksperter (Storelli et al).

Diffusjons MR (dMRI)



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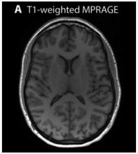

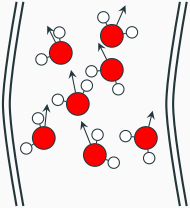

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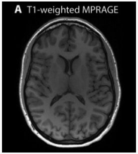
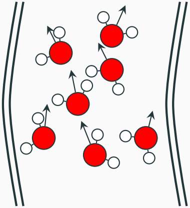
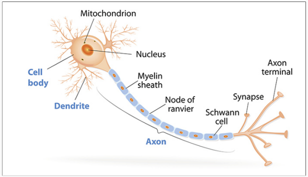
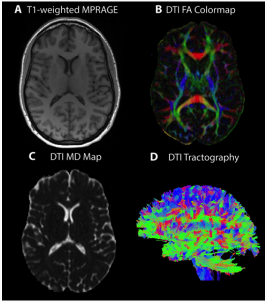






Queensland Brains Institute, Axons: the cable transmission of neurons, https://qbi.uq.edu.au/brain/brain-anatomy/axons-cable-transmission-neurons

Diffusjons MR (dMRI)



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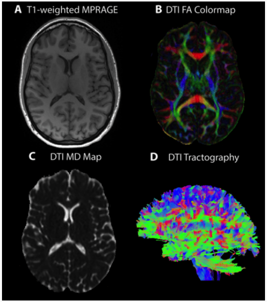

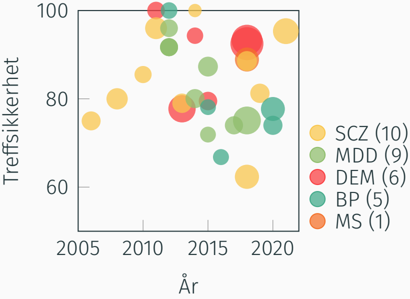

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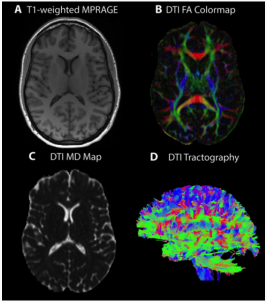
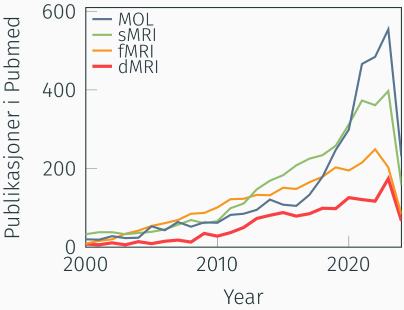
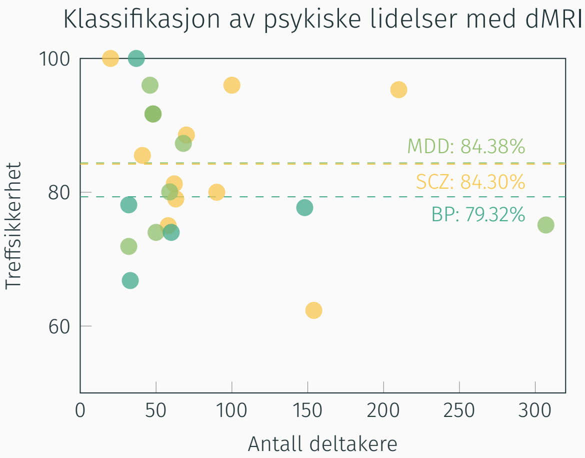




MOL:	((molecular[Title] AND imaging[Title]) OR PET[Title] OR SPECT[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)"
sMRI:	((structural[Title] AND MRI[Title]) OR sMRI[Title] OR T1[Title] OR T2[Title]) AND (machine learning OR ML OR deep learning OR DL OR prediction)
fMRI:	((functional[Title]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

Diffusjons MR (dMRI)

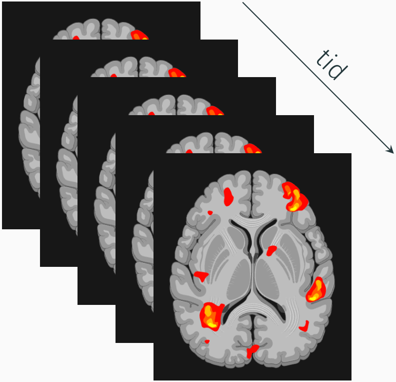


Diffusjons MR (dMRI)

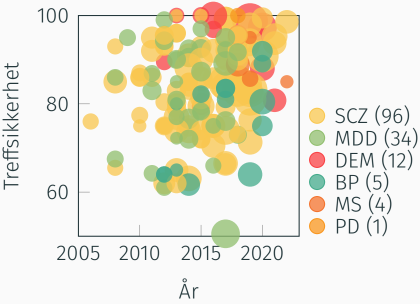
Diffusjons MR: Avbilder nervebaner og deres integritet.

- Vanskelig å finne prediksjonsstudier, de fleste fokuserer på å produsere biologisk innsikt.
- Flest studier for psykiske lidelser, spesielt SCZ og MDD, med høy gjennomsnittlig treffsikkerhet ($\sim$85%) men stor spredning (60-100%).

Funksjonell MR



Funksjonell MR



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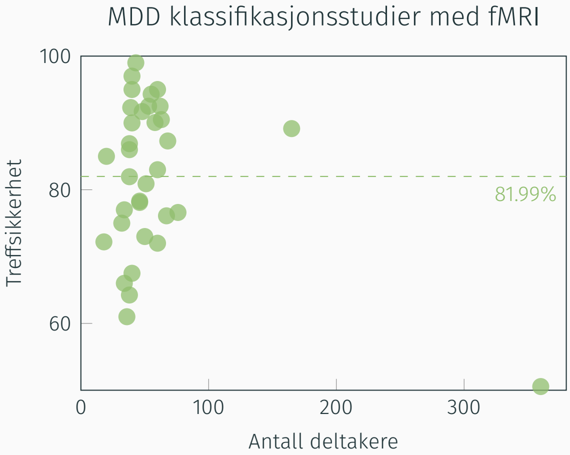

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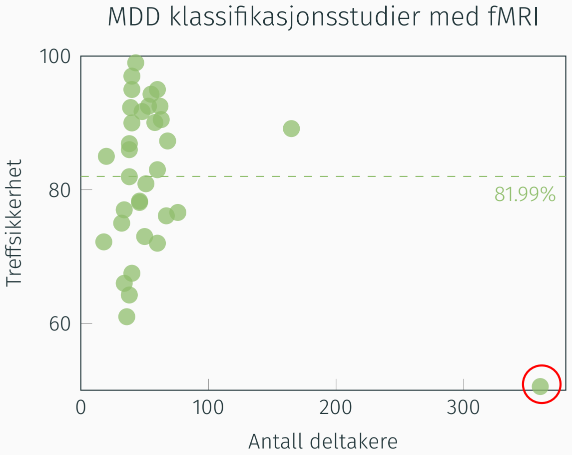
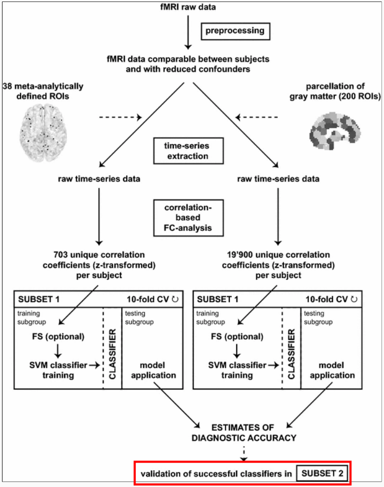


Sundermann, B., Feder, S., Wersching, H., Teuber, A., Schwindt, W., Kugel, H., ... & Pfleiderer, B. (2017). Diagnostic classification of unipolar depression based on resting-state functional connectivity MRI: effects of generalization to a diverse sample. Journal of Neural Transmission, 124, 589-605

Funksjonell MR



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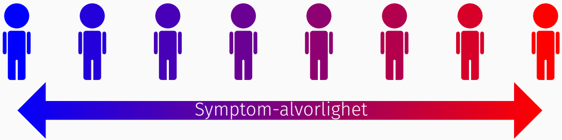
Funksjonell MR

(a) Main analysis									
Yielded no positive results									
(b) Subgroup analysis [most severely depressed patients (*n* = 60) and their corresponding controls (*n* = 60)]									
			CV in subset 1			Validation in subset 2			
FS	Features (*n*)	C-SVC-classifier	ACC (%)	SENS (%)	SPEC (%)	ACC (%)	SENS (%)	SPEC (%)	*p(FDR) ACC*
Models based on connectivity of meta-analytically defined regions									
./.	703	RBF (γ = 0.01), C = 10	60.0	60.0	60.0	55.0	46.7	63.3	0.171
t test[a]	141	lin, C = 0.1	65.0	63.3	66.7	57.5	45.0	70.0	0.087
t test[a]	141	RBF (γ = 0.01), C = 10	61.7	60.0	63.3	55.8	45.0	66.7	0.140
SVM[b]	141	RBF (γ = 0.01), C = 1	61.7	71.7	51.7	61.7	58.3	65.0	0.046*

Sundermann, B., Feder, S., Wersching, H., Teuber, A., Schwindt, W., Kugel, H., … & Pfleiderer, B. (2017). Diagnostic classification of unipolar depression based on resting-state functional connectivity MRI: effects of generalization to a diverse sample. Journal of Neural Transmission, 124, 589-605

Funksjonell MR

Funksjonell MR



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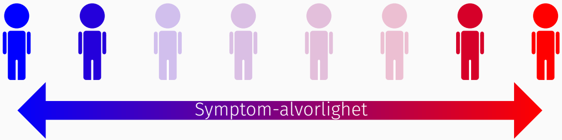
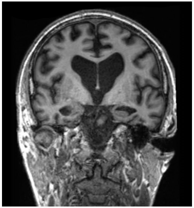


Funksjonell MR

Funksjonell MR: Et indirekte mål av hjerneaktivitet over tid.

- Mange prediktive studier å finne, flest for psykiske lidelser.
- Generelt høy gjennomsnittlig treffsikkerhet (80-85%), men stor spredning (50-100%).
- Sundermann et al. hadde problemer med å klassifisere heterogene MDD-pasienter, men fikk til å detektere pasientene med alvorligst symptomer (til en viss grad).

Molekylær avbildning



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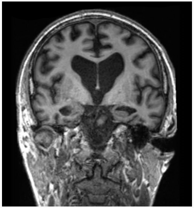

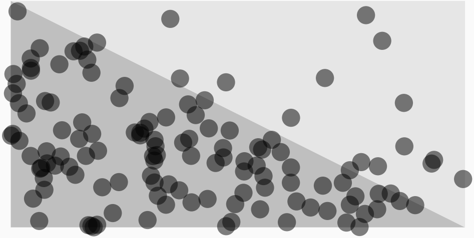

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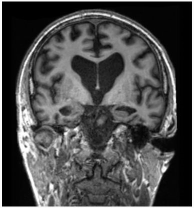

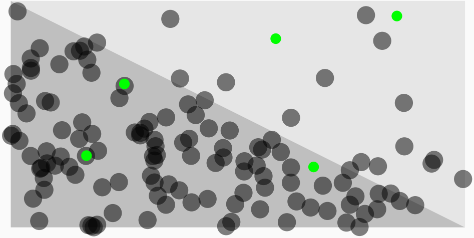

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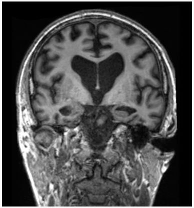

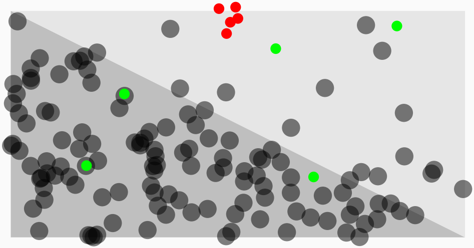

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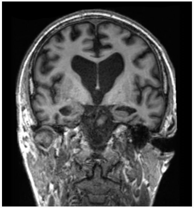

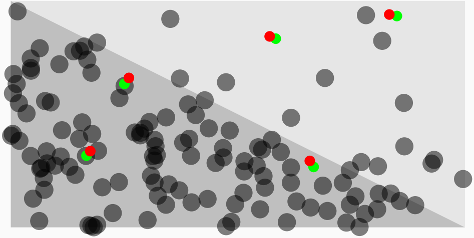

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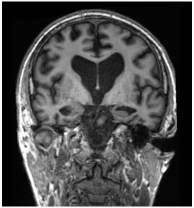

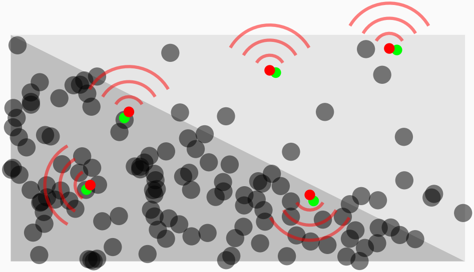

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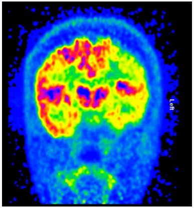

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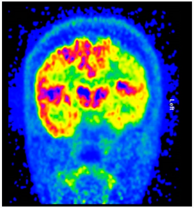

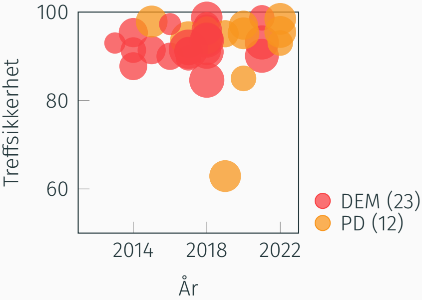

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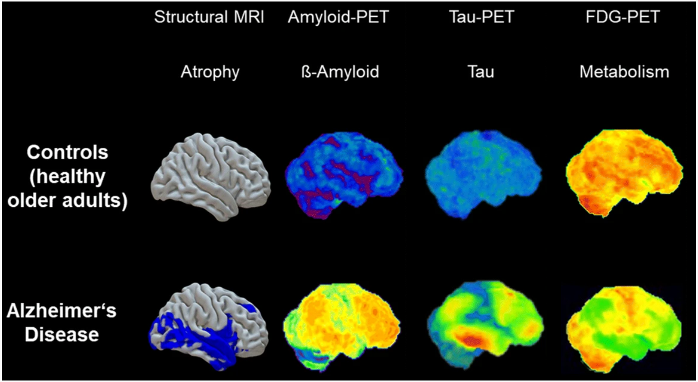
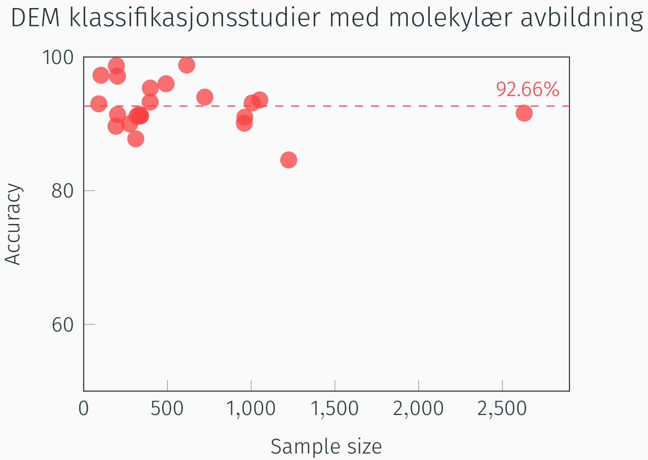


Chételat, G., Arbizu, J., Barthel, H., Garibotto, V., Lammertsma, A. A., Law, I., ... & Drzezga, A. (2021). Finding our way through the labyrinth of dementia biomarkers. European journal of nuclear medicine and molecular imaging, 48, 2320-2324

Molekylær avbildning



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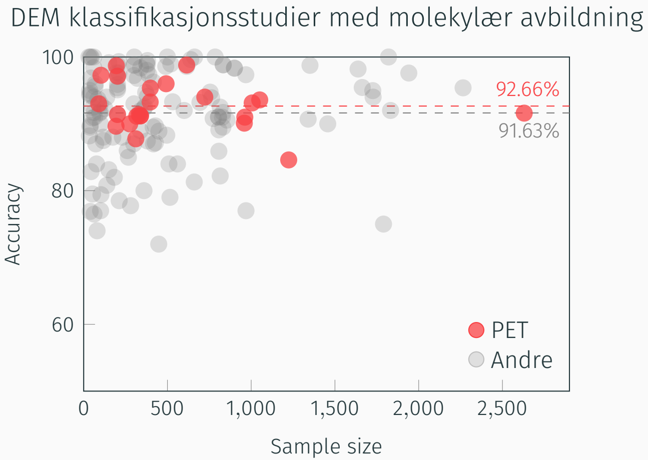


Molekylær avbildning

"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, alz.org/diagnosticcriteria

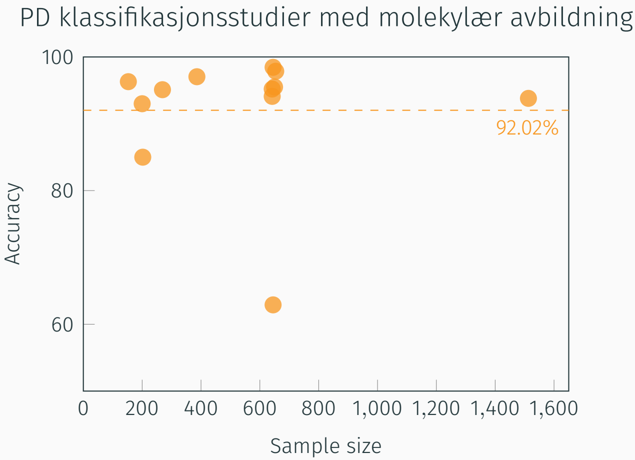
Molekylær avbildning

		Metrics				
		Se	Sp	Precision	F1-score	Support
Model	AD	75 % (15/20)	97 % (38/39)	94 % (15/16)	83 %	20
	FTD	95 % (18/19)	90 % (36/40)	82 % (18/22)	88 %	19
	CN	100 % (20/20)	97 % (38/39)	95 % (20/21)	98 %	20 acc 89.8%

		Se	Sp	Precision	F1-score	Support
Physician	AD	70 % (14/20)	87 % (34/39)	74 % (14/19)	72 %	20
	FTD	47 % (9/19)	92 % (37/40)	75 % (9/12)	58 %	19
	CN	90 % (18/20)	74 % (29/39)	64 % (18/28)	75 %	20 acc 69.5%

Rogeau, A., Hives, F., Bordier, C., Lahousse, H., Roca, V., Lebouvier, T., … & Lopes, R. (2024). A 3D convolutional neural network to classify subjects as Alzheimer's disease, frontotemporal dementia or healthy controls using brain 18F-FDG PET. NeuroImage, 120530

Molekylær avbildning



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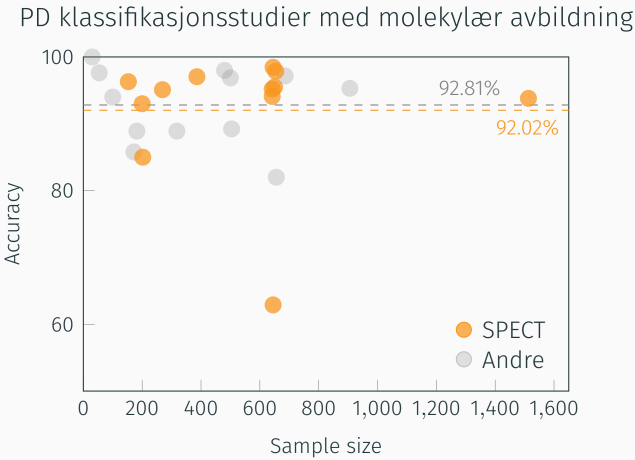


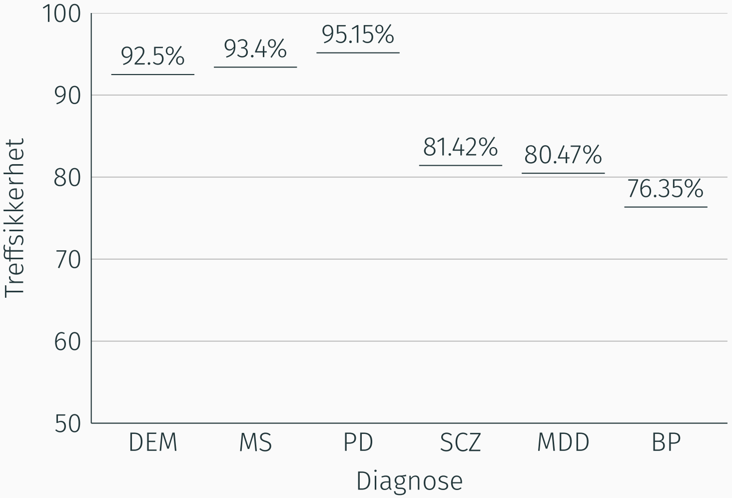
Molekylær avbildning

Molekylær avbildning: Lokaliserer og kvantifiserer tilstedeværelsen av spesifikke molekyler og partikler

- Brukt i studier for å klassifisere PD og DEM med gode resultater (treffsikkerhet >90%), men (noe overraskende) ikke bedre enn andre modaliteter.
- PET er et naturlig valg for å finne patologi relatert til AD, og kan brukes for å differensialdiagnostisere underliggende sykdom ved demens bedre enn mennesker (Rogeau et al).
- SPECT nyttig for å karakterisere degenerasjon av dopamin-produserende celler i PD.

Utfordringer og muligheter

Utfordringer: Prediktiv verdi



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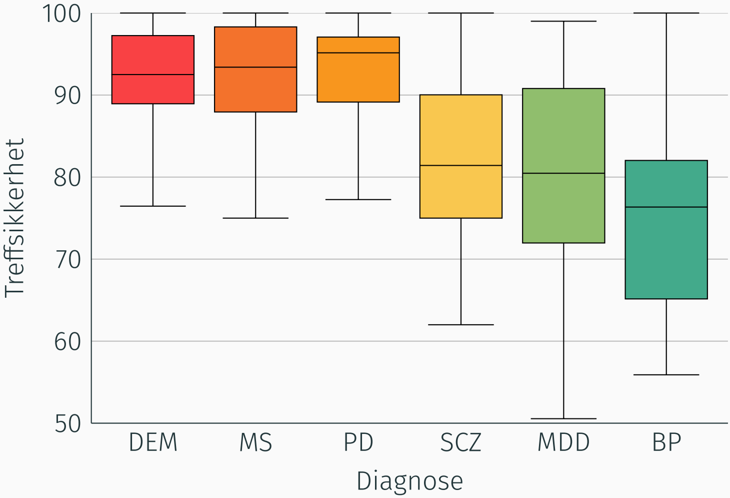

Utfordringer: Prediktiv verdi

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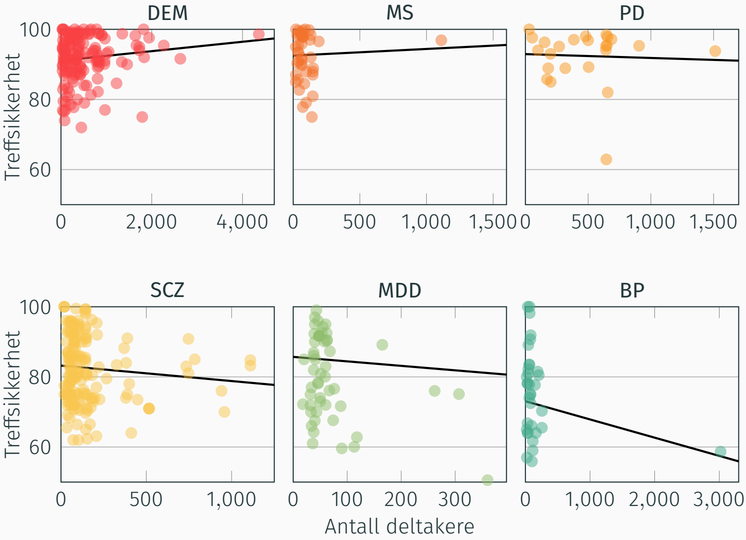
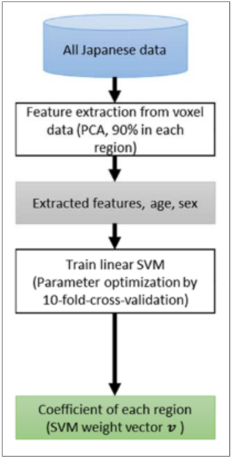


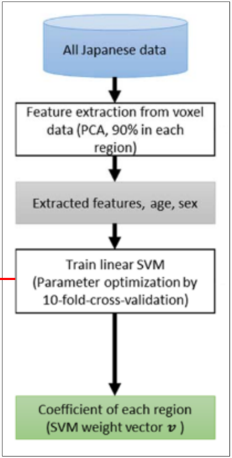
Utfordringer: Generalisering



Matsuo, K., Harada, K., Fujita, Y., Okamoto, Y., Ota, M., Narita, H., ... & Watanabe, Y. (2019). Distinctive neuroanatomical substrates for depression in bipolar disorder versus major depressive disorder. Cerebral Cortex, 29(1), 202-214

Utfordringer: Generalisering

88.1%



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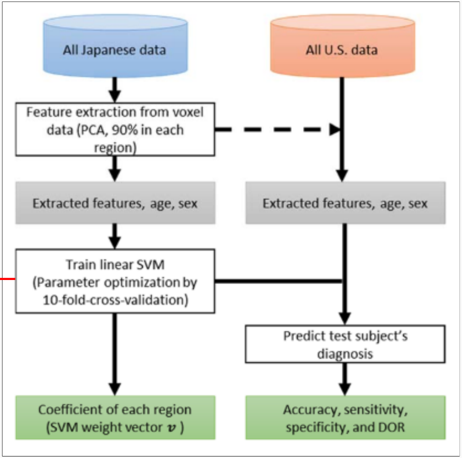

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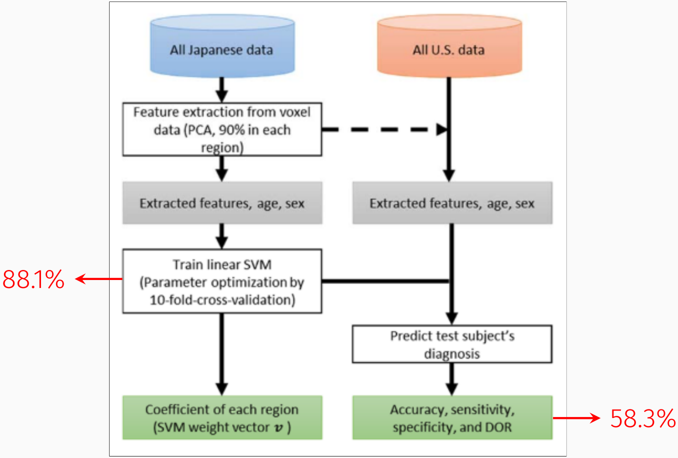

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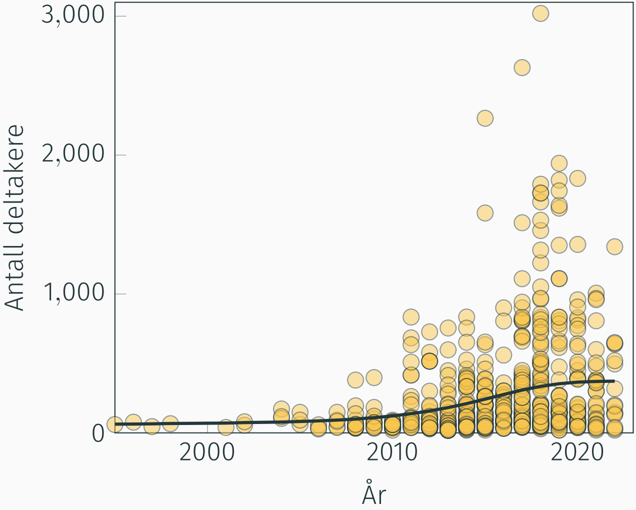
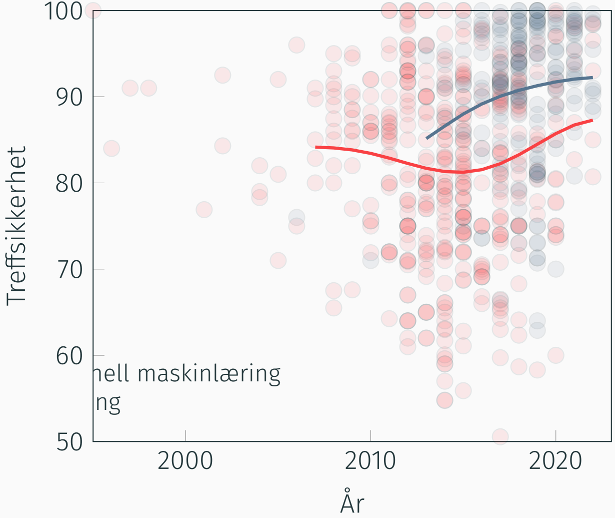
Muligheter: Større datasett



Muligheter: Bedre metoder



Oppsummering

En oversikt over hvordan kunstig intelligens og MR-data brukes i forsningslitteraturen for å predikere nevrologiske* sykdommer.

- En bred litteratur med studier som predikerer forskjellige utfall innen forskjellige tilstander med forskjellige typer MR-data.
- DEM og SCZ er de vanligste diagnosene å predikere.
- Strukturell og funksjonell MR de vanligste modalitetene.
- Generelt høy treffsikkerhet for DEM, MS, and PD (90%+)
- Lavere, men forsatt potensielt klinisk brukbare resultater for SCZ, BP, MDD ($\sim$80%).
- **Studier peker i vidt forskjellige retninger**, slik at litteraturen er vanskelig å tolke.
- **Bildemodaliteter som teoretisk er tett knyttet opp mot spesifikke sykdommer utkonkurrerer ikke andre modaliteter.**
- Større datasett og bedre metoder vil forhåpentligvis gi en mer enhetlig litteratur.

Takk for meg!

Takk for meg!

estenhl@uio.no