Multiple Sclerosis Research Group
Oslo University Hospital

Kick-off: Sys4MS oppfølging

Torsdag 30/8-18

OUS, Ullevål sykehus

Sys4MS

Einar August Høgestøl

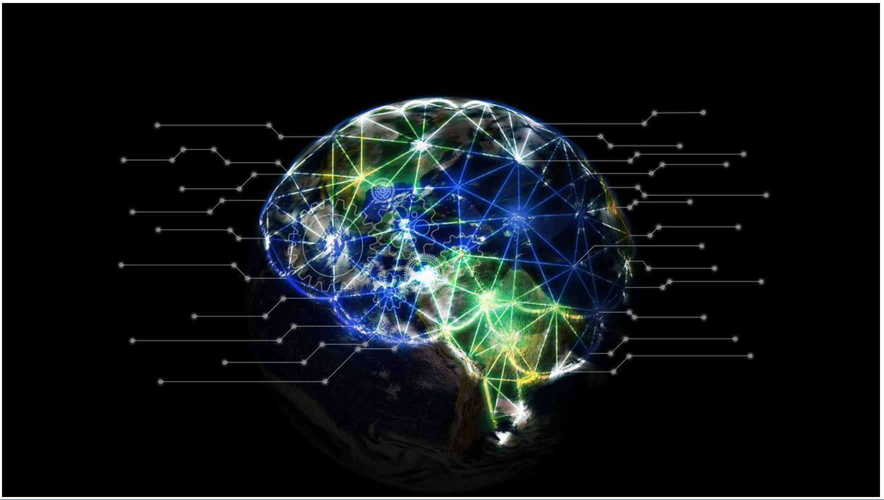
MD, Ph.D. student

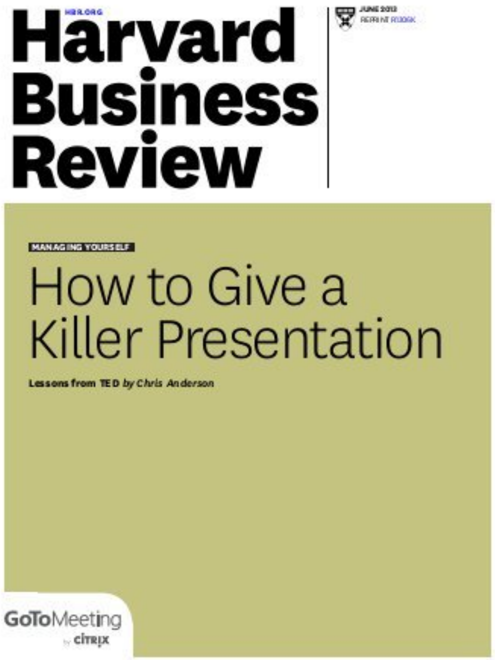
MS Research Group OUS / UiO

NORMENT

Agenda

- MS oppfølgingsstudien i Oslo
- fMRI artikkel
- Hjernealder artikkel
- NORMENT samarbeid
- MYO samarbeid





Oslo Longitudinal MS Cohort

Time point 1
2012/2013

76
MS patients

Oslo Longitudinal MS Cohort

Time point 2
2013/2014

72
MS patients

Oslo Longitudinal MS Cohort

Time point 3
2016/2017

62
MS patients

Sys4MS

Time point 1
2016/2017

95 MS patients

Oslo Longitudinal MS Cohort

Time point 4
2018/2019

~ 65
MS patients

Sys4MS

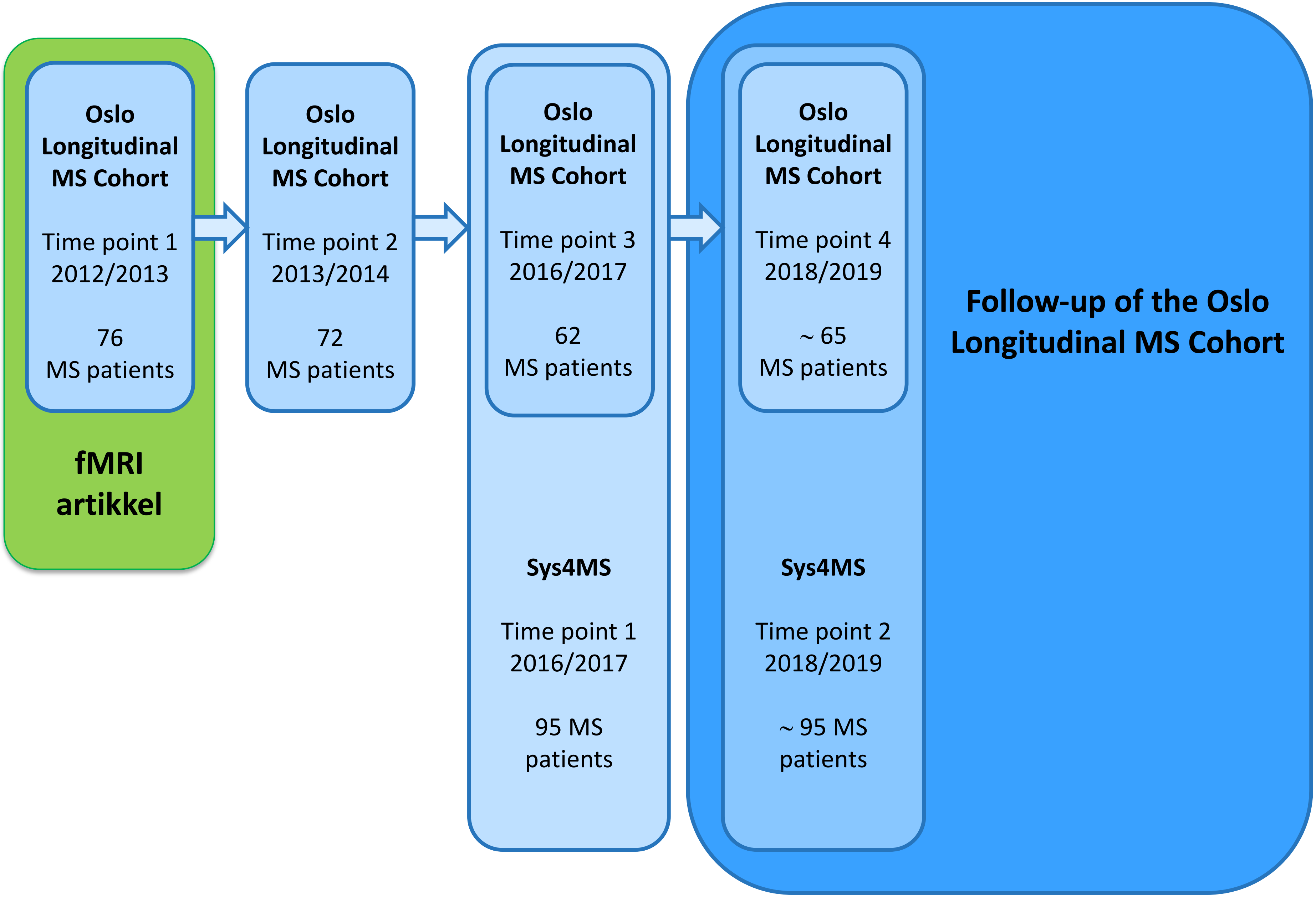
Time point 2
2018/2019

~ 95 MS patients

Follow-up of the Oslo Longitudinal MS Cohort

Ph.D til Gro O. Nygaard

Ph.D til Piotr W. Sowa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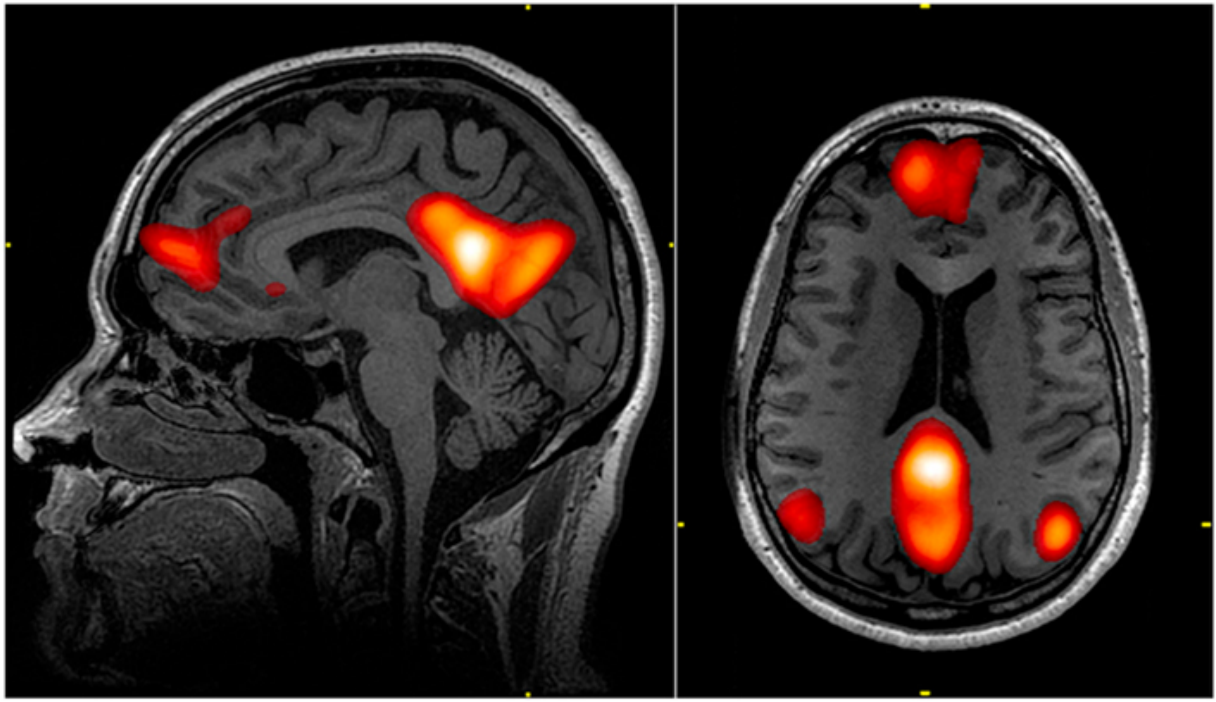
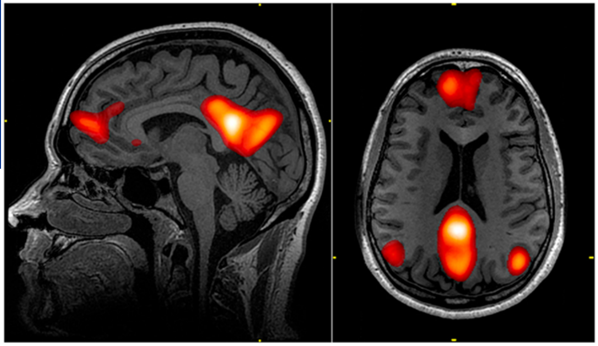
Funksjonell MR

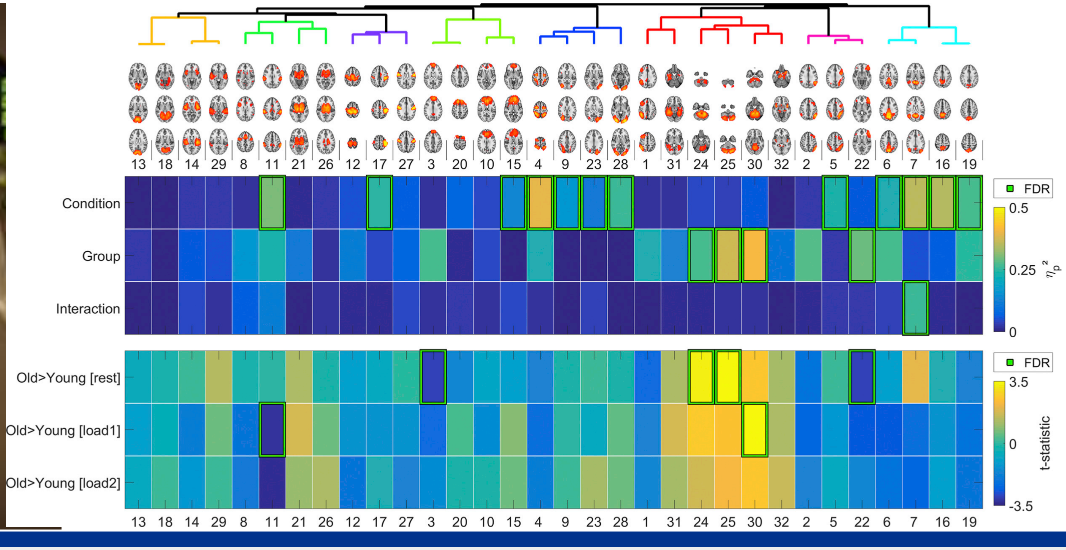
- Hvilemodus funksjonell MR undersøkelse (rs-fMRI)
  - Hjernens hvilenettverk (default mode network)
  - Nettverket mellom hjerneområdene som er mest aktivt når hjernen «hviler i våken tilstand»

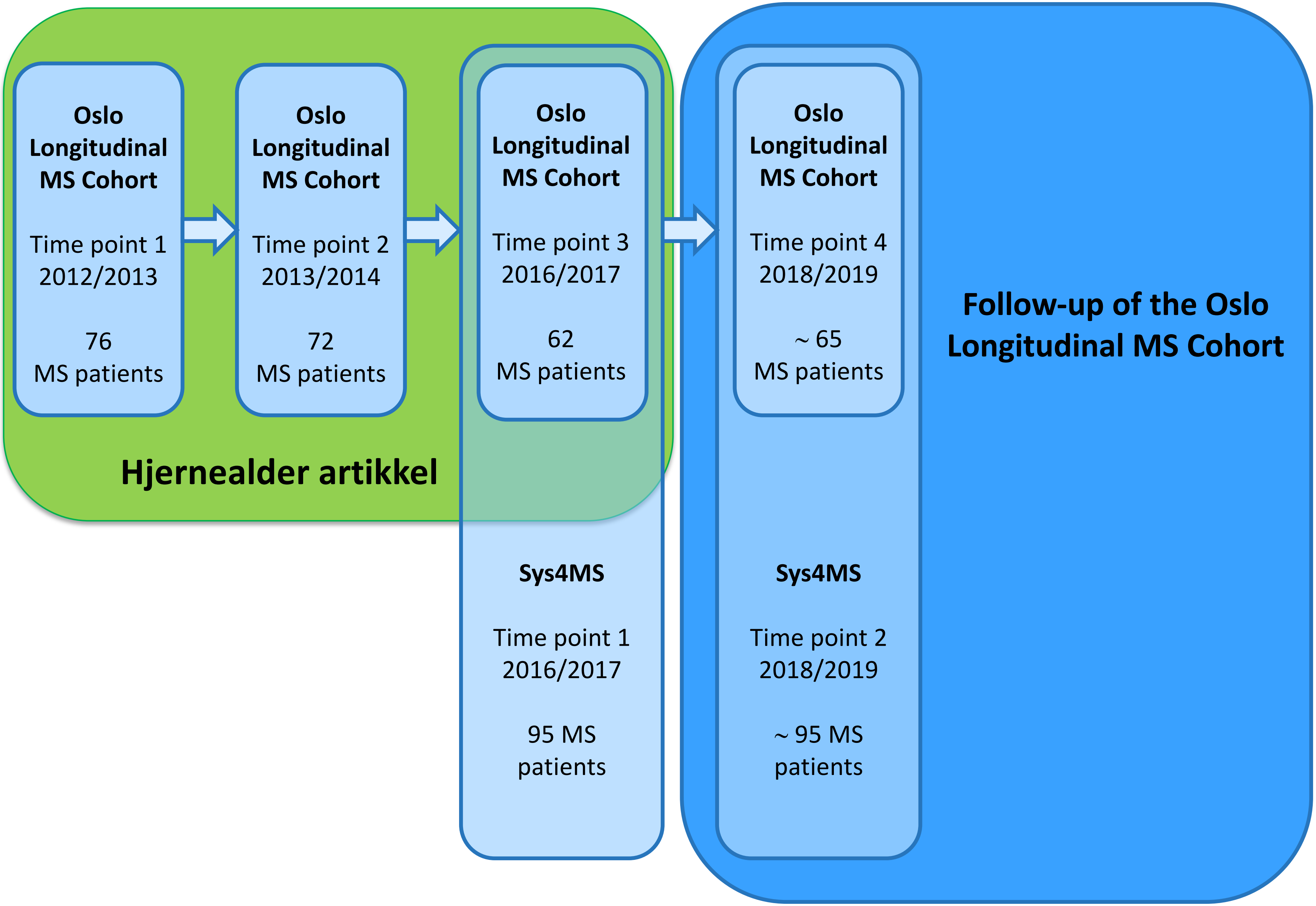


fMRI artikkel: Videre arbeid



- Tittel: "Functional connectivity alterations in multiple sclerosis "
  - rs-fMRI data fra tidspunkt 1 (n=73) and friske kontrollpasienter fra NCNG kohorten (n=263).
  - Første innsending kun fokus på hvilemodusnettverket. Nå omfattende utvidelse!

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Hjernealder prediksjon

Time point 1
Age 37
Brain Age 39

Time point 2
Age 38
Brain Age 44

Time point 3
Age 42
Brain Age 57

Time point 1
Age 40
Brain Age 36

Time point 2
Age 42
Brain Age 38

Time point 3
Age 45
Brain Age 34

Trends in Neurosciences

Opinion

Predicting Age Using Neuroimaging: Innovative Brain Ageing Biomarkers

James H. Cole[1,*] and Katja Franke[2,*]

Trends

Brain age can be predicted in individuals based on neuroimaging data using machine learning approaches to model trajectories of healthy brain ageing.

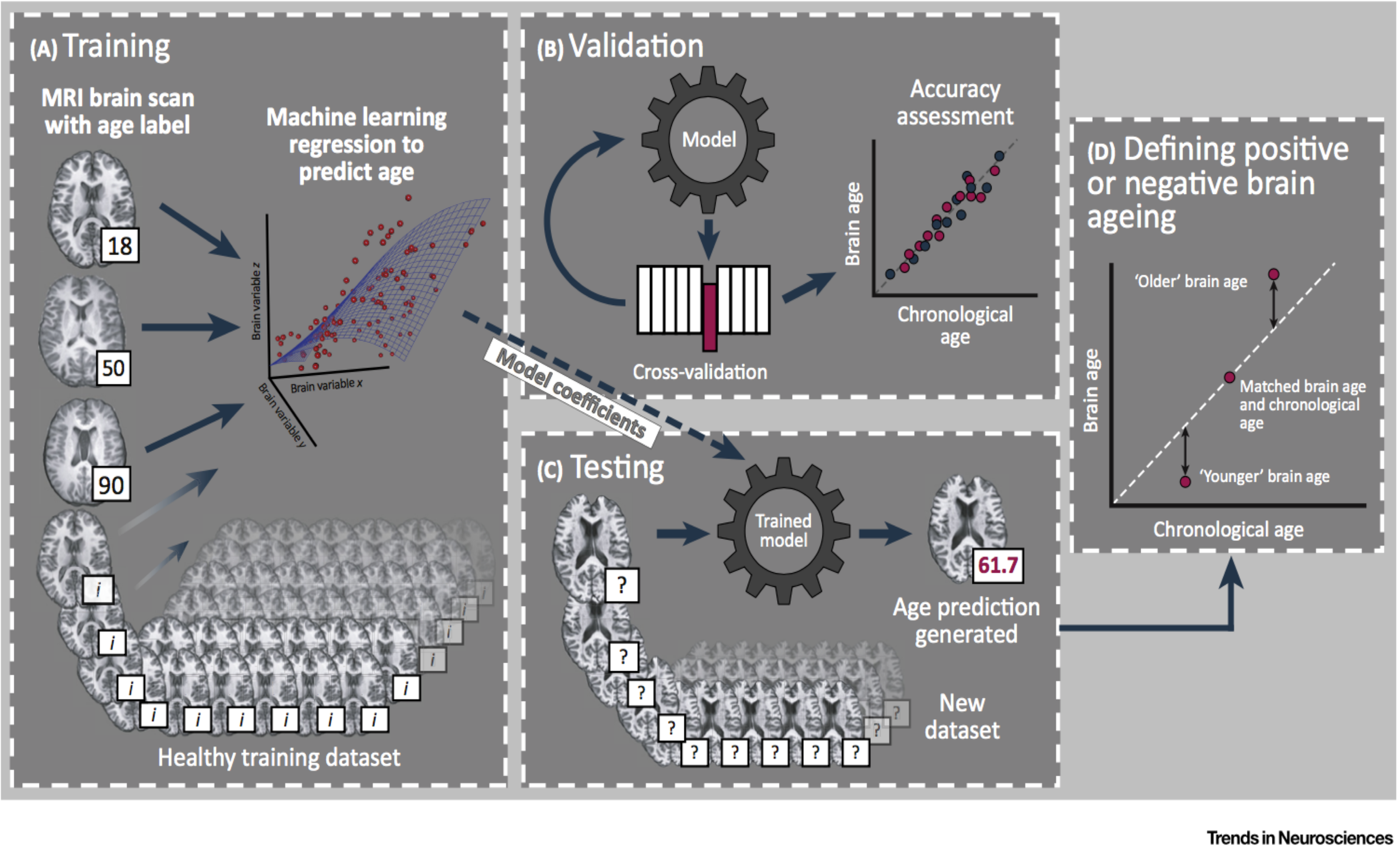
The predicted brain age for a new individual can differ from his or her chronological age; this difference appears to reflect advanced or delayed brain ageing.

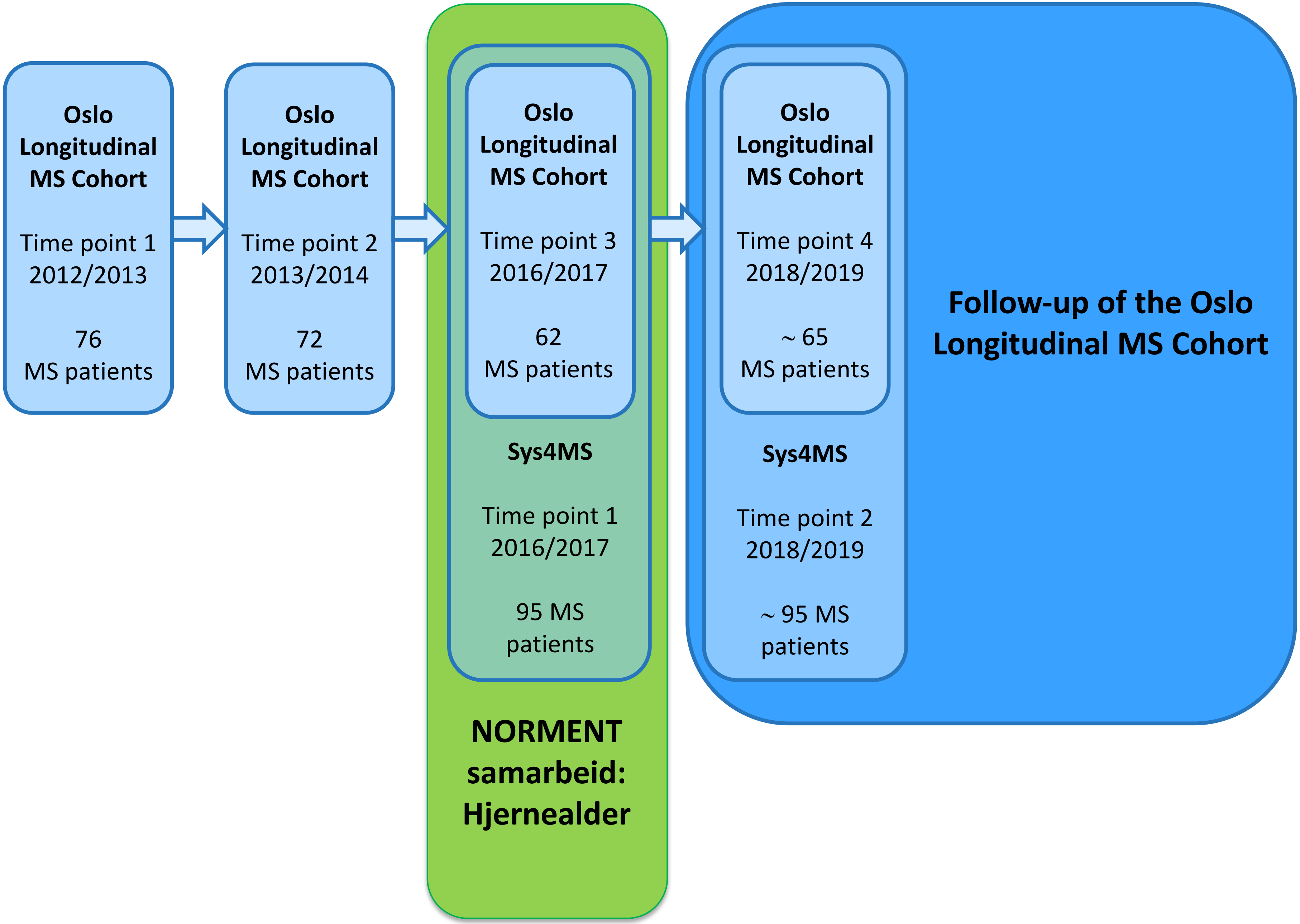
Brain age has been shown to relate to cognitive ageing and multiple aspects of physiological ageing and to predict the risk of neurodegenerative diseases and mortality in older adults.

Various diseases, including HIV, schizophrenia, and diabetes, have been shown to make the brain appear older. Further, brain age is being used to identify possible protective or deleterious factors for brain health as people age.

Brain age is being actively developed to combine multiple measures of brain structure and function, capturing increasing amounts of detail on the ageing brain.

How Brain Age Prediction Works

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NORMENT – Kaufmann, Tobias

- “Genetics of brain age suggests an overlap with common brain disorders”
  - N = 36.891
  - MS = 254
  - Submitted to bioRxiv 17/4

Article usage: April 2018 to May 2018

Show by month	Abstract	Pdf
Total	1,924	502

64

Tweeted by **113**

3 readers on Mendeley

See more details

Tweets referencing this article:

18 Apr 2018

Lars T. Westlye
@larswestlye

New preprint from our group demonstrates clinically relevant regional patterns of brain age deviations and partly shared genetic architecture with clinical traits. Massive collaborative effort led by amazing @TobKaufmann https://t.co/XdHURP94Xw

18 Apr 2018

Brain age prediction – samples

- Healthy controls in training sample n=26.535
- Several samples with brain disorders with typical onset age distributed across the life span

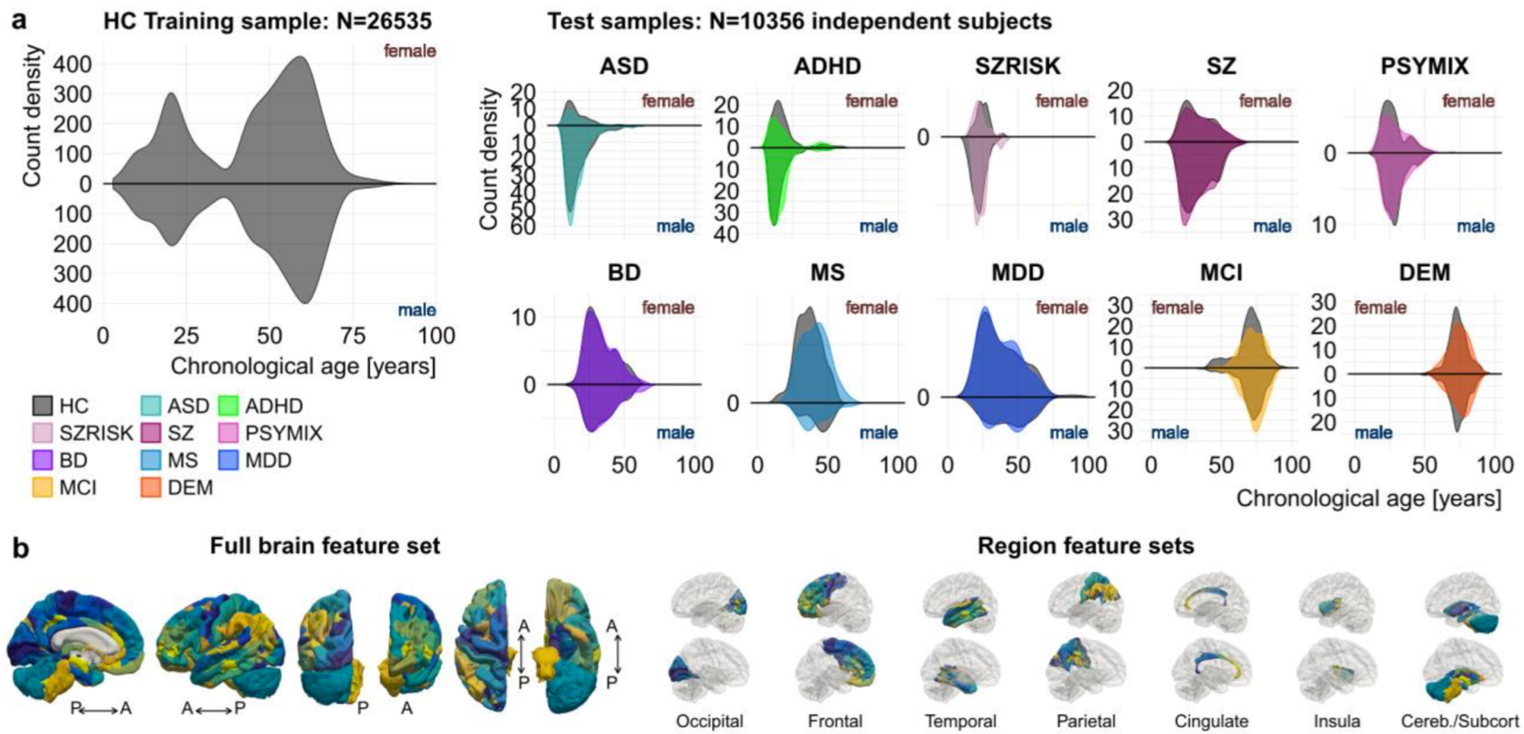
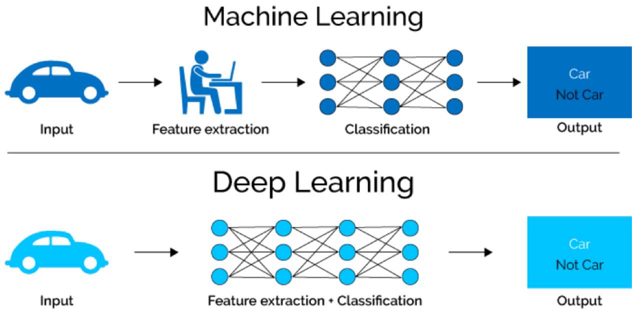


Figure 1: Sample distributions and brain features used for brain age prediction.

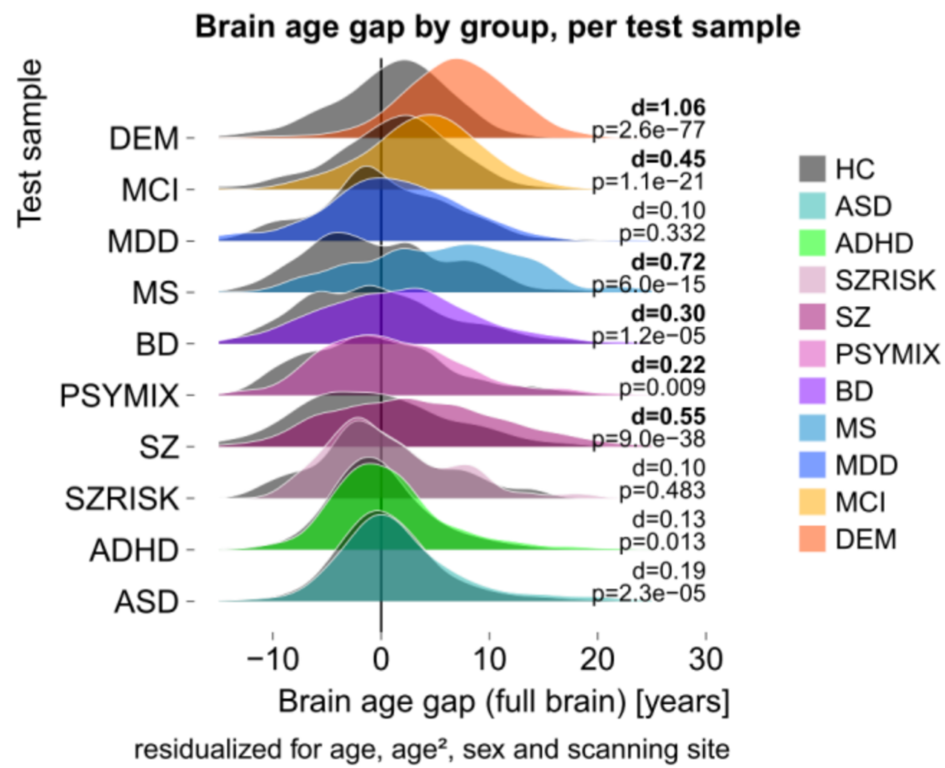
Brain age prediction – method

- Built a machine learning model for prediction brain age for each sex
  - Utilizing in total 1.118 different structural MRI features, we trained a brain age prediction model for each sex
  - High validity of the models, yielding high correlations between chronological and predicted age
    - Female: r=0.94
    - Male: r=0.95
  - Mega-analysis (across site analysis)
    - Controlled for age, age^2, sex and scanning site



Brain age prediction – mega-analysis

- Brain age gap (BAG): difference between chronological age and predicted brain age
- BAG increased in several brain disorders
  - DEM: 5.8 years
  - MS: 5.6 years
  - SZ: 3.9 years
  - MCI: 3.0 years
  - BP: 2.0 years
  - PSYMIX: 1.4 years
  - ASD: 1.1 years



Brain age prediction – brain regions

- Assessed the specificity of the spatial brain age gap patterns across clinical groups

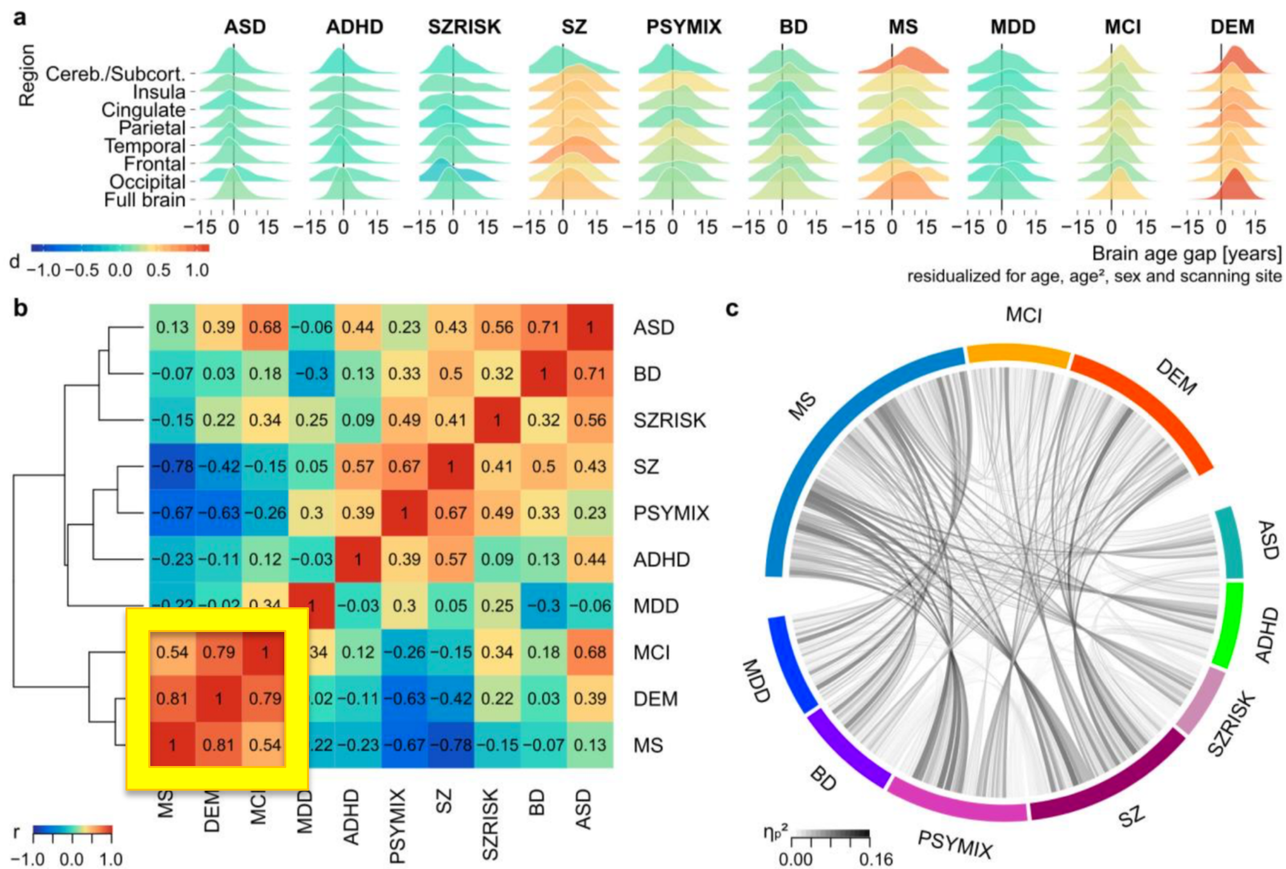


Figure 3: Several disorders displayed regional specific aging patterns.

Cerebellar and subcortical brain age gap most prominent in DEM (*d*=0.99) and MS (*d*=0.89).

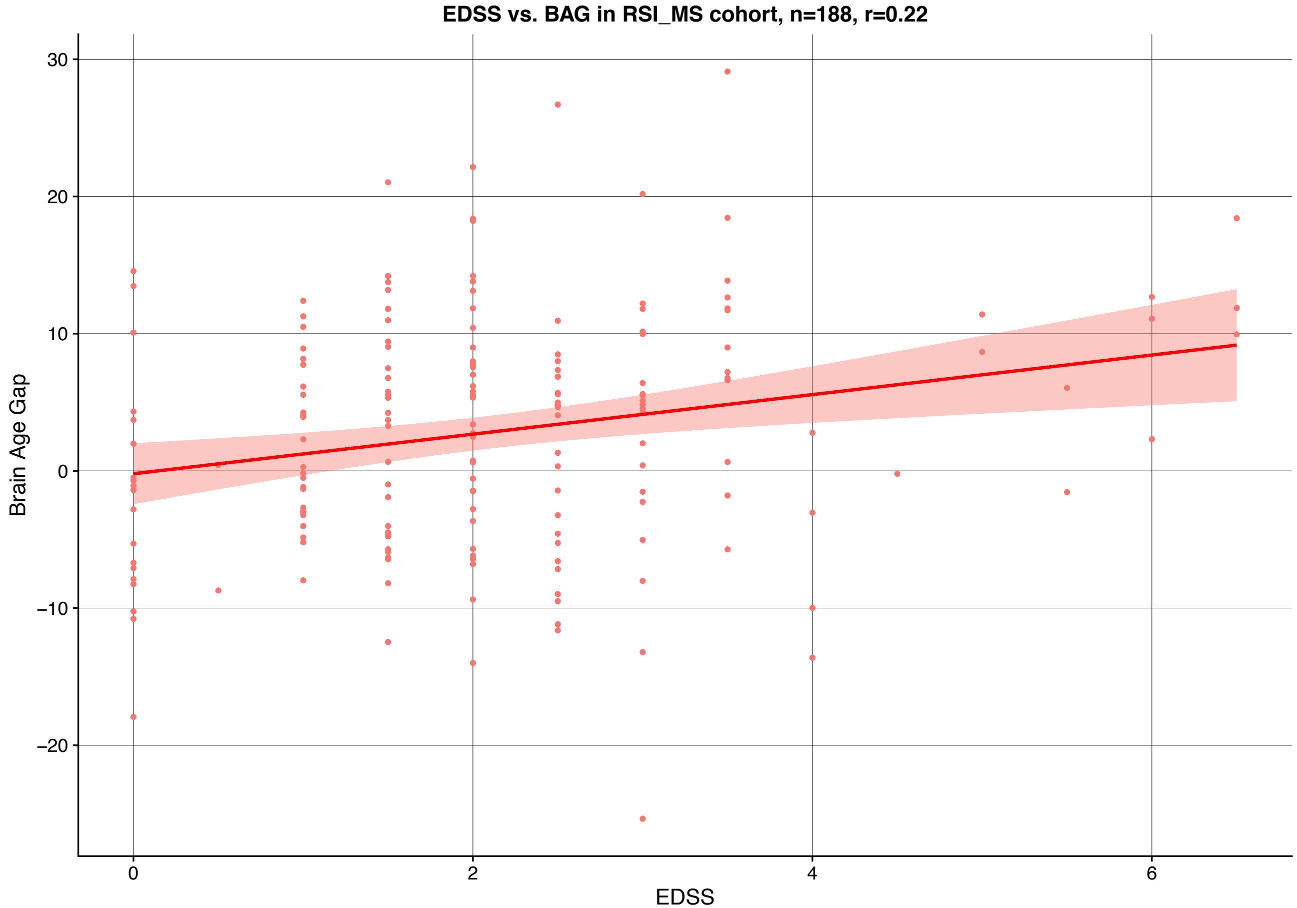
MS, MCI and DEM - same patterns.

Brain age prediction – functional relevance

- Associations with clinical and cognitive data

Figure 4. Region-wise brain age gaps were associated with cognitive and clinical scores.

Brain age prediction – EDSS in MS



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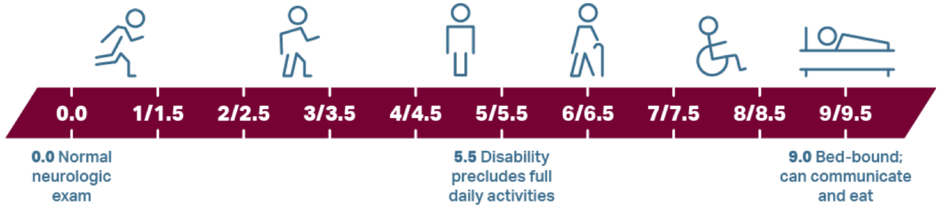


Brain age prediction – genetic architecture

- To what degree are brain age patterns genetically constrained?
  - GWAS data available from the UK Biobank (n=16.269)

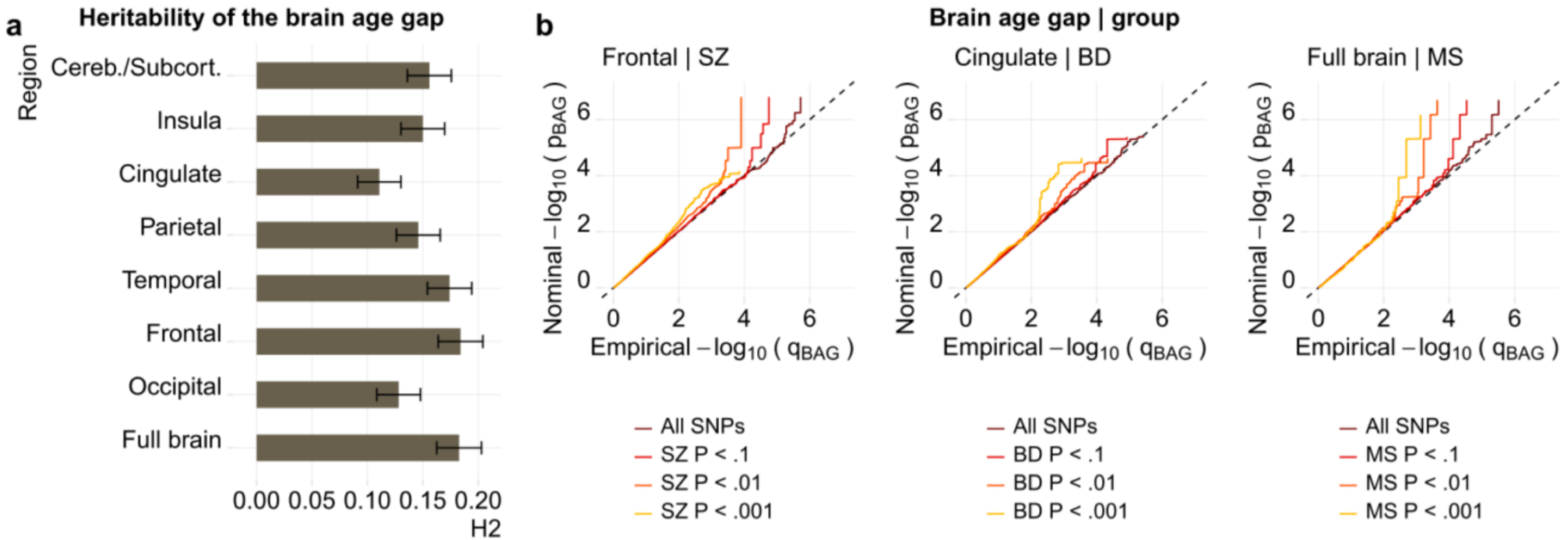
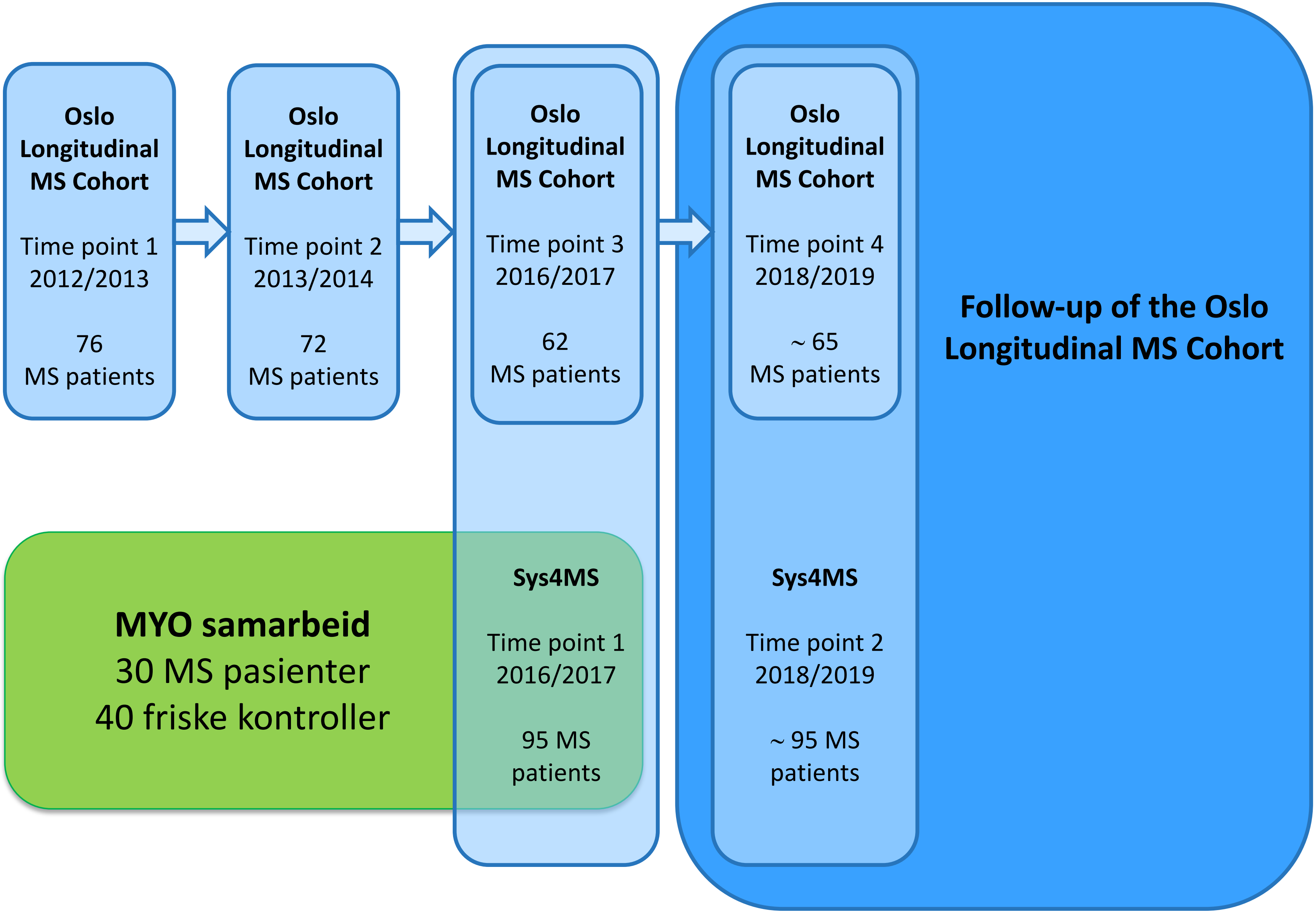


Fig. 5: **The brain age gaps are heritable and the genetic underpinnings overlap with those observed for several disorders.**

Brain age prediction – conclusions

- Several common brain disorders are associated with accentuated aging of the brain
- Distinct neuroanatomical distribution revealed in several disorders
- Functional relevance of brain age
- Brain age is heritable
- Overlapping genes implicated in the genetic underpinnings of brain age and common brain disorders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MYO samarbeid
30 MS pasienter
40 friske kontroller
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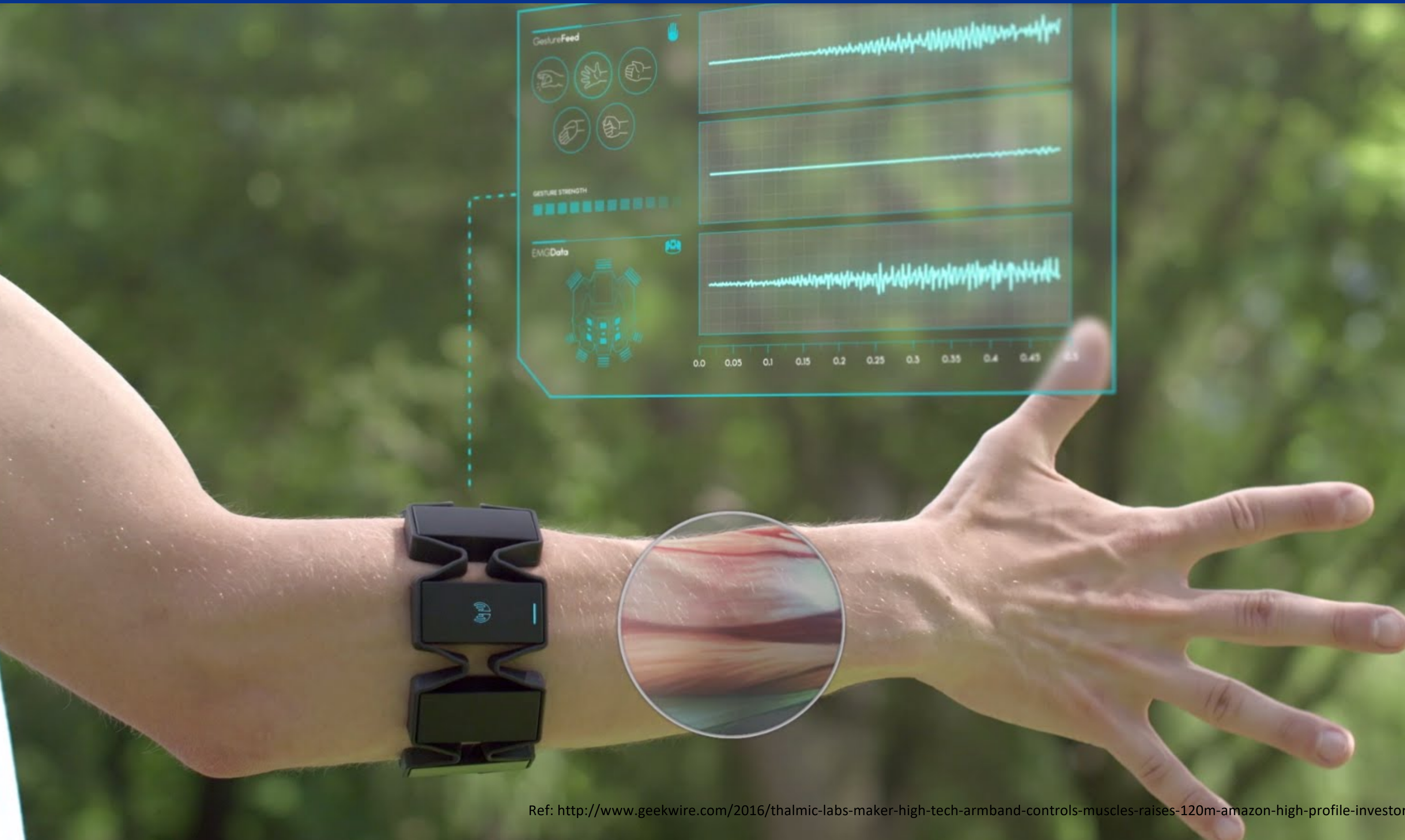
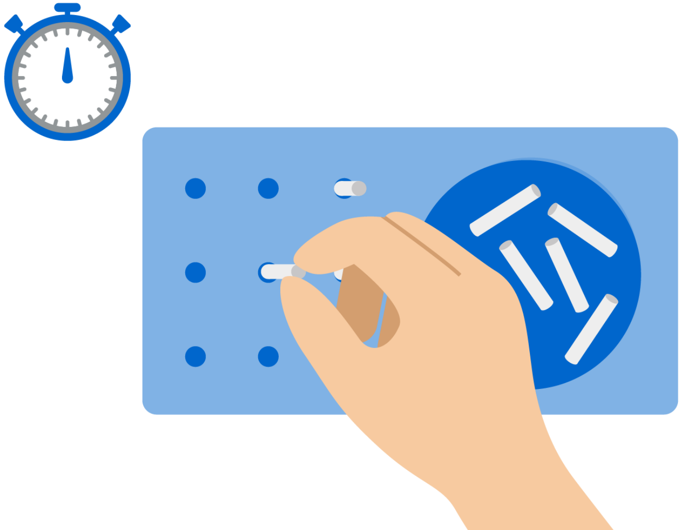
MYO (wearable electromyography device)



Ref: http://www.geekwire.com/2016/thalmic-labs-maker-high-tech-armband-controls-muscles-raises-120m-amazon-high-profile-investor

In collaboration with Uni. Nantes

- Professor Pierre-Antoine Gourraud (UCSF and Nantes)
- Novel multi-sensor device – MYO (www.myo.com)
- Pilot study to explore the possibilities of MYO acquisition in a clinical setting:



Master thesis: Ingerid M. Tutturen

- Title: “Use of wearable biosensor in clinical examinations of patients with multiple sclerosis”
  - Main supervisor: Professor Hanne F. Harbo

  - Co-supervisor: M.D. Einar August Høgestøl

- Defended 26/6-18

Aims of the study

- To ascertain whether the MYO device could differentiate between MS patients and healthy controls

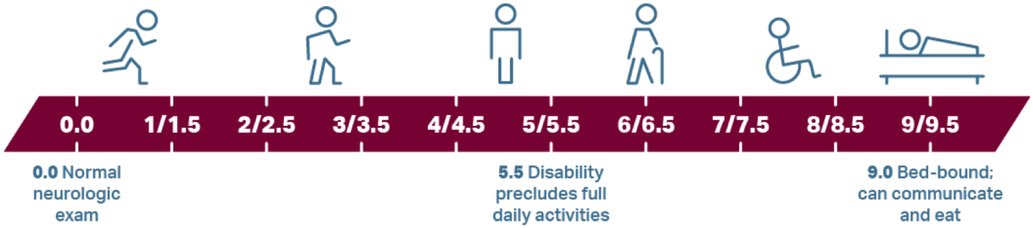
- Would the MYO results be superior in terms of accuracy to standard neurological examination in differentiation between MS patients and healthy controls

Test battery

- Nine Hole Peg Test (NHPT)
- Finger Tap
- Finger To Nose Test (FTNT)
- Foot Tap
- Heel To Knee Test (HTKT)
- Romberg's Test
- Timed 25-Feet Walk Test (T25FWT)

Summary MYO pilot project - Oslo

- 30 MS patients
  - All relapsing-remitting MS
  - Diagnosed between 2005 and 2015
  - 70 % female
  - EDSS mean 2.1 ±1.1
  - Treatment: None 20 %, first line 40 %, second/third line 40 %
- 40 healthy controls
  - Age and gender matched
  - Friends, family and colleagues (the usual)



Conclusions

- In this study we found that MYO was better at differentiating between MS patients and healthy controls than a standard neurological examination for the three tests Finger Tap, FTNT and T25FWT
- MYO "Timed 25-Feet Walk Test" was superior to the other tests with respect to area under ROC (0.92)
- Both sensitivity and specificity increased by combining tests
- A longitudinal study is necessary to assess whether MYO also could be more sensitive than a standard neurological assessment of disease progression

MS Forskningsgruppen – MR

- Gruppeleder: Professor Hanne F. Harbo
  - Mona K. Beyer – Nevroradiolog
  - Dan Rinker – Post. Doc, MSc
  - Gro Owren Nygaard – Nevrolog
    - ”Cognition, disease activity and MRI changes in early MS”
  - Piotr Sowa – Nevroradiolog
    - ”MRI biomarkers in multiple sclerosis. Perfusion weighted imaging and restriction spectrum imaging”
  - Einar August Høgestøl – MD, Ph.D. student
    - ”MRI and other biomarkers in early MS”
  - Synne Brune – MD, Ph.D. student

Takk for oppmerksomheten!

- Og takk for deres deltakelse og bidrag i vår forskning!

Facebook: «Multippel Sklerose Forskningsgruppen Oslo»

fMRI - Introduksjonsvideoer

- https://www.youtube.com/watch?v=Rb_mdzgw-Jc
- https://www.youtube.com/watch?v=nvB9hAarzw4

- Eksempel: https://youtu.be/l7iWbfvOycs