



NORMENT
Norwegian Centre for
Mental Disorders Research



Hvordan kan moderne hjerneforskning bidra til økt kunnskap om psykiske lidelser og utvikling av ny behandling?

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A decade for psychiatric disorders

There are many ways in which the understanding and treatment of conditions such as schizophrenia are ripe for a revolution.

A media circus surrounded President Bill Clinton's visit to a New York medical centre in 2004 for a quadruple heart bypass. Yet barely a whisper was heard about other high-profile individuals' visits there for the treatment of psychiatric disorders.

In Britain, the public donates £500 million (US\$800 million) each year to charities for cancer research. For mental-health research, the figure is a few million, and most of that is for work on neurodegenerative diseases such as Alzheimer's, rather than for earlier-onset conditions that can undermine people's entire lives, such as depressive disorders.

It is time for such disparities to be addressed in a more coherent and aggressive way than in the past. The stigma of psychiatric disorders is misplaced, their burdens on society are significantly greater than more publicized diseases in developed and developing nations alike,

characterized, they could lead to a number of alternative conditions. Here, above all, is where progress is needed in the form of reliable biomarkers to identify those at risk and to allow biomedical or cognitive interventions to prevent or mitigate the development of the disorders. Early intervention would lead to better outcomes.

A deeper understanding of the underlying biology is essential to improve diagnoses and therapies. New techniques — genome-wide association studies, imaging and the optical manipulation of neural circuits — are ushering in an era in which the neural circuitry underlying cognitive dysfunctions, for example, will be delineated. Tantalizingly, work in genetics is indi-

“Early detection and a clearer understanding of environmental factors may allow prevention of psychiatric disorders.”



Research topics



Genetics

Identify rare genetic variants or expression variation to reveal "missing heritability".



Brain Imaging

Determine new brain imaging phenotypes linking genes and core clinical phenotypes.



Antipsychotic Medication

Define new targets to optimize the ratio of beneficial vs. adverse effects of antipsychotics.



Outcome Predictors

Using genetic and environmental factors to estimate illness course and outcome.



NORMENT is a Centre of Excellence (CoE) funded by the Research Council of Norway.

Our main goal is to find answers to why some people develop severe mental illness.

[→ Read more about NORMENT](#)

News



[Beathe Haatveit will defend her PhD thesis on August 22, 2017](#)

Aug. 8, 2017 10:41 AM

Title: *Executive functioning in schizophrenia spectrum disorders: Methods of measurement and longitudinal course.*



[NORMENT researchers contribute in new book on cannabis](#)

July 6, 2017 1:18 PM



NORMENT in social media



The Research Council of Norway

Psykiske lidelser - hjernen

Kliniske syndrom

Deskriptive:

- *Atferd*

- *Symptomer*

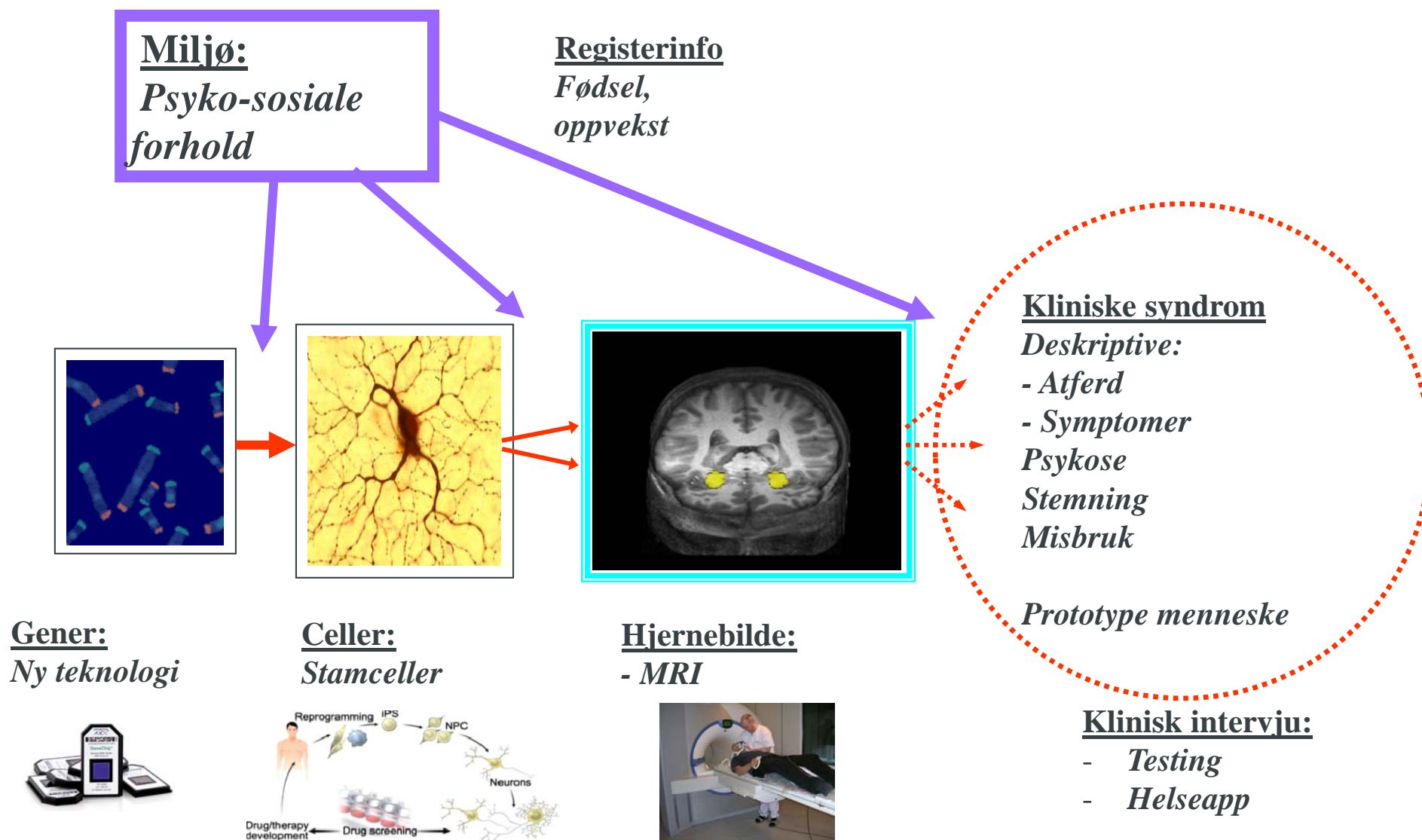
Psykose

Stemning

Misbruk

Prototype menneske

Psykiske lidelser - hjernen



Stor sykdomsbyrde (WHO 2010)

- Globalt
 - Mentale- og ruslidelser ledende årsak til uførhet
 - 37% økning 1990-2010
- Norge
 - viktigste årsak uføretrygd
- Tidlig innsykning, kronisk lidelser
- Livstidsprevalens
 - Autisme 1%
 - Schizofreni 1%
 - Bipolar lidelse 2%

THE LANCET **Global Health**



PSYCHIATRY

Beyond *DSM*: Seeking a Brain-Based Classification of Mental Illness

If a fright or despondency lasts for a long time, it is a melancholic affection.
—Hippocrates, *Aphorisms*, 400 B.C.E.

Since the time of the ancient Greeks, mental disorders have been classified according to their outward signs. But even in Hippocrates' day, attention was paid to the underlying causes. The word "melancholy" derives from the Greek word for black bile, an excess of which was thought to cause prolonged sadness.

Modern research in neuroscience and genetics has provided a more sophisticated understanding of mental illness, and harnessing this knowledge to improve the diagnosis of psychiatric disorders was a major impetus for undertaking a revision of the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* (*Science*, 12 February, p. 770). But even some of those leading the revision say there's still too little known about the biological basis of mental illness, and as a result *DSM* continues to be based on symptoms rather than causes. "We just don't know enough to do a lot better," says psychiatrist Steven Hyman, the provost of Harvard University and a member of the committee in charge of the new edition *DSM-V*

DSM criteria to frame their research questions, study sections used them to evaluate grant applications, journal editors used them to judge papers, and pharmaceutical companies used them to design clinical trials. At the same time, Hyman says, "it was clear that *DSM* was a poor mirror of nature."

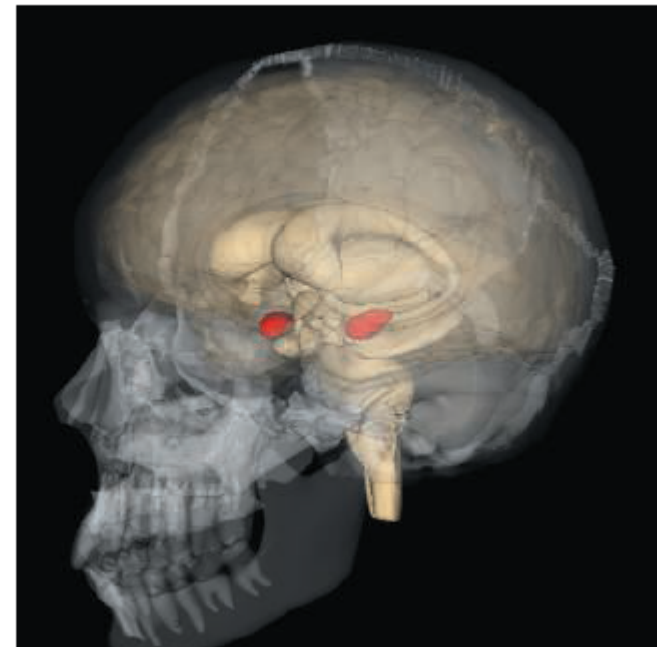
By way of illustration, he notes in a recent review article that the *DSM-IV* diagnosis of major depression requires that a patient have at least five of nine possible symptoms. In this scenario, it's possible for two patients to receive the same diagnosis with only one symptom in common. Their inner turmoil and its biological roots might differ substantially, but they could easily be lumped together in a study on "major depression." "We needed some way to break out of the cognitive box and encourage scientists to do research that disregards the current disease boundaries," Hyman says.

Hyman's successor at NIMH, Thomas Insel, made this a priority for the institute, and RDoC is the product. The draft document, to be posted on the RDoC Web site* next month, describes five

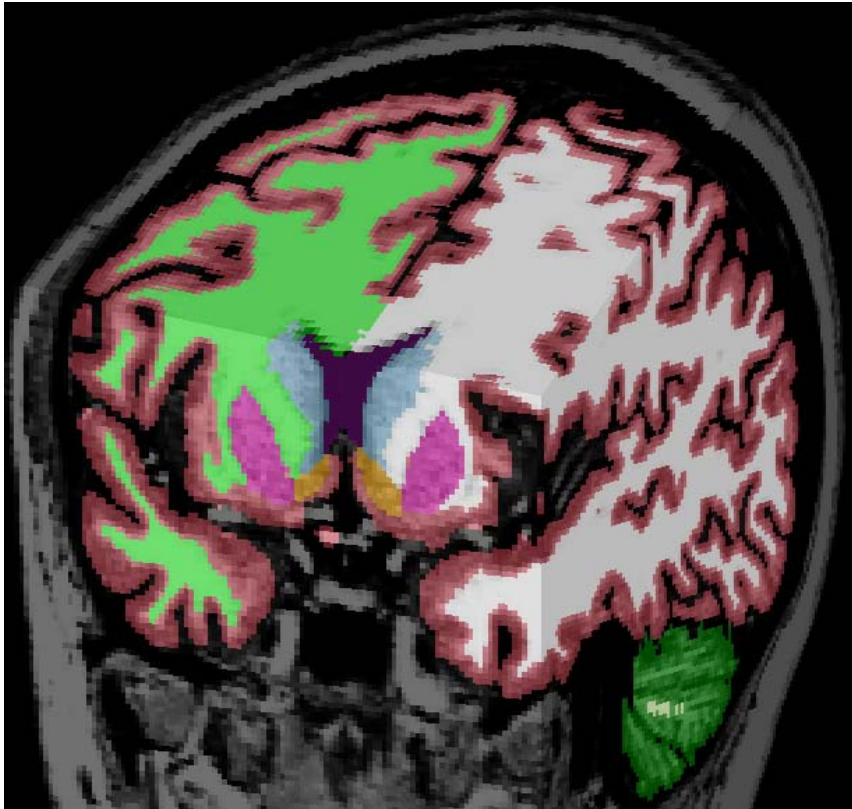
may involve multiple brain systems," he says.

Beginning this summer, workshops will bring together groups of experts to refine the RDoC entries and to identify gaps in the current understanding of the genetic risks, neural dysfunction, and behavioral problems associated with each one. Over the next 2 to 3 years, NIMH will encourage researchers to shift from using *DSM* criteria in their grant proposals to using the RDoC categories.

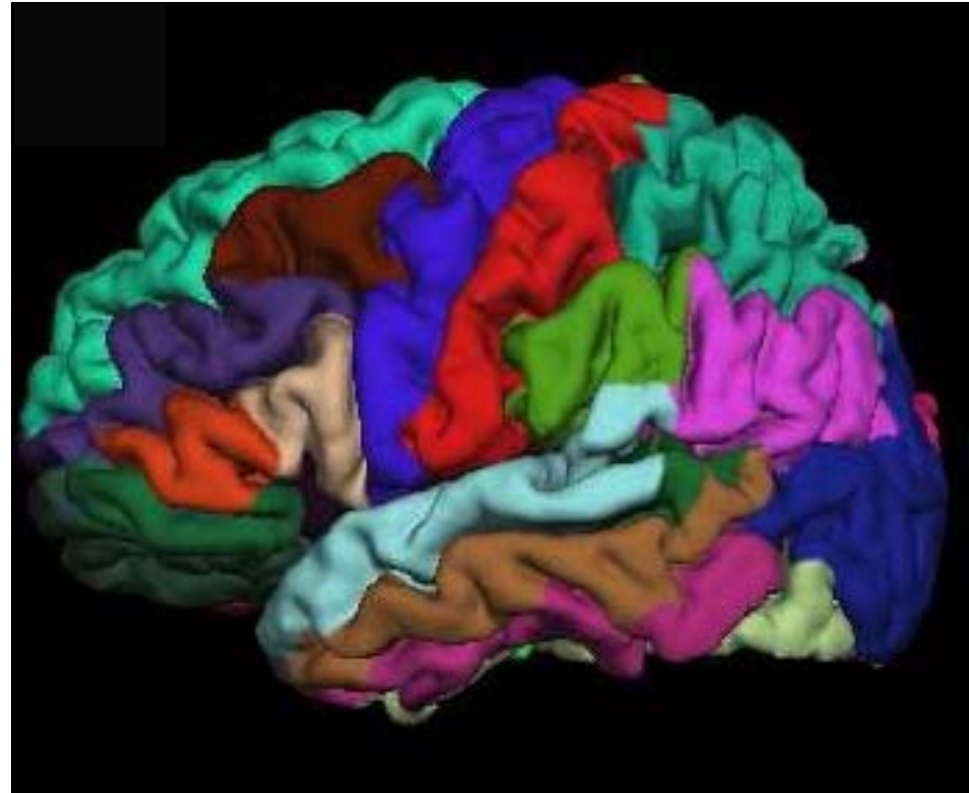
One goal of RDoC is to change the current practice of selecting research subjects based on their *DSM* diagnosis and to encourage studies that use biological indicators instead. A study on anxiety disorders, for example, might examine people who show a heightened amygdala



Hjerneavbildning - MRI

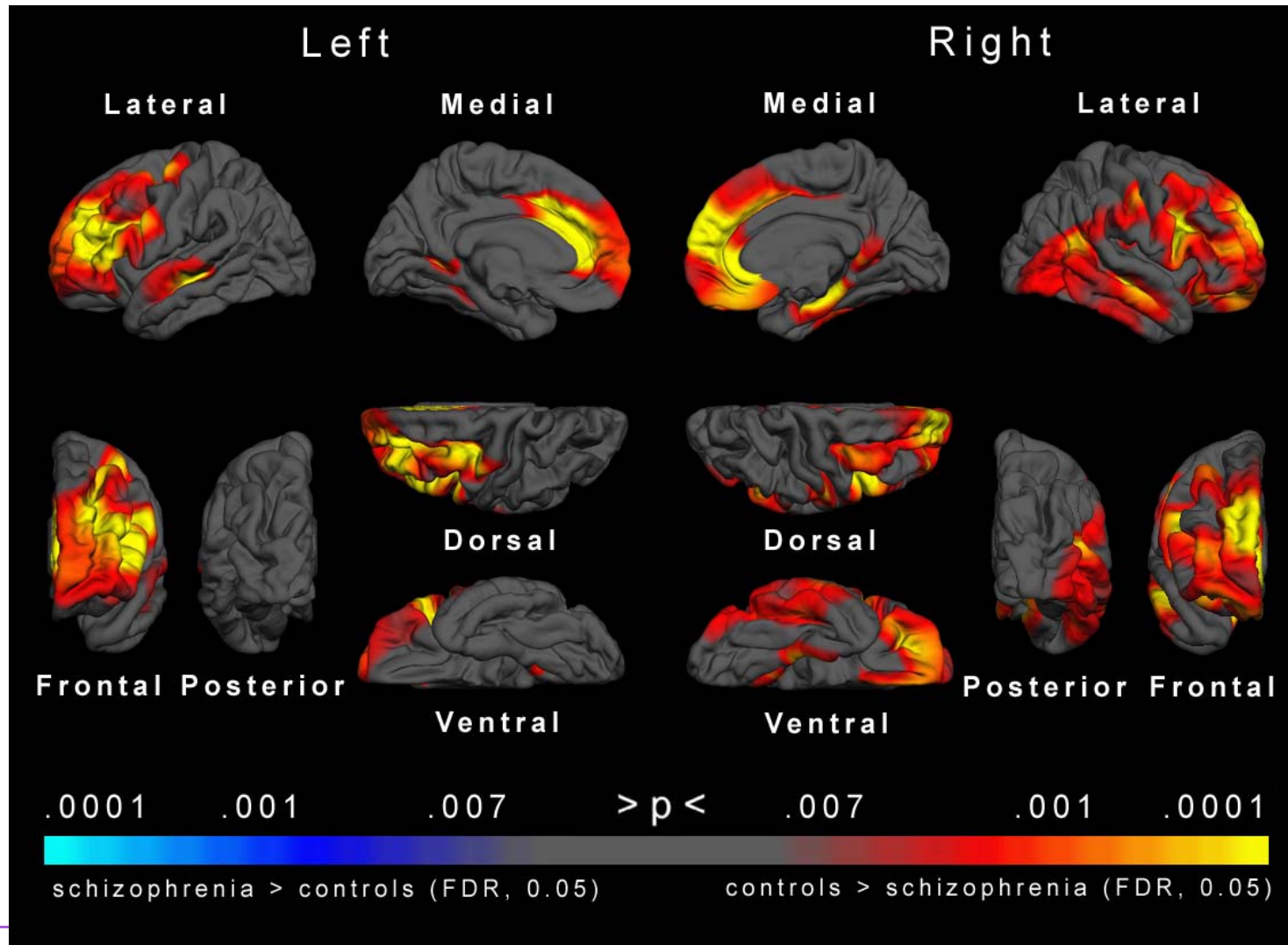


Subcortical Segmentation

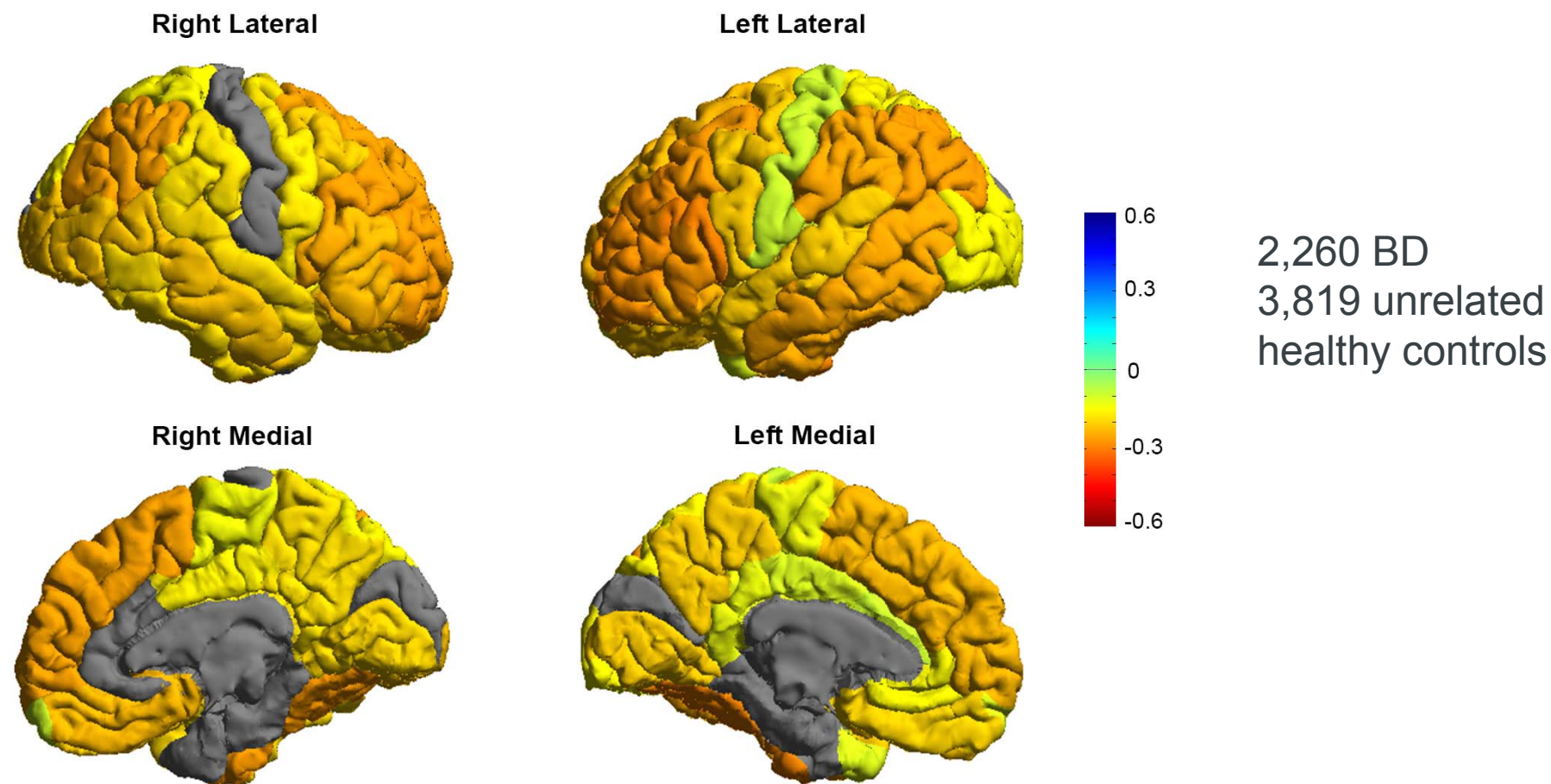


Cortical Parcellation

Schizofreni

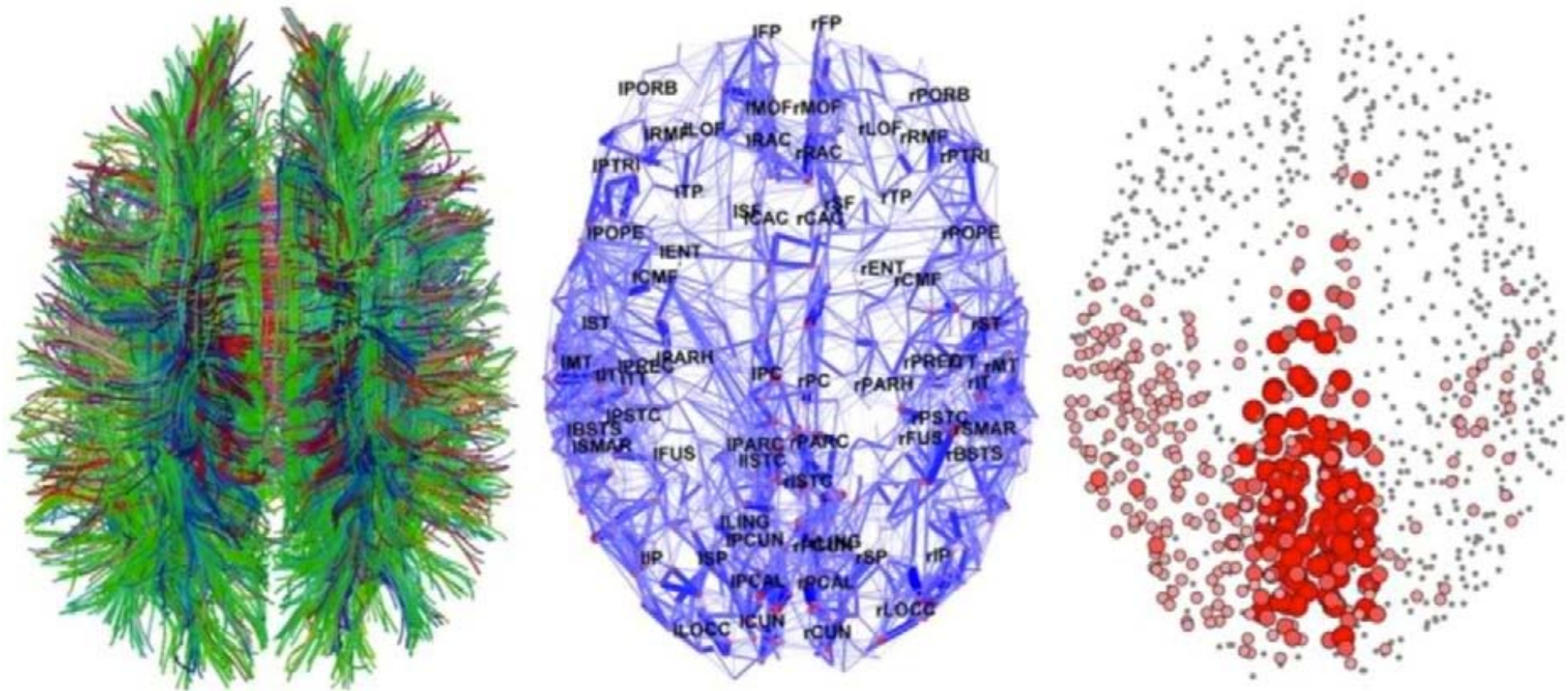


Bipolar lidelse

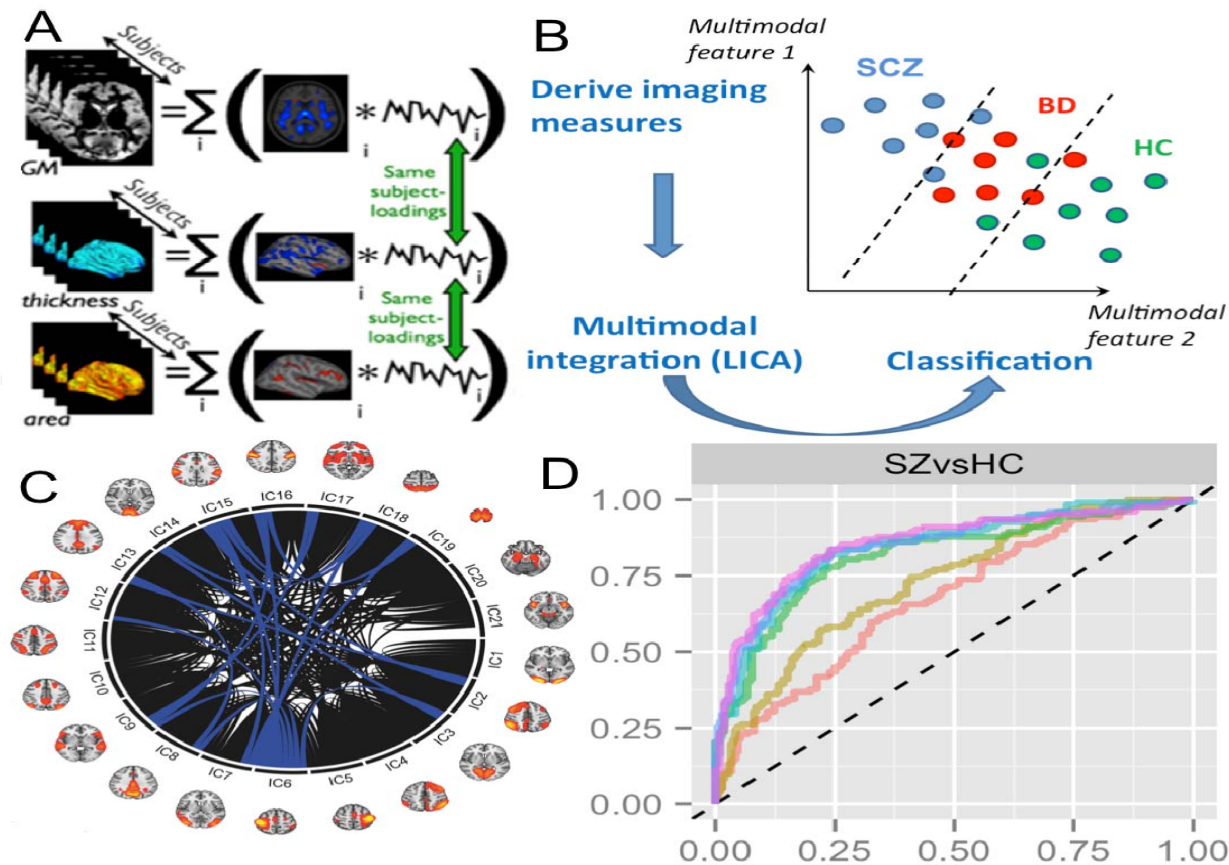


Konnektivitet

Struktur og funksjon – ny tilnærming

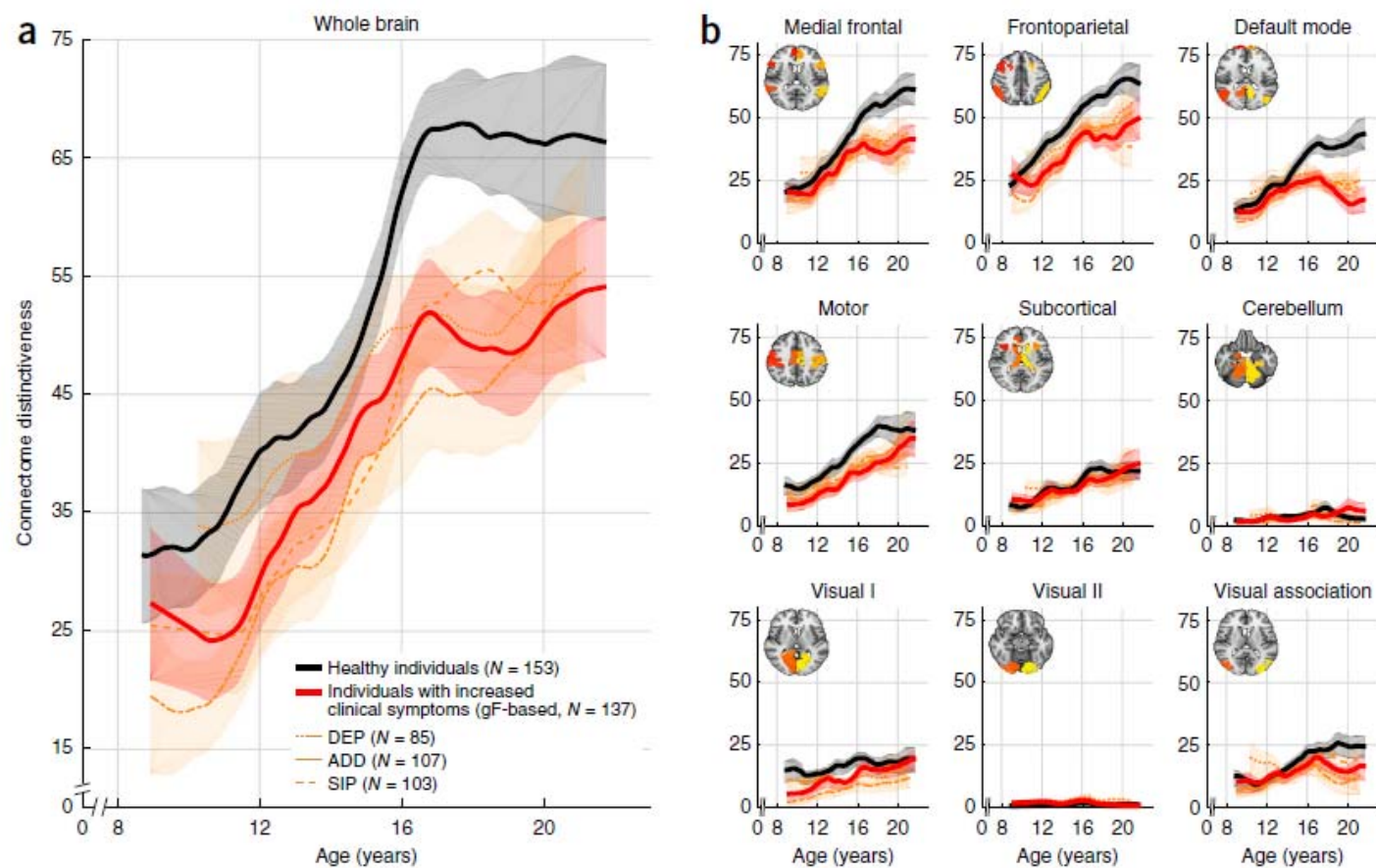


En multi-modal hjernebilde strategi



(A) Data-driven decomposition of multimodal MRI features, (B) machine learning based prediction and classification using multimodal brain MRI, (C) advanced network modeling to delineate brain connectivity features, (D) ROC curve representing for prediction of SCZ case-control (SZvsHC) status using combinations of brain and clinical information as predictors.

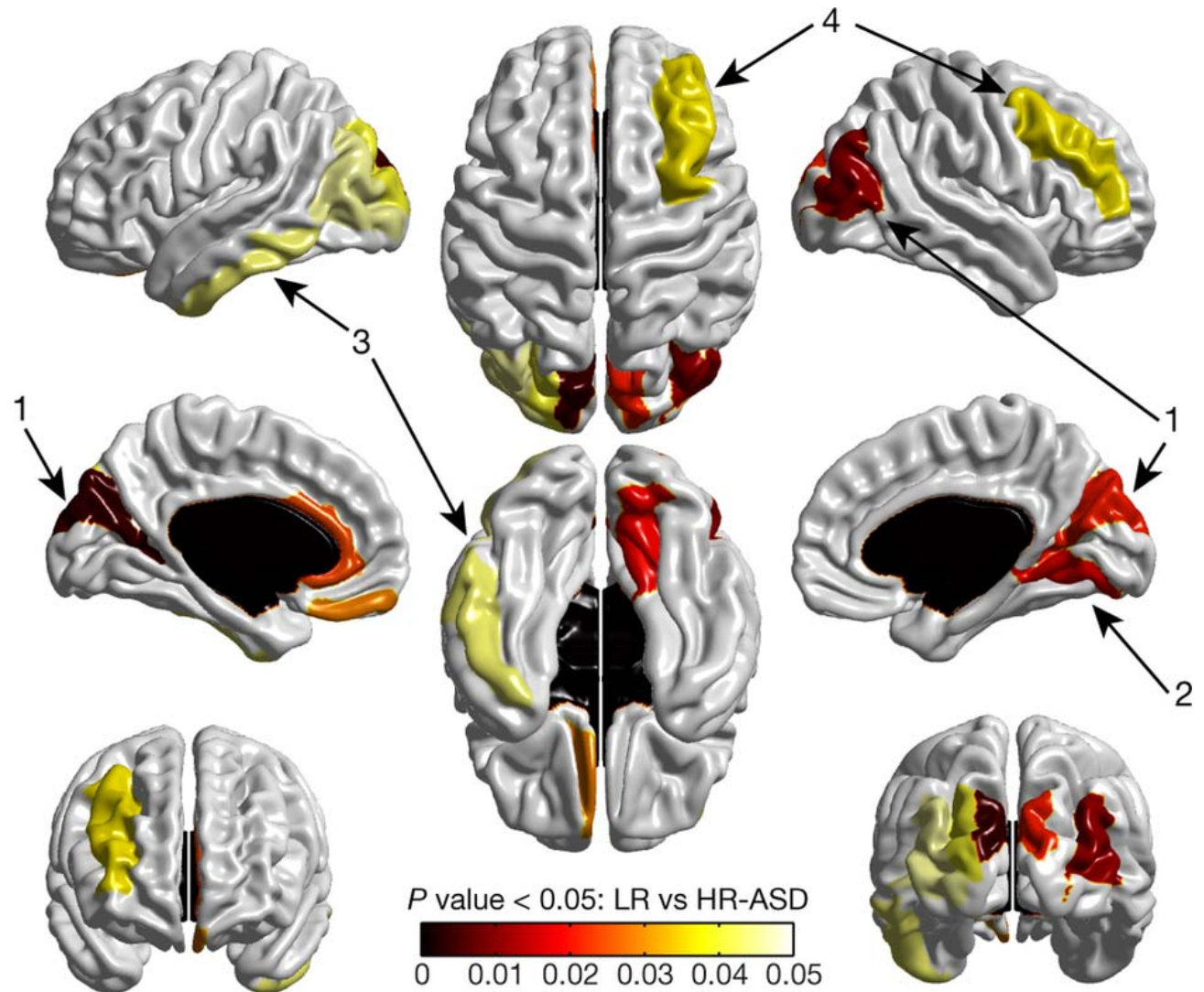
Hjerneavbildning – forutsi tegn på mental lidelse



Kaufmann et al., Nat Neurosci 2017

Autisme - utvidet overflateareal 6 - 12 måneder

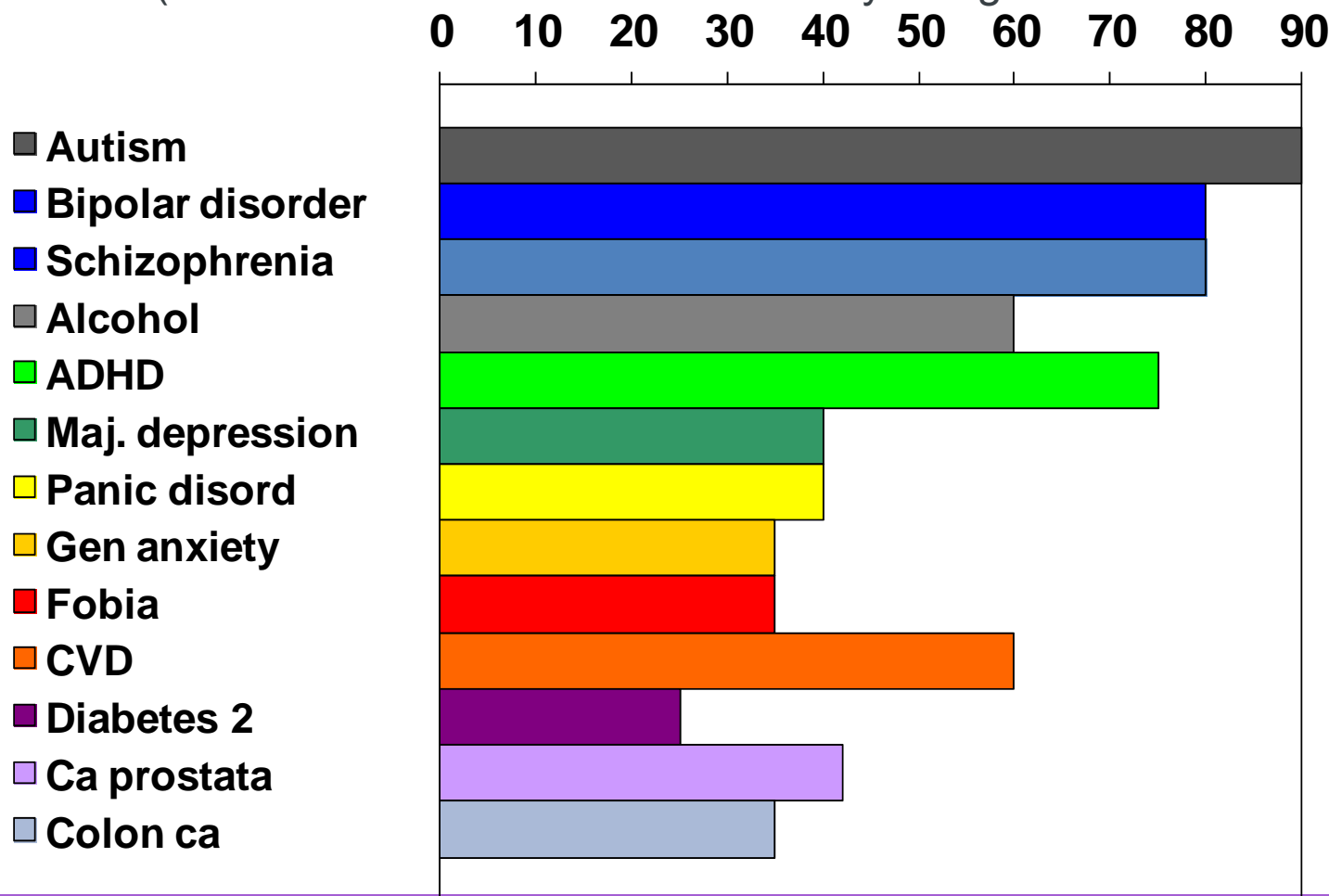
hyperexpansion of the cortical surface area between 6 and 12 months of age precedes brain volume overgrowth observed between 12 and 24 months



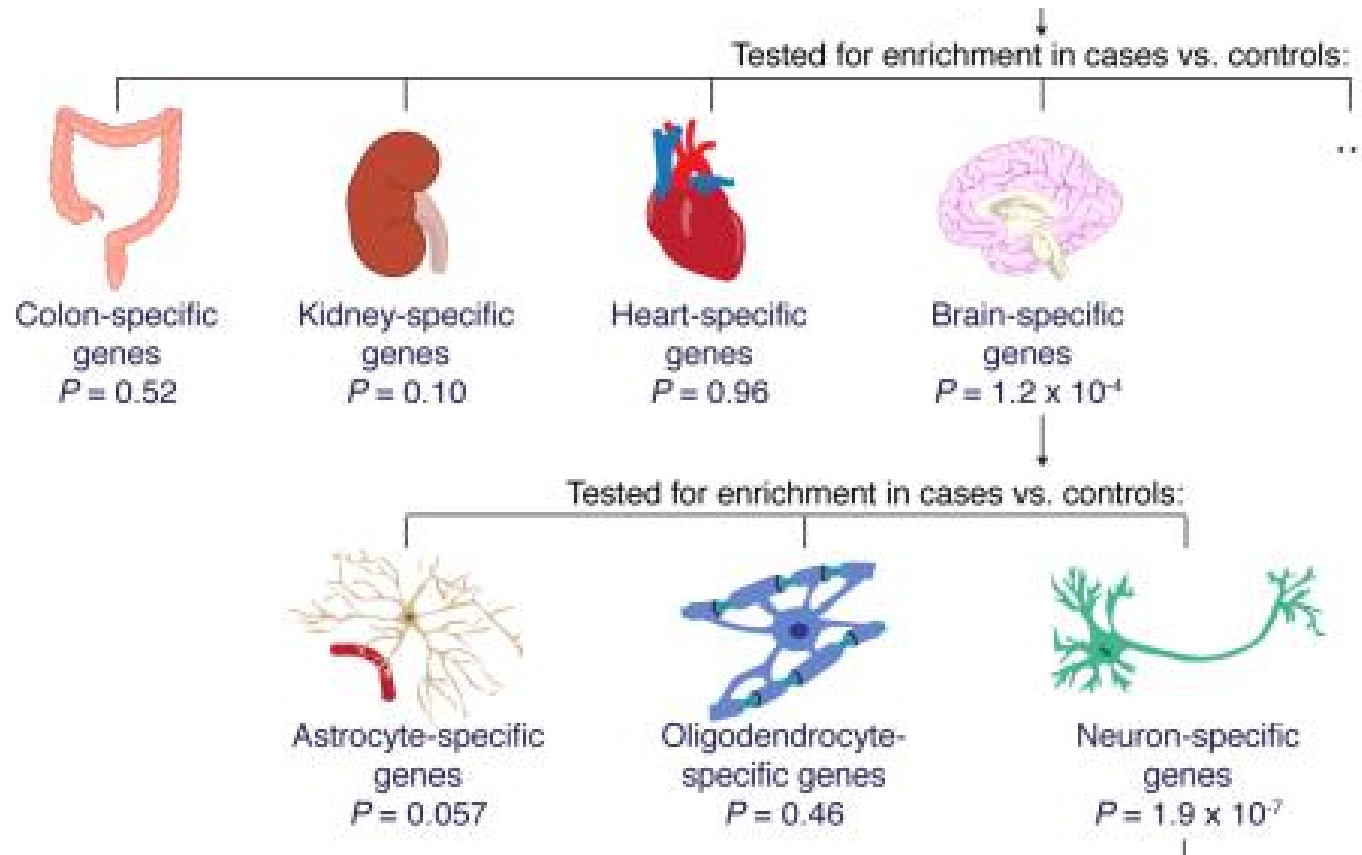
Hazlett Nature 2017

Psykiatri og arv

Heritabilitet (estimert andel av sårbarhet som skyldes genetiske faktorer)

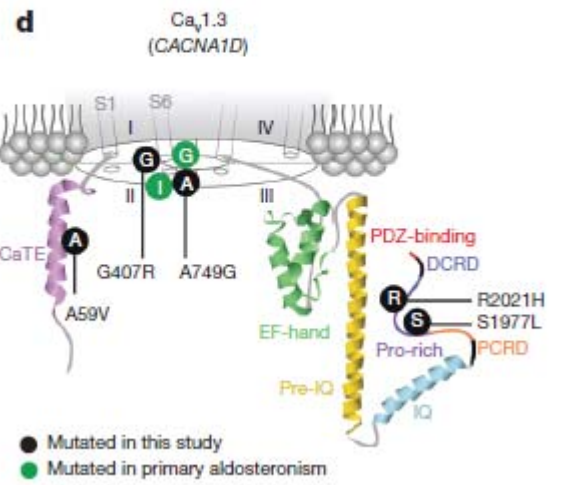
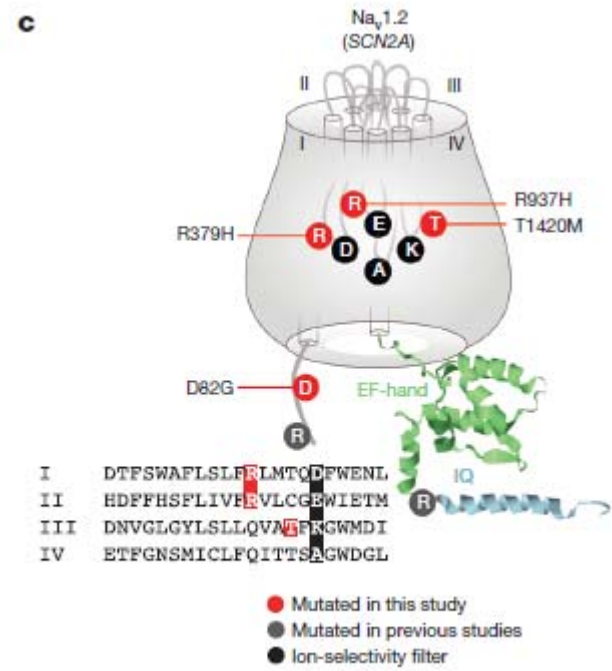
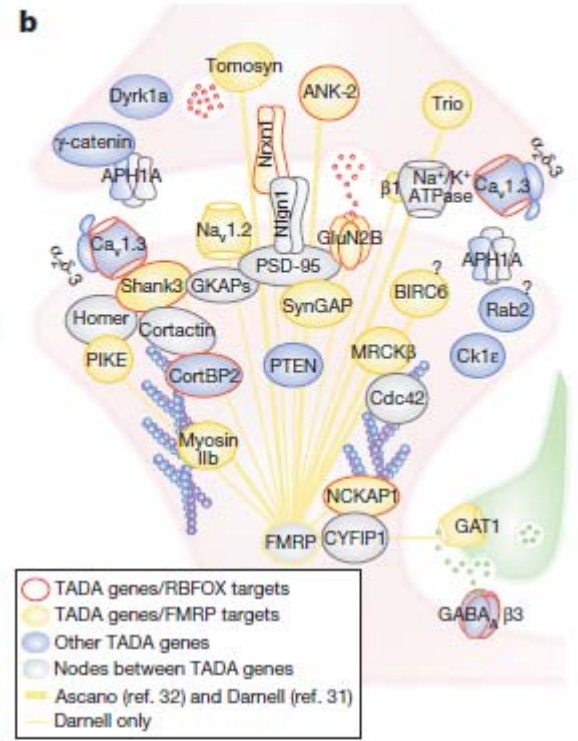
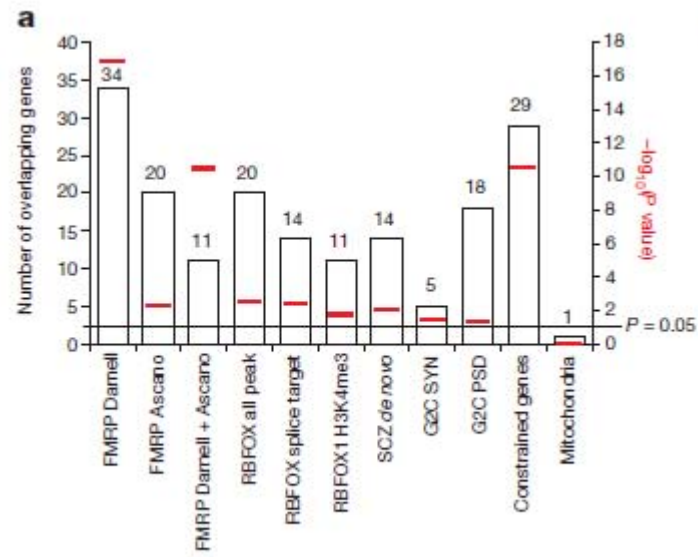


Schizofrenigener - hjerne



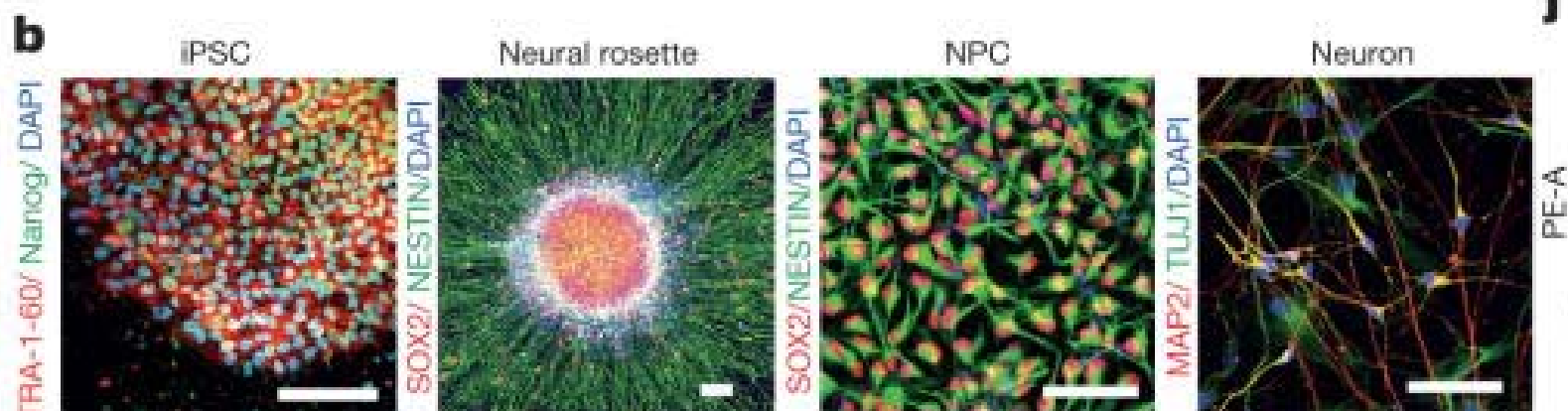
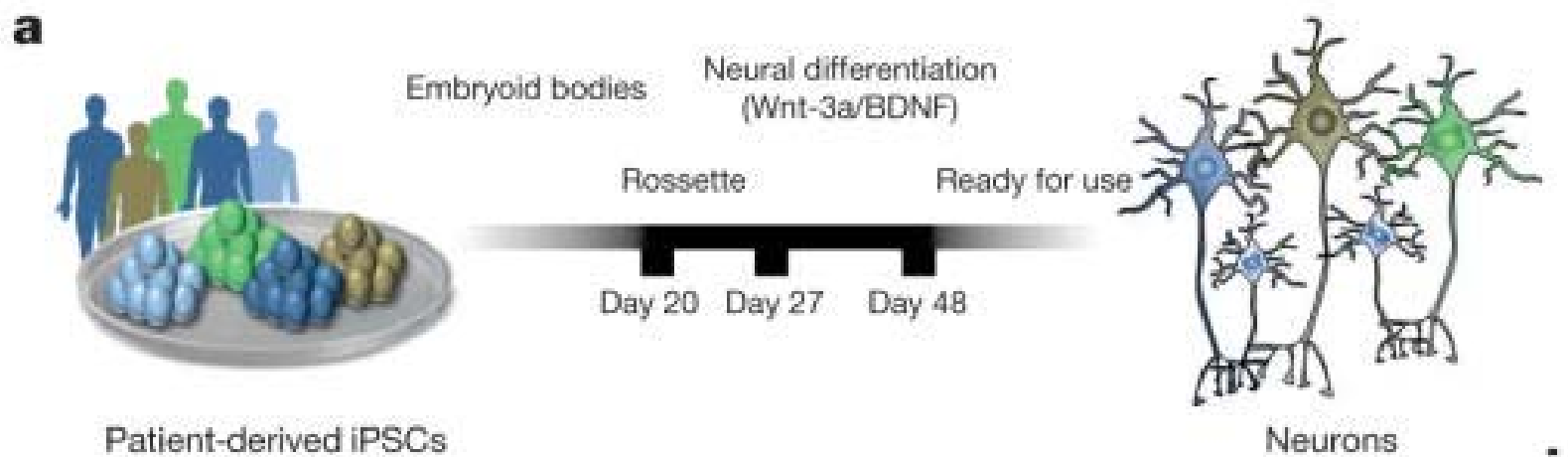
Autismmegener hjerne

- a. Ekspresjon
- b. Synapse
- c. Ionekanaler
- d. calcium



De Rubeis Nature 2014

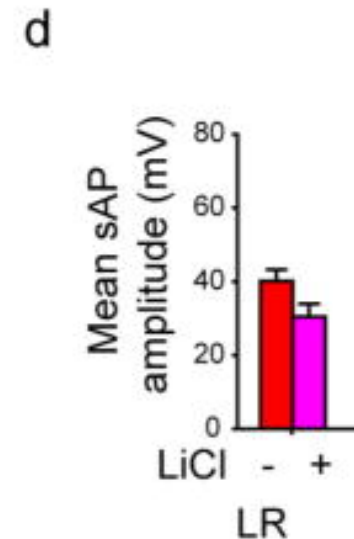
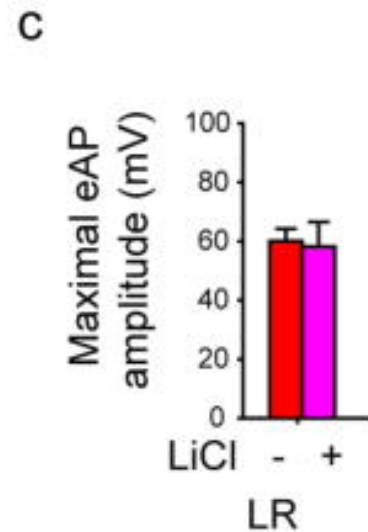
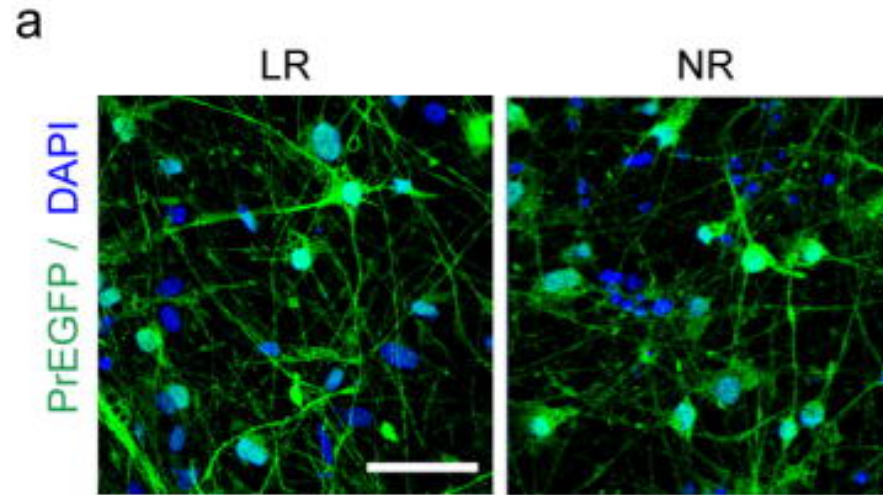
Bipolar lidelse nevronale stamceller



Mertens Nature 2015

Bipolar lidelser - litium- nerveceller

Litium påvirker
nerveceller



Mertens Nature 2015

Konklusjon

Autisme, schizofreni, bipolar lidelse

- 1) Stor global sykdomsbyrde
- 2) Klare funn hjerneavbildning
- 3) Risk gener koblet til hjernemekanismer

Nye metoder avdekker sykdomsmekanismer

Takk til

- Deltakerne i studiene
- NORMENT team
- UCSD; ENIGMA, PGC
- deCODE
- Regionale Helseforetak
- NFR
- KG Jebsen
- NORMENT Brukerråd

