

NORMENT Norwegian Centre for Mental Disorders Research

# NORMENT Annual Report 2021













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# Leader's Comments

It is also very important that we continued our success in 2021 was a year with great achievements at obtaining external grants, which will help financing our NORMENT on many levels, despite the challenges activities for years after the official Centre of Excellence caused by the Covid-19 pandemic. We continued grant ends. We received funding for the large EU H2020 with our well-organized digital work life, with project REALMENT that we are coordinating, as well as home office and Zoom meetings, similar to the a large Fellesløft project from the Research Council of situation for our collaborators across the world. Norway. We also received funding for scientific renewal projects to scientists Tobias Kaufmann, Christian Tamnes and Dan Quintana, and young talent grants to Tiril Gurholt, Fortunately, it was possible to continue the clinical Torbjørn Elvsåshagen and Dan Quintana. This funding will secure a high level of activity in the coming years.

Fortunately, it was possible to continue the clinical assessments and perform lab work during the year, although with strict infection control routines. We were also lucky to have some periods back in the offices and labs with physical contact before the new wave of Covid-19 hit at the end of the year. Several teams were able to have physical group meetings, and a few key events were not digital, such as the Early Career Researchers Meeting. Some of the PhD defences and doctoral dinners were also done in the good old way.

I think an important reason for our ability to prevent the negative effects of the pandemic is the contribution from each of the NORMENT staff members. By maintaining a compassionate work atmosphere, with personal support and friendships, and everyone contributing to the team spirit, we help to make each other better.

On most deliverables and output measures, 2021 was a large success, with more and better scientific publications than any preceding year. Several of our publications this year had a high impact, also illustrated by the publication awards to Centre researchers from both the Haukeland University Hospital and the Oslo University Hospital. Scientists at the Centre also received the Innovation Prize from Oslo University Hospital. This illustrates how longterm focus on excellence, with frontline infrastructure including data collection and methodology development, as well as synergy projects across disciplines and talented coworkers, is a very good solution for scientific discoveries.

Further examples of the scientific quality come from the awards in 2021. I was very lucky to receive the Norwegian Health Association's Dementia Research Award, which was based on many years of teamwork. In addition, one junior researcher received Excellence and Poster Awards at the large ECNP meeting.



The NORMENT dissemination activities also continued the successful application of online platforms in 2021. Our social media activity on Twitter and Facebook has increased, and we organized a webinar series together with the Norwegian Bipolar Association and hosted two webinars about environmental risk factors in schizophrenia and how our work at NORMENT can constribute to better treatments. Further, our newsletter reached more stakeholders, including health care workers and user groups.

I would again thank all NORMENT staff for their hard work in 2021, and I am impressed with your accomplishments. It is a pleasure and privilege to be the Director of the NORMENT centre with such outstanding colleagues, and I am convinced we will be able work with exciting project well beyond the time period of the Centre.

alunder

Ole A. Andreassen Centre Director



# Scientific Highlights 2021

Our research resulted in many exciting and important findings in 2021, of which several were published in prestigious scientific journals with NORMENT researchers as lead authors.

Jordi Requena Osete and colleagues used advanced stem cell technology to study effects of Lithium treatment and found that Lithium increases mitochondrial respiration in iPSC-derived neural precursor cells from Lithium responders (Molecular Psychiatry).

Weigiu Cheng and colleagues determined the overlapping genetic architecture between brain structure variation and schizophrenia risk genes, based on data from almost 140 000 individuals (JAMA Psychiatry). A subset of the genetic variants was associated with immunity, suggesting that immune functions may be associated with cortical development and the pathology of schizophrenia.

Ole A. Andreassen headed a large genome-wide association study of more than 40,000 people with bipolar disorder in the Psychiatric Genetics Consortium. The group of researchers – many of them from NORMENT – discovered genetic variants associated with bipolar disorders type I and II, implicating abnormal neurotransmission, and highlighted differences across sub-groups (Nature Genetics).

Torbjørn Elvsåshagen and co-authors studied the thalamus structure in the brain and identified the first genetic variants linked to thalamic nuclei volumes. They also reported an overlap between genetic architectures of the thalamic nuclei and ten neurological and psychiatric disorders (Nature Communications).

Dennis van der Meer and co-authors identified novel polygenic variants determining the folding of the human brain applying advanced statistics and large number of brain imaging data (Science Advances).

We also identified important characteristics of psychotic disorders that may be useful for clinical outcome and prediction of illness course. These include adverse life events (Ottesen et al., Psychological Medicine), immune factors (Engh et al., Schizophrenia Bulletin), cognitive functions (Flaaten et al., Psychological Medicine), sleep (O'Connell, Biological Psychiatry), brain plasticity (Valstad et al., Schizophrenia Bulletin), substance use (Lagerberg et al., Frontiers Psychiatry), and antipsychotic medication (Akkouh et al., Schizophrenia Bulletin; Hoekstra et al., NPJ Schizophrenia).

Ida Sønderby was lead author on two ENIGMA consortium papers related to copy number variants (CNV), reporting that the 1q21.1 distal CNVs are associated with cerebral and cognitive alterations in humans (Translational Psychiatry), and reviewed the effects of copy number variations on brain structure and risk for psychiatric illness (Human Brain Mapping).

NORMENT researchers were also involved in a number of other international studies, including clinical high risk for psychosis (ENIGMA Working Group et al., JAMA Psychiatry), schizophrenia (Blokland et al., Biological Psychiatry), and bipolar disorder (Mishra et al., Molecular Psychiatry).

For a complete list of NORMENT publications in 2021, see page 82



Osete et al., Molecular Psychiatry, 2021

# Prizes and Awards



### **Dementia Research Prize to Ole A. Andreassen**

Professor Ole A. Andreassen received the Dementia Research Prize from the Norwegian Health Association (Nasjonalforeningen for folkehelsen) on February 2. Andreassen received the prize for his contribution to more knowledge about the genetic causes of dementia and breakthroughs in research that has provided new insight into disease mechanisms. The Dementia Research Prize is awarded to a researcher that has excelled through outstanding research on dementia. The prize consists of a monetary award of NOK 200.000 and a graphic print.

### **Excellence and Posters Awards to Claudia Barth**

Postdoctoral fellow Claudia Barth received both an Excellence Award and a Poster Award from the European College of Neuropsychopharmacology (ECNP) during their annual congress in Lisbon on October 2-5. Barth was awarded the prizes for her work on sex differences related to hormones and brain structures in schizophrenia. The title of the poster abstract was "Sex differences in hippocampal subfield volumes and relationship to testosterone measures in schizophrenia and bipolar disorders".



### Innovation Award

Senior researcher Trine Vik Lagerberg and Database manager Thomas Doug Bjella were awarded Oslo University Hospital's Innovation Award <u>2021</u> on September 16, for developing the app"MinDag". The app is used by patients with mental illness to measure symptoms over time. The goal is to aquire more knowledge about why symptoms often vary in time, and how different symptoms and lifestyle factors are connected.



### Award for Young Researchers

Senior researcher Daniel Quintana received the Award for Young <u>Researchers</u> from the Royal Norwegian Society of Sciences and Letters in February 2021, for his impressive research on the hormone oxytocin. His work has improved our understanding of the oxytocin system and its function in human behavior and physiology.





### Paper Awards

Researchers Oleksandr Frei and Dennis van der Meer received the Prize for Outstanding Paper of the fall 2020 from Oslo University Hospital, for the paper titled: "Understanding the genetic determinants of the brain with MOSTest". The paper was published in Nature Communications and involved contributions from several people from NORMENT.

Researcher Jordi Requena Osete received the Prize for Outstanding Paper of the spring 2021 from Oslo University Hospital, for the paper titled: "Lithium increases mitochondrial respiration in iPSC-derived neural precursor cells from Lithium responders". The paper was published in Molecular Psychiatry and involved contributions from several NORMENT researchers.

Professor Erik Johnsen and Associate professor Rune Kroken received the Prize for Best Publication from the Research Depart-

ment, Division of psychiatry at Haukeland University Hospital, for the paper titled: "Amisulpride, aripiprazole, and olanzapine in patients with schizophrenia-spectrum disorders (BeSt InTro): a pragmatic, rater-blind, semi-randomised trial". The paper was published in 2020 in Lancet Psychiatry.

### **Other Awards**

PhD candidate Petter Jakobsen and Professor Ketil Joachim Ødegaard received the Best Poster Award on October 7, on "Forskningens dag" at the Division of Psychiatry, Haukeland University Hospital, for the poster titled "Motor Activity Analyses Distinguish Manic and Euthymic Mood States in Bipolar Disorder".

Researcher Dennis van der Meer received the Early Career Investigator Award, from the International Society of Psychiatric Genetics on August 3, 2021.











# About the Centre



The Norwegian Centre for Mental Disorders Research (NORMENT) is a research centre focusing on understanding the causes and mechanisms underlying severe mental illness. The goal is to better understand why some people develop psychotic symptoms (perceptual disturbances, hallucinations, delusions) and mood disturbances (depression, manic episodes). Ultimately, the hope is that by understanding more about how and why mental illness develops, we can contribute to increase the quality of prevention and treatment.

NORMENT was established as a Norwegian Centre of Excellence (CoE) in July 2013, with a 10-year CoE grant from the Research Council of Norway, as well as being funded by several other institutions.

The Centre is based on collaboration between the University of Oslo (host institution), the University of Bergen, Oslo University Hospital, and Haukeland University Hospital. The research on severe mental illness has a long history both in Oslo and Bergen and is based on many years of collaboration across the current NORMENT sites. In Oslo, the main research project preceding the Centre of Excellence was a network project called the "Thematically Organized Psychosis" (TOP) study, a thematic effort focused on psychotic disorders. The term "TOP" is still used about the main study protocol at the Centre, in which a large number of people have participated over the years.

In 2021, more than 200 people with various professional backgrounds such as Medicine, Psychology, Biology, Neuroscience, Mathematics, Statistics, Engineering, and Administration were involved at NORMENT, either as employees or affiliated to the Centre.

The research at NORMENT is being carried out in 15 research groups. The main research topics include Genetics (genetic susceptibility and heritability), Brain Imaging (brain structure and function), Outcome Prediction (estimation of illness course and outcome), and Clinical Intervention (test out new treatment). Most, if not all, research activities depend on a tight collaboration and efficient use of resources across different research groups and scientific disciplines. An important aim is to create a synergy effect where ideas, knowledge, and competence at the Centre as a whole become greater than its individual components. Using a "vertical synergy" approach, severe mental illnesses are studied across different levels and by combining different methods, to get the most complete picture of mechanisms involved in these complex disorders.

Most of NORMENT's research is made possible thanks to a large growing database where several thousand participants, both people with mental illness and healthy individuals, have generously volunteered to take part in extensive and timeconsuming clinical assessments, neuropsychological tests, and brain imaging. Inclusion of new participants into the studies represents a major activity at the Centre, also thanks to state-of-the-art facilities and an outstanding team of technical



and administrative support personnel. NORMENT also has a focus on user involvement and has an active User Council and an employed User Representative that give valuable perspectives and input.

The last years, NORMENT has contributed to a series of important discoveries which have been published in leading international scientific journals such as Science, Cell, Nature Genetics, JAMA Psychiatry, Molecular Psychiatry, Biological Psychiatry, and Schizophrenia Bulletin. NORMENT has so far:

- gained new knowledge about the immune system and related genes in mental illness
- developed novel and promising statistical tools to study mental disorders
- shown how advanced stem cells methods can be used to develop better medication
- determined that complications before or during birth may affect brain development and play an important role in psychiatric illness
- identified gene variants related to specific regions and properties of the brain
- detected how brain connections evolve during development and are associated with mental health
- identified factors affecting illness progress and outcome, such as childhood trauma and its interaction with genes
- shown that cannabis use reduces the age of onset in bipolar disorder

In the years to come, the research at NORMENT will continue to follow up on new disease mechanisms, based on the discoveries of more risk genes for schizophrenia and bipolar disorder. In this regard, a promising new area of research is to use human stem cells developed from skin cells to investigate molecular and cellular mechanisms in mental illness. We will integrate this experimental work with clinical trials and interventions to follow up our discoveries and ensure clinical impact.

We will also integrate our new clinical outcome findings and continue improving our approaches for analysing large amounts of data ("big data") to obtain clinically relevant tools. The Centre will maintain a leading role in the development and implementation of new digital tools, and other eHealth technology. Altogether, we aim to contribute substantially to a better understanding, care and treatment of severe mental disorders.

been involved in discoveries of new gene variants associated with severe mental illness, including large international studies reporting over 100 gene variants related to schizophrenia and 30 risk variants associated with bipolar disorder

# **Vision Statement**

NORMENT's primary objective is to explore and reveal the underlying pathophysiology of psychotic disorders based on recent discoveries of genetic risk factors, develop tools for stratification and outcome prediction, and translate findings into clinical interventions.

The main research topics at the Centre are Genetics, Brain Imaging, Outcome Prediction, and Clinical Intervention, which are reflected in the following subgoals:

- 1. Disclose the complete genetic architecture of psychotic disorders and determine their functional impact
- 2. Identify novel brain imaging phenotypes linking genes and clinical phenotypes in a longitudinal setting
- 3. Use genetic, environmental and clinical factors to predict disease progress and outcome
- 4. Translate pathophysiological discoveries into clinical and pharmacological interventions

We benefit from the homogeneity of the Norwegian population (genetic background, health care system, registries) as the basis for collecting large samples of affected and unaffected people. These individuals are characterized with the same clinical, cognitive, biochemical and imaging protocols to identify new disease mechanisms which are then studied functionally in animal and cell culture models. The aim of this "vertical synergy" approach is to obtain different levels of understanding by bringing together transdisciplinary expertise and methods.



# **Scientific Aims**

# **GENETICS:** Disclose the complete genetic architecture of psychotic disorders and determine their functional impact

Large international genetic studies including NORMENT studies have generated evidence of novel risk genes. Emerging data show overlapping genetic architecture in bipolar disorder and schizophrenia, and involvement of many genes with small effects (polygenic architecture), but also rare variants and copy number variants with larger effects.

Still, the identified genetic variants explain only a small fraction of disease susceptibility. We have developed statistical models supporting that there is a large potential for gene discovery in bipolar disorder and schizophrenia, with relatively small increase in sample size.

### Aims:

- Uncover new rare genetic variants conferring risk of bipolar disorder and schizophrenia
- Leverage new statistical methods to determine the polygenic architecture of bipolar disorder and schizophrenia
- Discover biomarkers and biological mechanisms of psychosis risk genes

### BRAIN IMAGING: Identify novel brain imaging phenotypes linking genes and clinical phenotypes in a longitudinal setting

Non-invasive MRI technology provides a large opportunity to identify genetically determined brain pathology in patients with psychotic disorders. We will use these methods in our integrated study of brain abnormalities related to clinical characteristics, including developmental trajectories.

### Aims:

- Explore brain network dynamics in psychotic disorders and associated phenotypes
- Identify genetic determinants of brain abnormalities
- Determine brain abnormalities underlying key clinical phenotypes and their genetic architecture

### OUTCOME PREDICTION: Use genetic, environmental and clinical factors to predict disease progress and outcome

The first episode of schizophrenia and bipolar disorder remits in the majority of patients, but with significant risk for relapse. Psychotic disorders thus have a wide range of possible trajectories, which underlines the importance of ascertaining early predictors of treatment response and of clinical outcome.

We will delineate the course of key clinical and cognitive characteristics, with structural and functional imaging, expanding to the genetic and molecular levels of explanation in a longitudinal design. We expect that these multifactorial data and novel statistical tools will enable us to better predict course and outcome with a clinically useful level of confidence.

### Aims:

- Define clinical trajectories from premorbid stages and related pathophysiological processes
- Identify gene-environment interactions at critical phases of neurodevelopment with relation to clinical outcome, including mortality
- Develop prediction and stratification tools for disease course and outcome

### CLINICAL INTERVENTION: Translate pathophysiological discoveries into clinical and pharmacological interventions

It is a major challenge to move from statistical genetics associations in large samples, to the underlying disease mechanisms of psychosis in individual patients. We will use our rich database and stem cells technology to study immune- and lipid-related pathways based on our previous findings.

### Aims:

- Determine immune and lipid-related mechanisms in psychotic disorders
- Develop a stratification approach based on immune dysfunction profiles
- Perform immune system-related interventions in psychotic disorders







# Governing Board

Chair: Dag Kvale

Professor Head of Institute

Board member: Marit Bjartveit

### Board member: Trine Waaktaar

Clinic Manager Division of Mental Health and Addiction Oslo University Hospital

Professor Vice Dean of Studies Faculty of Social Sciences University of Oslo





stitute of Clinical Medicine University of Oslo



### Board member: Marit Bakke

Professor Vice Dean for Research Faculty of Medicine and Dentistry University of Bergen



### Board member: Hans Olav Instefjord

Director Divison of Psychiatry Haukeland University Hospital





# Scientific Advisory Committee

**Terry Jernigan** 

Professor University of California San Diego



### Professor Terry Jernigan:

Professor in Cognitive Science, Psychiatry, and Radiology, and Director of the Center for Human Development, University of California, San Diego (UCSD), USA, as well as Co-Director of the Coordinating Center for the ABCD Study.

### Professor Michael Foster Green:

Professor-in-Residence at the Department of Psychiatry and Biobehavioral Sciences and the Semel Institute for Neuroscience and Human Behavior at the Geffen School of Medicine at the University of California Los Angeles (UCLA), USA. He is also Director of the Treatment Unit of the Department of Veteran Affairs VISN 22 Mental Illness Research, Education, and Clinical Center (MIRECC).

### Professor Peter Falkai:

Professor of Psychiatry and Psychotherapy and Chairman of the Department of Psychiatry and Psychotherapy of the Ludwig-Maximilian University in Munich, Germany. He was Chairman of the DGPPN from 2011-2012 and Chairman of the Council of National Societies (NPAs) of the European Psychiatric Association (EPA) from 2012-2014. As of 12 April 2021, he is President of the European Psychiatric Association (EPA).



### Their tasks are as follows:

- Provide advice to the NORMENT leadership in strategic decisions.
- Contribute to NORMENT's research activity by • evaluating and advising on the activities within each of the research groups of the Centre and by acting as scientific advisors to the Centre Director.
- Take an active part in NORMENT's annual meetings. Participate in preparing an annual written evaluation. Contribute by giving an annual lecture at postgraduate level.





### Scientific Management

Eight Core Researchers (CR) with complementary expertise from different disciplines constitute the scientific management of the Centre.

- Ole A. Andreassen, Professor, University of Oslo
- Ingrid Melle, Professor, Oslo University Hospital
- Vidar M. Steen, Professor, University of Bergen
- Ingrid Agartz, Professor, University of Oslo
- Srdjan Djurovic, Professor, Oslo University Hospital and University of Bergen
- Stéphanie Le Hellard, Professor, University of Bergen
- Lars T. Westlye, Professor, University of Oslo
- Erik Johnsen, Professor, Haukeland University Hospital

In addition to being part of the scientific leader team, each CR is the head of a Research Group (see page 31).



Top left to right: Stéphanie Le Hellard, Ingrid Agartz, Srdjan Djurovic, Erik Johnsen, Ingrid Melle, Lars T. Westlye , Ole A. Andreassen, Vidar M. Steen.





### User Council

NORMENT's User Council represents the user community and consists of individuals who have lived experience, competency and expertise related to mental health. The members of the User Council give valuable input and hence complement and support the Centre in its effort to carry out research that is relevant for society.

The User Council meets four times a year and provides input to research strategy, gives advice on practical research protocols, gives input to grant applications and is consulted on matters that affect participants in the studies. The User Council also contributes to dissemination activities, and the members of the Council help strengthen the communication between NORMENT, the user organizations and the community at large.

In 2021, the members of the User Council were: Lena-Maria Haugerud, Fred Gerkum, Fabian Stang and Karoline Fløystad Thorsen.

### **User Representatives**

To strengthen the user perspective in the research, NORMENT has employed parttime User Representatives in both Oslo and Bergen.

The User Representative in Oslo, Cecilie Busch-Christensen, participates in daily activities at the Centre and brings the user perspective into group meetings, project planning, grant applications, practical operation procedures, and dissemination activities with a focus on Facebook and public events. Busch-Christensen coordinates NORMENTs User Council as well as the stakeholder forum of the EU-project CoMorMent. Furthermore, she is involved in projects where the user perspective is particularly relevant, such as the development of smartphone apps and other digital methods of data collection, and acts as a link to user organizations, such as the Norwegian Bipolar Association.

The User Representative in Bergen, Anne Blindheim, is associated with the Bergen Psychosis Research Group, and coordinates the stakeholder forum "PEK". This forum, consisting of people with lived psychosis experience and next of kin, meet once a month and give feedback to research projects. Blindheim is also involved in developing protocols and contributing to manuscripts as well as acting as a discussion partner for researchers.





# **Technical and Administrative Support**

In order to perform excellent research, NORMENT is dependent on well-organized support functions that ensure a stable and efficient infrastructure. The Centre is lucky to have a great team of technical and administrative personnel who continuously work to fulfil these functions in a good way. Support functions span from IT assistance and project economy to communication and project coordination.

Technical and administrative support has become increasingly important as the Centre has grown from about 80 employees in 2013 to more than 200 people involved in 2021. In addition, NORMENT affiliates are located at several sites in Oslo and Bergen, and are employed at four different institutions (University of Oslo, University of Bergen, Oslo University Hospital, Haukeland University Hospital).

Both the size and organization of the Centre demand well-working systems for internal communication and information flow. During the pandemic, digital platforms have been more important than ever, and here support personnel have had a central role. Most Centre meetings in 2021 have been on Zoom, and the NORMENT intranet, Wiki and Slack have been increasingly used for exchange of both formal and informal information across the Centre.

Technical support for data storage and computational platforms is also essential. The database with all research data is carefully quality controlled and stored on a secure server that is available across the Centre. Database staff clean and prepare data for analysis and ensure data security and adherence to national and international regulations. Support personnel also keep track of project budgets and yearly reports required by funding agencies, and work to improve central administrative systems, procedures and protocols that that are essential for an efficient research organization.



The Centre administration is located in Building 49, Ullevål Hospital, Oslo

# **Core Resource Units**

The daily infrastructure for collection, storage, and processing of scientific data at NORMENT is divided into seven different Core Resource Units (CRU). These are sections that are responsible for and have expertise in different methodological aspects of the data collection, and reflect that the Centre has a strong focus on "vertical synergy" and thereby the integration of various research methods and approaches.

Most scientific projects at the Centre include several Core Resource Units, since they are based on data collected from different groups and involve both clinical and other information about the participants.

The main responsibilities of the different Core Resource Units are described below.

### **Clinical CRU**

Leader: Ingrid Melle Manager clinical assessment: Trine Vik Lagerberg

The Clinical CRU has the main responsibility for recruitment and standardized scheduled clinical assessments of participants with psychotic disorders in the core research studies at NORMENT. This includes development and maintenance of the common clinical assessment protocol and quality assurance of assessments. The quality assurance includes standardized training of assessment team members, quality assurance and reliability of ratings, preparation of data for entry into the clinical database, and supervision of assessment team members. The assessment team consists of PhD students and research assistants with clinical qualifications to do diagnostic and symptom assessments, in most cases psychiatrists/psychiatric residents or clinical psychologists from the "Illness trajectories and functional outcome", "Mechanisms of psychopathology", and "Biological psychiatry" research groups at the Centre.

### **Cognitive CRU**

Leader: Torill Ueland Manager cognitive assessment: Hanne Christine Mohn

The Cognitive CRU conducts neuropsychological assessment of participants recruited for the core research studies at NORMENT. This includes assessment of patients with psychotic disorders and healthy control individuals at all time-points (baseline and follow-up). The group provides neuropsychological reports for clinical participants. The work of the group also includes development and maintenance of the cognitive assessment protocol and quality assurance of assessments. Quality assurance includes standardized training of assessment team members, calibration to ensure reliability of ratings, as well as preparation of data for entry into the database, and supervision of assessment team members. The assessment team responsible for the clinical participants consists of clinical psychologists and PhD students with qualifications to do neuropsychological assessments. The assessment team responsible for assessing healthy controls consists of psychology students and master degree holders.

### **Database and Biostatistics CRU** Leader: Ole A. Andreassen

Manager: Thomas Bjella

The main purpose of the Database and Biostatistics CRU is to develop and maintain secure and accessible storage structures, analytical tools, and communication platforms that facilitate and accelerate the process between data collection and data distribution at NORMENT. The unit is connecting the seven Core Resource Units at the Centre, and is integral in defining data properties for all research groups. This includes: 1) Database solution for integration of multidisciplinary data: Setting up a common procedure for data formatting, data transfer and data storage across all units; 2) Communication: Better and transparent communication lines, and regular update intervals on all data; 3) eHealth: eNORMENT service, make all data collection from electronic data capture systems; 4) Ethics and GDPR: Ethical approval for digital consent, and remote web form access; 5) Biostatistics service: Distribute method descriptions and guidelines for big data analysis, and provide code and consultation for data analysis.



**Neuroimaging CRU** Leader: Ingrid Agartz Manager MRI: Lars T. Westlye, Manager EEG: Torbjørn Elvsåshagen

The Neuroimaging CRU has the main responsibility for providing solid state-of-the-art methodology and infrastructure for magnetic resonance imaging (MRI) and electroencephalography (EEG) in the study of severe mental illness. This includes implementation of standard protocols for MRI and EEG, coordination between different research projects at the Centre, and a close collaboration with the Core Facility at the Department of Radiology, Oslo University Hospital. The Neuroimaging CRU works to guarantee streamlined logistics from collection to storage and processing of imaging data, including access to optimal methods for large-scale as well as innovative imaging (e.g. brain structural, functional, blood flow, metabolism, whole body scanning, electrophysiology), and aid to research groups both within and outside NORMENT. The CRU is also responsible for coordination of internal procedures and routines, follow-up of clinical aspects of MRI (e.g., incidental findings), and training of new staff.

### **Biobank and Stem Cells CRU** Leader: Srdjan Djurovic

The Biobank and Stem Cells CRU coordinates all biobank activities at NORMENT. This includes biological sampling (blood, urine, saliva etc.), treatment of samples (storage, tracking, retrieval), quality control, and shipment between different partners. The CRU also coordinates with the Norwegian Institute of Public Health, and contributes to data capture, organization and data flow. The Biobank and Stem Cells CRU has also established the required competence and facilities for human induced pluripotent stem cell (hiPSC) technology unit in our Centre allowing investigation of neuronal cells from participants. Validated iPSCs are differentiated to neural progenitor cells (neural conversion) and regionalized neuronal subtypes, as well as astrocytes/glial populations under standard in-house methods. Further activities will be aimed to develop a psychopharmacological screening platform for psychiatric disorders using iPSC-derived neurons.

### **Functional Genomics CRU**

Leader: Vidar M. Steen Co-leader: Stéphanie Le Hellard

The Functional Genomics CRU has expertise and infrastructure for large-scale analysis of the genome, focusing on global gene expression and epigenomics. The team is also equipped for explorative studies and validation experiments in relevant cell cultures and animal models. The current prioritized tasks are RNA sequencing and DNA methylation assays of the clinical samples (patients with schizophrenia spectrum disorders or bipolar disorder as well as healthy controls). We are also responsible for implementation and development of bioinformatic tools for data analysis, including multi-omic methods for integration of corresponding genomic, transcriptomic and epigenomic data.

### Pharma and Intervention CRU Leader: Erik Johnsen

The Pharma and Intervention CRU has the main responsibility for facilitating, coordinating and running intervention studies with medicinal products and other treatments for mental disorders. The CRU furthermore follows individuals with mental disorders in a long-term perspective in order to identify markers and predictors of the course of the disorders, as well as effects and side effects of treatment. The CRU includes three research groups covering the areas 1) Pharmacology and intervention, 2) Affective disorders, and 3) Predictive and pharmacological imaging.



# **Research Groups**

Group Leader and a particular focus area of research, but there is a close collaboration across groups and scientific disciplines, as reflected in the "vertical synergy" approach at the Centre (see page 12).

The number of Research Groups increased from eight to fifteen during 2018, when we entered the second phase as a Centre of Excellence. Some of the new groups are already well-established at their institutions, while others have just recently started. The inclusion of new groups is also part of our career development strategy to give early-stage researchers more responsibility and experience.

All Research Groups and Group Leaders are listed below. Each group has a formal affiliation to one specific Core Researcher (CR) in the scientific management, as shown below:

|                 | CR<br>Melle  | CR<br>Andreassen  | CR<br>Agartz  | CR<br>Westlye                      | CR<br>Djurovic                             | CR<br>VM Steen                          | CR<br>Le Hellard                                   | CR<br>Johnsen  |
|-----------------|--|---|---|------------------------------------|--|---|--|--|
|                 |  |   |   |                                    |  |   |  |  |
| Research Groups | Illness<br>Trajectories<br>and Outcome<br>Prediction<br>(Melle)<br>Mechanisms of<br>Psychopathology<br>(Lagerberg)<br>Cognitive<br>Mechanisms<br>and Outcome<br>(Ueland) | Precision<br>Psychiatry<br>(Andreassen)<br>Biological<br>Psychiatry<br>(NE Steen) | Imaging Psychosis<br>(Agartz)<br>Forensic<br>Psychiatry<br>(Haukvik)<br>Translational<br>Electrophysiology<br>(Jönsson) | Multimodal<br>Imaging<br>(Westlye) | Stem Cells<br>and Mechanisms<br>(Djurovic) | Molecular<br>Risk Factors<br>(VM Steen) | Epigenetics of<br>Mental Disorders<br>(Le Hellard) | Pharmacology<br>and Intervention<br>(Johnsen)<br>Affective Disorders<br>(Ødegaard)<br>Predictive and<br>Pharmacological<br>Imaging<br>(Grüner) |

In addition to our eight Core Researchers (see page 23), we have seven Group Leaders:





# Illness Trajectories and Outcome Prediction Group Leader: Ingrid Melle

## About the Group

Psychotic disorders show large variations in course and outcome. Early course parameters, including length of untreated illness and initial treatment response, are among the most important predictors of long-term outcome. Our aim is to identify symptom trajectories and correlates through prospective longitudinal studies of first-treatment participants. The group studies the longitudinal development of negative and psychotic symptoms including the opposite outcomes of full functional recovery versus treatment resistance and suicide, with a specific focus on the correlates of vulnerability factors. In 2020 we completed the 10-year follow-up of first episode cases in the TOP study with quality assurance of data. We also started a 20-year follow-up of previous participants in the TIPS study.

The results of our long-term studies indicate that the first year of treatment, in particular factors associated with first treatment response, is pivotal to long-term outcomes. We are thus starting out a new longitudinal study with more indepth characterization of developments over the first treatment year. For this purpose, we have re-designed the firstepisode research protocol. We will also use digital symptom registrations in the new study.

### **Main Projects**

Development of psychotic disorders from first treatment:

- Development of negative symptoms
- Development of treatment resistance •
- Development of substance use
- Development of full functional recovery •
- Risk of suicidal behavior and suicide
- Subjective experience of outcome

### Scientific Achievements 2021

- We have studied the role of substance use for the development of negative symptoms over the first year of treatment (Ihler et al).
- We have participated in two studies of the interaction between early trauma, premorbid adjustment, and treatment response (Hegelstad et al, Ottesen et al).

# Mechanisms of Psychopathology Group Leader: Trine Vik Lagerberg

## About the Group

The group aims to expand the understanding of mechanisms underlying the significant symptom variation seen in psychotic disorders over time and between individuals. We aim to provide rich clinical characterisations and to investigate the relationship between core affective and psychotic symptoms on one hand, and affective dysregulation, substance use and circadian rhythms on the other. To do so, we have developed and implemented digital tools (smartphone application, actigraphy) designed to prospectively capture a fine-grained picture of several dimensions of symptoms and behaviour.

In collaboration with other groups in the centre, we will combine such observations with data from cognitive, brain imaging, genetic and biochemical assessments. The group is also investigating how digital tools can be used in a clinical setting to boost treatment in bipolar disorder, and as a tool for assessing treatment response in clinical trials. The group is responsible for the research activities in a specialized clinical research unit for bipolar disorder at Nydalen District Psychiatric Centre.

## Main projects

- Digital monitoring of illness fluctuations in psychotic disorders (MinDag)
- Affective lability across psychotic disorders
- Substance use in bipolar disorder
- Clinical features of bipolar disorder: psychotic symptoms, illness insight and circadian rhythm
- Vitamin D supplementation in psychotic disorders RCT (Plan D)

## Scientific Achievements 2021

- The prevalence of substance misuse is reduced over the first year of treatment in bipolar disorder. Continuing alcohol alcohol misuse and those who never misused alcohol. The impact of cannabis misuse on affective relapse is unclear and needs further investigation (Lagerberg et al.).
- Affective lability (and particularly oscillations between anxiety and depression) is associated with reduced social impairment such as higher symptom levels, premorbid function and duration of untreated illness (Høegh et al.).
- Comorbid substance use disorders in bipolar disorder are not associated with a higher risk of receiving inadequate in France, and with reduced lithium use in Norway (Icick et al.).



misuse is associated with higher risk of affective relapse, while there is no difference in relapse risk for those stopping

function in psychotic disorders. This relationship is independent from other well established risk factors for functional pharmacological treatment. Cannabis use disorders are independently associated with increased use of antipsychotics

# **Cognitive Mechanisms and Outcome**

Group Leader: Torill Ueland

## About the Group

The aim of the group is to capture the variation and course of cognitive functioning in psychotic disorders and to identify mechanisms underlying cognitive dysfunction and cognitive heterogeneity. Our goal is to provide better prognostic guidance and improved individualized intervention programs including cognitive remediation.

Our studies require both large scale datasets of cognitive performance in combination with other biomarkers, as well as smaller richer datasets measuring cognition in the same individual over time. Achieving our aims entails using cognitive and clinical data, brain imaging data, genetic data and biochemical assessments, in collaboration with other research groups in the Centre.

### Main Projects

- Long term course of intellectual functioning and cognition in first-episode schizophrenia spectrum disorders and bipolar disorder.
- Cognition and negative symptoms in first-episode schizophrenia spectrum disorders: Long term course and associations to functional outcome.
- Cognitive heterogeneity and underlying mechanisms in psychotic disorders.
- Inflammation and cognition in psychotic disorders.

### Scientific Achievements 2021

- IQ trajectories in schizophrenia and bipolar disorder are characterized by initial declines from premorbid levels to illness onset, followed by long-term increases but with maintained developmental deficits (Flaaten et al.).
- Physical neglect experienced in childhood is associated with cognitive theory of mind in homicide offenders with schizophrenia (Vaskinn et al.).
- Higher self-efficacy and more disorganized symptoms are predictive of fewer subjective cognitive complaints despite more objective cognitive impairments in schizophrenia (Haugen et al.).
- Men convicted of rape have a markedly inferior ability to infer the mental states of others (Friestad and Vaskinn).
- Together with other groups in the Centre we have showed that cognitive control mediates the association between childhood trauma and increased waist circumference in severe mental disorder (Lunding et al) and found shared genetic loci between major depression and intelligence (Bahrami et al).

# **Precision Psychiatry** Group Leader: Ole A. Andreassen

### About the Group

The group uses big data and new analytical methods to clarify causes and risk factors of severe mental disorders to improve diagnosis and treatment, and enable precision medicine tools for prevention and treatment stratification. We apply state-of-the-art methodology to examine data from NORMENT and large databases that include several million individuals. This includes the groundbreaking Norwegian Mother and Child cohort (MoBa), which we have recently genotyped and will become a key resource in understanding the longitudinal trajectories of mental disorders in the coming years.

Using these unique datasets, we develop mathematical models to understand variation in the human genome, to improve our ability to identify genetic and environmental factors contributing to disease development. Together with information from other modalities, such as brain imaging and clinical data, we aim to predict disease onset and treatment response. This research is performed in close collaboration with international researchers and global consortia, with a strong focus on Nordic partners to leverage the large potential of registries and biobanks. The group's long-term goal is to develop the framework for precision medicine approaches - to apply the discoveries of causal factors in clinical practice - which has great potential in psychiatry.

### Main Projects

- Identifying genetic risk factors for mental and neuropsychiatric disorders (PGC) and mapping imaging genetics factors in mental disorders (ENIGMA), leading bipolar disorder and Alzheimer's disease projects.
- Identifying gene environment interplay in neuropsychiatric and mental disorders in Nordic samples (Tryggve) to identify resilience factors, and neurodevelopmental mechanisms (MoBa).
- Characterize comorbidity and longitudinal development of severe mental disorders, and role of lifestyle factors (CoMorMent).
- Psychopharmacological treatment stratification using real-world data (REALMENT) and lithium effect (R-LINK). Develop statistical genetics tools, based on uni- and bivariate mixture models (MiXeR), multivariate omnibus statistical test (MOSTest), and improve prediction and stratification with machine learning approaches.
- Understand cross-disorder genetic overlap to inform psychiatric nosology and understanding molecular mechanisms underlying mental disorders.

### Scientific Achievements 2021

- Discovered genetic variants associated with bipolar disorders implicating abnormal neurotransmission, and highlighted differences across sub-groups (Mullins et al.).
- Determined the overlapping genetic architecture between brain structure variation and schizophrenia risk genes (Cheng et al.).
- Discovered genetic variants associated with Alzheimer's disease implicating immune mechanisms (Wightman et al.). Identified novel polygenic variants determining the folding of the human brain (van der Meer et al.).
- Identified overlapping genetic architecture between severe mental disorders and mental traits such as sleep (O'Connell et al.) and neurological disorders including Parkinson's and migraine (Smeland et al., Bahrami et al.).









# **Biological Psychiatry** Group Leader: Nils Eiel Steen

### About the Group

The group investigates biological mechanisms in schizophrenia and bipolar disorder by integrating genetic, biological, environmental and clinical data in a translational approach. We use the richly characterized TOP/NORMENT sample in combination with data from international genetic consortia and health registries. Several biological processes related to severe mental disorders and their treatment are investigated with a special focus on inflammation and mechanisms of cardiovascular comorbidity as well as candidate metabolism pathways and the endocrine stress regulation system.

The overall goal is to increase the knowledge of the underlying biological mechanisms of these disorders with potential implications for prevention, treatment, course prediction and diagnostics. Our aims include gaining knowledge of underlying immune mechanisms of severe mental disorders, identifying pathophysiological pathways, and identifying stress-related mechanisms of severe mental disorders.

### **Main Projects**

- The immune system and severe mental disorders, genetics and associations to clinical characteristics and pharmacological treatment
- Cardiovascular risk and disease in severe mental disorders occurrence and mechanisms
- Sex-dependent somatic and pharmacological aspects in severe mental disorders
- The role of stress and psychophysiology in severe mental disorders •
- Metabolomic and proteomic biomarkers of severe mental disorders

### Scientific Achievements 2021

- Aberrant levels of the cytokines BAFF and APRIL and association with psychotic symptoms in severe mental illness (Engh et al.).
- Childhood trauma predispose for central obesity in severe mental illness mediated by diminished cognitive control (Lunding et al.).
- Adiponectin associated with cardiovascular disease risk in severe mental illness regardless of antipsychotic drug treatment (Reponen et al.).
- Extensive polygenic overlap between bipolar disorder and cardiovascular disease phenotypes with mixed effect directions (Rødevand et al.).
- Shared genetic mechanisms between loneliness, severe mental illness and cardiovascular disease risk (Rødevand et al.).

# **Imaging Psychosis** Group Leader: Ingrid Agartz

### About the Group

The focus of the group is brain neuroanatomy studied with advanced magnetic resonance imaging (MRI) methodology and how it relates with aetiology (genes and environmental factors) and early life risk factors (e.g. obstetric complications) as well as with the clinical phenotype, substance use, immune markers, infection exposure and medication. Advanced MRI phenotypes are used (e.g. cortex thickness, volume and area, myelin mapping, contrast, DTI).

We investigate large cohorts of schizophrenia or bipolar disorders. In longitudinal follow-up studies, we investigate brain trajectories over 13 years. One subproject (Youth-TOP) focuses on early-onset psychosis in adolescents, their brain development over time, the biomarkers, and early risk factors. We participate in several international consortia and coordinate two international collaborations on adolescent psychosis.

### Main Projects

- MRI studies of primary sensory and motor brain regions in psychosis disorders.
- Importance of birth and pregnancy complications to brain development and cognition in severe mental illness across the age range.
- Bridging neuroscience research with clinical applications, using machine learning approaches and multiparametric myelin mapping in psychotic disorders.
- Clinical investigation and follow-up of Youth-TOP participants at the University of Oslo and Karolinska Institutet, Stockholm.
- Coordination of ENIGMA-EOP study and cognitive networks for adolescents with early-onset psychosis.

### Scientific Achievements 2021

- We reported test-retest reliability and reproducibility of myeloarchitecture in the cerebral cortex of the MR T1w/T2wratio, and optimization for its use in clinical studies (Nerland et al).
- Specificity of volumetric differences in individual amygdala nuclei shows reductions that are more widespread in schizophrenia (Barth et al.).
- Cytomegalovirus exposure during lifetime shows sex-dependent association with dentate gyrus volume in the hippocampus in severe mental illness (Andreou et al).
- In comparison with healthy peers, adolescents with early-onset psychosis are impaired on all cognitive domains demonstrating age effects and minor sex effects (Smelror et al).
- The default functional connectivity network is weaker in several cortical brain regions (Hilland et al).







# **Forensic Psychiatry** Group Leader: Unn Kristin H. Haukvik

### About the Group

The group has an interdisciplinary approach to the study of violence and aggression in severe mental disorders. Our main focus is to study biopsychosocial factors involved in violent behaviour, and how they interact to affect violence risk in severe mental disorders, by combining thorough clinical investigation with advanced brain imaging methods and registry data. As a thematic research group, we collaborate closely with the other research groups within the Centre.

We also explore the potential legal implications of our research, in the intersection between law and neuroscience. We use frontline MRI-methodology to explore neurobiological underpinnings of violence and aggression, and combine this knowledge with social and psychological factors to understand the patterns leading to violent behaviour in severe mental disorders and map targets for treatment and prevention. We aim to link our research to the Norwegian medical model of criminal insanity and to contribute to strengthening legal rights of patients and reduce the stigma associated with violence in severe mental disorders.

### **Main Projects**

- Violence in severe mental disorders; biological, psychological, and social patterns (sTOP).
- Violence in psychosis: towards neuroimaging-informed prediction of violence risk?
- Insight and phenomenology in psychotic disorders with comorbid violence.
- Neuroinflammatory biomarkers of aggression in severe mental disorders: clinical implications for prevention and treatment.
- Reworking the medical model of criminal insanity in the intersection between law and science empirical data and the legal significance of psychosis.

### Scientific Achievements 2021

- People with psychosis and a history of violence show brain-wide white matter disruptions compared to non-violent persons with psychosis (Tesli et al).
- Violent offenders without and without psychosis have widespread white matter abnormalities compared to healthy persons but do not differ from each other (Tesli et al).
- Psychopathy scores correlates with white matter in the corpus callosum (Tesli et al).
- Psychopathy scores are not related to amygdala volume or volumes of the amygdala nuclei (Bell et al).
- Patients with psychosis and a history of violence have smaller volumes of several nuclei of the amygdala (Bell et al).

# Translational Electrophysiology Group Leader: Erik Gunnar Jönsson

## About the Group

The group studies nerve cell function in patients with psychosis and other psychiatric disorders using electroencephalography (EEG) and related electrophysiological methods. The electrophysiological indices are also analyzed in connection with clinical symptoms, genetic variation, morphological variation in the brain, computerized models of nerve cells, and stem cell based methods.

The group aims to examine whether EEG-based indices of synaptic function and neuronal excitability regulation are altered in schizophrenia and bipolar disorder. We assess effects of novel schizophrenia and bipolar disorder genetic risk loci on the EEG-based indices and to examine whether the EEG-based indices can be used to predict illness severity in schizophrenia and bipolar disorder.

## **Main Projects**

- Genes and the synapse in severe mental illnesses: From stem cells and in vivo brain function to clinical implications models of synaptic function).
- and synaptic function).

## Scientific Achievements 2021

- Analyses showed decreased cortical plasticity in schizophrenia and bipolar disorder (Valstad et al).
- We found that heart rate variability was reduced and associated with symptoms severity in psychosis spectrum disorders (Benjamin et al).
- controls.





(examination of synaptic function in vivo using electrophysiological techniques in individuals with psychotic disorders and healthy controls, in vitro using iPSC-derived neurons from the same participants, and in silico using computational

Sensory and motor networks in psychotic disorders: From structure and function to phenomenology (examination of the relationship between brain myelination, aberrant sensory processing and phenomenology of psychotic disorders). Equivalence class formation and cortical synaptic function in autism spectrum disorders (examination of the role of synaptic function and plasticity in the autism spectrum disorders and the relationship between equivalence formation

Preliminary analyses of a novel EEG-based index indicated increased cortical excitability in bipolar disorder relative to

# Multimodal Imaging

Group Leader: Lars T. Westlye

### About the Group

To characterize the dynamic mechanisms of mental disorders across life, we use different brain imaging approaches, with a particular emphasis on combining measures of structural and functional connectivity with clinical and genetic information.

Structural and functional brain characteristics are highly heritable, and our research aims at increasing our understanding of how genes, environments and gene-environment interactions influence mood, cognition and risk of mental disorders during sensitive periods in life, in particular during childhood and adolescence.

### **Main Projects**

- Brains and minds in transition (BRAINMINT): The dark side of neuroplasticity during sensitive life phases.
- MoBaBrain: Parsing the developmental and genetic architecture of risk and resilience in the adolescent brain.
- IMPLEMENT: Improved personalized medicine through machine learning in mental disorder.
- BRAINCHART: Normative brain charting for predicting and stratifying psychosis.
- COMMITMENT: CoMorbidity Modeling via Integrative Transfer machine-learning in MENTal illness.

### Scientific Achievements 2021

- Cardiometabolic risk factors (e.g. smoking, high blood pressure) are associated with brain age and accelerated brain ageing (Beck et al.).
- Recent studies suggest that the thalamus has a broader role in cognition and common brain disorder than previously assumed; here, we identified the first genetic loci linked to thalamic nuclei volumes and found overlap between genetic architectures of the thalamic nuclei and ten neurological and psychiatric disorders (Elvsåshagen et al.).
- Independent mental health profiles with low phenotypic correlation share genetic underpinnings, suggesting a shared biology among symptom profiles (Roelfs et al.).
- Systematic mapping of the heterogeneity of schizophrenia and bipolar disorder between individuals is the better way forward in computational psychiatry than comparing group averages (Wolfers et al.).
- The shared effect of oxytocin-pathway genetics helps provide a better understanding of why social metabolic dysfunction often co-occurs in severe mental illnesses (Winterton et al.).

## Stem Cells and Mechanisms Group Leader: Srdjan Djurovic

### About the Group

The group's current research aims are to perform molecular genetic analysis to increase the knowledge and expertise in psychiatric genetics and genomics and to identify the molecular networks underlying psychiatric disease as well as to continually develop an organization to support psychiatric genetic and stem cell studies with design and planning.

Our research group is also responsible for the management and operation of the biobank and stem cell facilities at NORMENT. This CRU includes sampling, treatment of samples (storage, tracking, retrieval) and shipment between different partners, as well as data processing/coordination to ensure quality of associated data for the collected biobank samples.

### **Main Projects**

- Human induced pluripotent stem cell (hiPSC) technologies in psychiatric molecular genetics.
- Neuro-immune interactions.
- Identifying the polygenic basis of the human brain and neurodevelopmental disorders.

### Scientific Achievements 2021

- Development of novel protocol for the differentiation and characterization of iPSC-derived cortical spheroids (Osete et al.).
- Optimization of the co-culturing protocols of iPSC- derived neurons and astrocytes, screening platform for characterization of iPSC-derived astrocytes under baseline and inflammatory conditions, as well al., Osete et al., Akkouh et al.).
- Identification of molecular networks underlying psychiatric disease (Holmgren et al., Szabo et al., Akkouh et al.).
- Genome-wide pleiotropy analysis and genetic overlap between neuropsychiatric traits (O'Connell et al.).





Psychopharmacological screening platform for psychiatric disorders using iPSC-derived neurons.

Large-scale investigations of the role of copy number variants in disease, brain phenotypes and cognition.

aspsychopharmacological screening platform - using RNA-Seq, fluorescent microscopy, and various functional assays, incl. multidisciplinary platform combining cell electrophysiology, calcium imaging as well as voltage imaging (Szabo et





# **Molecular Risk Factors** Group Leader: Vidar M. Steen

### About the Group

Our group aims at identifying and understanding genetic and biological factors that are involved in illness mechanisms and therapeutic response during pharmacological treatment of schizophrenia and bipolar disorder. We use a combination of clinical data, biomarker screening and functional studies in patient samples and various experimental models.

Our main research interest is at present directed towards the role of metabolic factors and inflammation processes in development of psychosis and during antipsychotic treatment. The group is also responsible for running the Genomics Core Facility at the University of Bergen, to provide guidance and service on large-scale genomic analyses, such as whole genome-, exome- and RNA sequencing.

### Main Projects

- The effect of drug-related weight gain and lipid disturbances on psychotic symptoms, cognitive function and brain myelin in patients with schizophrenia
- Transcriptional changes in peripheral blood during drug treatment in patients with psychotic disorders: A crosssectional and longitudinal study
- The molecular mechanisms of antipsychotic-induced metabolic effects
- Low grade inflammation and innate immune responses in peripheral blood as trait or state markers of psychosis
- Genetic risk factors for disease susceptibility and treatment outcome in schizophrenia and bipolar disorder

### Scientific Achievements 2021

- Sex-specific associations between serum lipids and psychotic symptoms were demonstrated in first-episode psychosis patients (Gjerde et al.).
- Elevated numbers of neutrophilic granulocytes in peripheral blood can be observed in patients with schizophrenia, but it is still unclear if it is a cause or consequence of the disorder (Sandberg et al.).
- Completed lipidomic profiling of from longitudinal serum samples of psychosis patients treated with amisulpride, aripiprazole or olanzapine in a randomized controlled trial.

# **Epigenetics of Mental Disorders** Group Leader: Stéphanie Le Hellard

### About the Group

Major mental disorders such as psychotic disorders have a complex and multifactorial etiology. Both genetic and environmental risks have been described and their interaction is still uncertain. We study how the pathology, the genetic factors and the environmental factors can modify the genome by modifying regulatory elements of the genome (epigenetic modifications). Our aims are to understand how environmental risk factors interact with the genetic risk at the epigenetic level, to identify epigenetic biomarkers for disease status, environmental exposure and treatment.

The group consists of people with background in genetics, statistics, medicine and informatics who together bring their complementary expertise to try understanding the interaction between genetic and environmental risk in mental disorders. We work in close collaboration with clinicians. We use datasets generated in house or publicly available that combine genetic, epigenetic and gene expression datasets for mental disorders (mostly schizophrenia and bipolar disorders) that are in addition well annotated for environmental factors. We have generated DNA methylation profiles in large samples of patients with bipolar disorders, schizophrenia or ADHD and matched controls.

During the pandemic, we also initiated the recruitment of population to study the effects of the pandemic on mental health.

### Main Projects

- Identify epigenetic modifications associated with environmental exposure (cannabis, trauma, birth complications, etc)
- Identify epigenetic modifications associated with treatment (pharmacological, ECT, exposure therapy)
- Identify epigenetic modifications regulated by genetics in the brain
- Characterize peripheric effects of cannabis in the blood
- Characterize the effects of the COVID19 pandemic on mental health

### Scientific Achievements 2021

- Psychiatric traits can be associated to the same genes but not necessarily the same genetic variants within the genes, i.e. pleiotropy at the gene level.
- DNA methylation differences are associated with cannabis use, exposure to trauma in childhood and asphyxia at birth (manuscripts in submission).
- There has been a small increase in symptoms of depression and anxiety during the COVID-19 pandemic, especially in vulnerable groups (Hagen et al., Unnarsdottir et al.).
- Participated in large consortia studies to identify genetic association in brain morphology and mental disorders (e.g. Sonderby et al.).
- Provided expertise support to identify epigenetic associations in mental disorders, e.g psychotic experience (Navarro et al.).









# Pharmacology and Intervention

Group Leader: Erik Johnsen

## About the Group

We study schizophrenia spectrum disorders at several levels in an integrated fashion, including clinical symptoms and signs, treatment effects and side effects, brain imaging measures, as well as molecular vulnerability and disease mechanisms. The research group has more than 15 years of experience in conducting researcher initiated drug trials independently of pharmaceutical industry. The group overlaps with the Bergen Psychosis Research Group at Haukeland University Hospital and the University of Bergen.

The main aims of the research group is to identify differential effectiveness among antipsychotic drugs, and to identify predictors of effects and side effects of treatment at the individual level. We want to unravel disease mechanisms and potential new treatment targets, in addition to assess the value of immune-modulating treatment in psychosis, and the value of omega-3 fatty acids in ultra-high risk of psychosis.

### **Main Projects**

- The Norwegian Prednisolone in Early Psychosis Study (NorPEPS): A double-blind, randomized, placebo-controlled addon effectiveness study of prednisolone in early psychosis.
- The Neuroinflammation in Adolescents with Psychosis Project (NAPP): An observational cohort-study of young people with psychosis.
- The Non-Pharmacological treatment of Psychosis study (NonPharm): An observational cohort study following individuals with psychosis seeking treatment without the use of antipsychotic drugs.
- The Placebo-controlled Trial in Subjects at Ultra-High Risk for Psychosis With Omega-3 Fatty Acids in Europe (PURPOSE): A randomized placebo-controlled study of omega-3 fatty acids in ultra-high risk for psychosis to prevent transition to psychosis.
- Stems cells in schizophrenia project: Using stem cells to model antipsychotic drug response.

### Scientific Achievements 2021

- Sex differences exist between effectiveness and side effects of antipsychotic drugs (Hoekstra et al.).
- Substance use does not have a major impact on side effects antipsychotic drugs (Alisauskiene et al.).
- Periods of non-use compared to periods of use of antipsychotic drugs are associated with doubled mortality risk in schizophrenia (Strømme et al.).

# Affective Disorders Group Leader: Ketil J. Ødegaard

### About the Group

We study bipolar disorders and other illnesses of depression using different methods and approaches. Our studies focus on psychopharmacology, neurostimulating treatment, sensor technology, registry research, cognitive function, genetics and brain imaging in bipolar disorders and other illnesses including depression.

The research group has a translational focus with the aim of contributing to increased etiological knowledge of pathophysiological processes in affective disorders, mainly through clinical intervention studies. The group also covers the Bergen Bipolar and Depression Research group at Haukeland University Hospital and consists of collaborating researchers with joint projects on mood disorders.

### **Main Projects**

- The Pharmacogenomics of Bipolar Disorder study (PGBD): Identification of genes for lithium response in a prospective sample.
- Monitoring of bipolar disorder using sensor technology (part of INTROMAT-study).
- underlying response to electroconvulsive therapy.
- Blue-blocking glasses as additive treatment for mania: A randomized placebo-controlled trial.
- Cognitive residual symptoms in MDD. Cognitive remediation in order to prevent new episodes.

### Scientific Achievements 2021

- Neuronal circadian rhythm abnormalities are present in Bipolar disorder and most pronounced in Li-Non responders. Rhythm deficits may be partly reversible through stimulation of entrainment pathways (Mishra et al.).
- Significant clinical predictors of lithium treatment failure in BD include baseline anxiety symptoms, functional impairments, negative life events and lifetime clinical features such as a history of migraine, suicidal ideation/ attempts, and mixed episodes, as well as a chronic course of illness. (Lin et al.).
- Volume increases in gray matter areas can be detected 2 h after a single ECT session (Brancati et al.).
- Suicidal and violent ideation in inpatients with mental health disorders are associated with young age and the absence of diagnoses of psychotic disorders. In addition, suicidal ideation is associated with several core clinical factors (Furnes et al.).
- Longitudinal effect of ECT on gray matter volume may not explain superior ECT response in Psychotic major depression, and further investigation is needed (Takamiya et al.).







The Global ECT-MRI Research Collaboration (GEMRIC): Establishing a multi-site investigation of the neural mechanisms



# Predictive and Pharmacological Imaging

Group Leader: Renate Grüner

## About the Group

We explore and develop novel neuroimaging biomarkers, across scales and in time, to better understand underlying disease mechanisms and monitor the course of illness/ treatment effects in mental health and disorders. The majority of the work is on challenge image data acquisition, processing and visualization and link neuroimaging data to other variables such as cognition, psychiatric symptoms, inflammation and more. The research group includes members at the Haukeland University Hospital and the University of Bergen.

### **Main Projects**

- Multimodal integration of DTI, fMRI, sMRI and MRS data in psychosis patients
- Excitatory/inhibitory neurotransmission: relation to hallucinations and medication
- Dynamic connectivity analysis of functional connectivity networks in psychosis patients
- Explore novel diagnostic and treatment approaches
- Adapt computational resources and explore prognostic features

### **Scientific Achievements 2021**

- Applications of Transcranial direct current stimulation (tDCS)
- Exploring olfactory hallucinations (Wehling et al.)
- Investigate microstructural changes using TBSS in auditory hallucinations
- Establishment of pipeline for dopamine tracer for PET/MR, applications of 31P MRS
- Comparison of unimodal and multimodal image data analysis strategies in auditory hallucinations



# **Collaboration Across Research Groups**

NORMENT is a cross-disciplinary research centre, Being a Centre of Excellence provides great opportunities to broaden and strengthen our cooperation, align research where sharing of competence and infrastructure goals, and profit from of our complementary expertise is a key principle. We have set aside about half of and valuable infrastructure, as well as performing more the Centre of Excellence grant to fund our core cost-efficient research through strong leadership and an infrastructure (Core Resource Units), to enable integrated approach. Further, there is a large degree of easy access to state-of-the-art methodology, sharing of postdoctoral fellows and support personnel infrastructure for recruitment and assessment of across different groups, and several PhD students have been co-supervised by seniors and members of different participants, and database and biobank services. research groups at the Centre. Most if not all research activities at the Centre depend on this tight integration and efficient use of resources across different research groups.

A large degree of NORMENT's research is generated from multidisciplinary projects, and this is also the framework for new project developments and grant applications. Collaborative projects within the Centre are organized through the monthly Synergy Meetings and named Synergy Projects with project lists available on our intranet.

The projects are grouped under different research topics, such as Cannabis, eNORMENT (electronical data collection), Genetics, Imaging Genetics, Immunology, Methylation, mRNA, MRI, and Polygenic Risk Score.

There are specific added values of this cross-disciplinary approach that are related to the main research topics and aims of the Centre:

- 1. Genetics: Combine large amounts of genetic data with relevant environmental factors, and move this to experimental studies in human stem cells.
- 2. Brain Imaging: Use advanced imaging technology to study brain characteristics in large groups of participants who are also genotyped and extensively clinically characterized, a sample which is unique internationally.
- Outcome Prediction: Determine the association between genes, environment, and their effect on different illness trajectories, with the potential of leading to new tools for prediction and early identification of illness.
- 4. Clinical Intervention: Translate genetic, immunological, imaging, and other pathophysiological findings into clinical and pharmacological interventions to improve treatment.











# Top Day 2021

# 11 June - Zoom

### Ole A Andreassen: 09:00 Introduction and overview of today's program Guy Hindley: Charting the landscape of genetic overlap 09:15 between mental disorders and brain related traits beyond genetic correlation Maren C. F. Werner: PhD summary; Genetic and non-genetic 09:35 factors related to immune abnormalities and treatment resistance in severe mental disorders 09:55 Coffee break Line Widing: Clinical and premorbid characteristics of 10:15 patients with DSM-IV Psychotic disorder NOS Margrethe C. Høegh: 10:35 PhD summary; Affective lability in psychosis spectrum disorders 11:00 **Coffee break** Synve Hoffart Lunding: 11:15 Childhood trauma and smoking Mathias Valstad: PhD summary; Synaptic plasticity aber-11:35 rations in severe psychiatric disorders assessed with an EEG paradigm 12:00 Lunch break **Rikka Kjelkenes:** Mapping normative trajectories of cog-13:00 nitive performance and its relation to psychopathology and polygenetic risk in the PNC sample Natalia Tesli: PhD summary; Imaging violence in psy-13:20 chosis - Using MRI to investigate neurobiological correlates of violence in psychotic disorders 13:45 **Coffee break** Nora Slapø: Bridging the gap between cortical brain 14:00 structure and function in healthy controls and in patients with psychotic disorders

### Adriano Winterton:

14:20 PhD summary; The Oxytocin Pathway in Severe Psychiatric Disorders and Metabolic Syndrome

# **Researcher Training**

NORMENT also emphasizes guiding of early stage NORMENT offers a range of training and development opportunities for our PhD students, researchers by involving them in grant writing and postgraduate researchers, and other research encouraging them to participate in the postdoctoral and staff. About 60 PhD students and 30 postdoctoral mentor programme at the Universities of Oslo and Bergen. fellows worked at or were affiliated with the These programmes include courses in career planning, Centre in 2021. During the year, there have been research management, and external funding. Early stage various meetings with the aim to provide the best possible researcher training. Scientific sharing scientists may also participate in international research and synergy across domains were important education and training at the University of California San Diego (UCSD) in the USA, funded in part by the Research topics at these events and are underlying Council of Norway (INTPART grant). principles for all research activities at the Centre.

## **PhD Education and Training of Researchers**

The PhD students at NORMENT are enrolled at the mandatory PhD education programme at the University of Oslo and University of Bergen. In addition, several PhD students are members of the Norwegian Research School in Neuroscience (NRSN) which organizes courses, training, and a conference for PhD candidates in neuroscience nationwide. NORMENT is also involved in the National Research School in Bioinformatics, Biostatistics and Systems Biology (NORBIS), where PhD students and postdocs may attend courses in genetic analyses and statistics.

During 2021, NORMENT organized regular research meetings where PhD students and postdocs across research groups and scientific disciplines presented their projects, results and future plans. There were also regular workshops in academic writing and clinical supervision, as well as group meetings organized by the different research groups at the Centre where PhD students and postdocs presented their research.

The yearly TOP Day is also an important arena for PhD students to get training in dissemination of their research. The term "TOP" comes from the name of the main study at the Centre, the "Thematically Organized Psychosis" Study. In 2021, the TOP Day was organized as a digital meeting on June 11. After a general introduction and update by Centre leader Ole A. Andreassen, 10 PhD students from various groups and scientific backgrounds presented their research projects, to share ideas and give each other feedback on topics ranging from genes to clinical symptoms.

### **Career Development**

Another important aspect of the researcher training is a continuous focus on career development of early career investigators. The Career Development Task Force at the Centre organized two grant writing workhops during 2021 and started the process of planning a seminar series on career development in 2022, organized by early career researchers.







Photos from different NORMENT activities.



26. november

"Transferrable skills, getting the most out of your skillset"









### **Early-Career Researchers Meeting**

The Early Career Researchers Meeting was established in 2015 as a yearly one-day meeting for PhD students, postdocs and other researchers who are at an early stage in their career. The meeting is fully planned by the early career researchers themselves and is an arena to discuss topics that they consider important to their scientific development and career.

The 2021 meeting took place on November 26, and could fortunately be organized as a physical event at the Norwegian Academy of Science and Letters in Oslo. The title of the meeting was "Transferable skills, getting the most out of your skillset", and about 50 people attended.

Comic writer Øystein Runde was invited as a keynote speaker to share his experiences from science communication and give advice on how to improve our own dissemination skills. Selected speakers affiliated with NORMENT presented various aspects of transferable skills and provided examples from their work inside and outside of academia.

The meeting also had an interactive session challenging all participants to use their creativity to make an advertisement for a new drug. The session was led by Øystein Runde, and a winning team was selected. This was a fun and inspiring part of the meeting, and people enjoyed some social activity after a long period of digital meetings due to the pandemic.

### **Synergy Meetings**

The Synergy Meetings are monthly meetings alternating between Oslo and Bergen, where researchers at all levels can present ideas and preliminary data to facilitate interactions and discussions. These meetings reflect NORMENT's overall focus on "vertical synergy", in which the aim is to obtain different levels of understanding by bringing together transdisciplinary expertise and methods.

An important part of the meetings is to initiate new collaborative projects and discuss ongoing projects across the Centre. Each meeting ends with a to-do list, and the Synergy Projects lists on our internal webpages are updated.

During 2021, there were seven Synergy Meetings in total. All meetings were digital due to the pandemic, with 60-80 people participating. The meetings covered broad topics such as *Pharma and interventions, Epigenetics and environment, Biological models, Developmental factors, Population cohorts, Cardiovascular comorbidity, and Longitudinal studies.* 

### **Annual Retreat**

The Annual Retreat is the main social and scientific event for everyone at NORMENT and is normally organized as a two-day meeting at a conference hotel in Oslo or Bergen. Due to the pandemic, we had to go digital again. The meeting took place on Zoom on September 16-17 with almost 150 participants. The overall theme for this year's retreat was New Horizons: Translation from Research to the Clinic, with a focus on future opportunities in mental health research, and reflecting the Centre's goal of generating new knowledge that can be used to improve treatment and the quality of life of individuals suffering from severe mental disorders. See the full program on page 50.

This ambition requires an integrated approach which allows for the convergence of many different perspectives. Therefore, the event included contributions from speakers in thematically organized sessions covering both technologies, treatment, politics, and global science.

## NORMENT ANNUAL RETREAT 2021 New Horizons: Translation from Research to the Clinic 16 – 17 September, Zoom

Five international keynote speakers were invited to give inspiring talks of relevance for everyone at the Centre. Professor Danielle Posthuma from the Vrije Universiteit Amsterdam presented recent research on large-scale genetics and analytical tools, while Professor Catherine Harmer from the University of Oxford gave a talk on the integration of pharmacological and psychological treatments. Ole Johan Borge, Director of health research and innovation at the Research Council of Norway, gave an overview and advice on future mental health research funding.



During the session on global science, Professor Dan Stein from the University of Cape Town shared his experiences from global mental health research, while Professor Unnur Valdimarsdóttir, University of Iceland, presented the COVIDMENT project, a Nordic research consortium on mental health during the COVID-19 pandemic. In addition, several researchers from the Centre gave talks on current projects and plans related to the main topic.



An interactive session was also included at the meeting, to promote social and fun activities with colleagues across the Centre. People were divided into smaller groups, solving tasks and puzzles together as part of an "escape room" game that challenged both our collaborative, cognitive, and creative skills!

As opposed to last year's retreat, a poster session was part of the program this year. Almost 30 researchers from the Centre contributed with scientific posters that were published on a dedicated website for everyone to visit. Presenters were also encouraged to make a brief video recording of themselves telling about the study, and several people used this dissemination opportunity. During the poster session, presenters were also available in breakout rooms in Zoom to answers questions from the audience. All posters were evaluated by our Scientific Advisory Committee, and three prizes were awarded to posters showing high clinical utility, in accordance with the main topic at the meeting.

The main poster prize was awarded to PhD student Maria Fagerbakke Strømme for her study titled "Mortality and non-use of antipsychotic drugs after acute admission in schizophrenia: A prospective total-cohort study". With this prize also comes a grant of NOK 10.000 from the Dr. Einar Martens Foundation to be used on research. Two runnersup prizes were awarded to PhD student Guy Hindley for his poster "Dissecting the shared genetic determinants of migraine and mental disorders", and to Researcher Monica Aas for the poster "Physical activity and childhood trauma experiences in patients with schizophrenia or bipolar disorders". See other posters on page 51.



Maria Fagerbakke Strømme won the 2021 poster prize.

## Annual Retreat 2021

Program 16-17 September

| 09:00 - 09:30   | 9:00 - 09:30 Welcome address and status of<br>NORMENT  |  | Committee - Marit Haram:<br>Welcome day 2  |
|---|--|--|--|
| Ν   | Session 1: Technologies<br>1oderator: Stephanie Le Hellard   | Session 3: Po  | <b>plitics, society and clinical implicati</b><br>Moderator: Marit Haram   |
| 09:30 - 10:00   | Danielle Posthuma:<br>Large-scale genetics and analytical tools.   | 09:10 - 09:40  | Ole Johan Borge:<br>Future mental health research fu   |
| 10:00 - 10:15   | Q&A  | 09.40 - 09.55  |  |
| 10:15 - 10:30   | Coffee break   | 05.40 - 05.55  | Androas Pingon:  |
|   | Srdjan Djurovic:   | 09:55 - 10:15  | Research possibilities in the cli  |
| 10:30 - 10:50   | in the era of precision medicine:<br>research at NORMENT   | 10:15 - 10:35  | Martin Tesli:<br>The socioeconomic environment<br>mortality in schizophrenia   |
| 10.20 - 11.10   | Oleksandr Frei:<br>Big data tools in psychiatric genetics and  | 10:35 - 10:45  | Coffee break   |
| 10.50 11.10   | neuroimaging   |  | Social session - Escape room   |
| 11:10 - 11:30   | Trine Vik Lagerberg:<br>eHealth - using digital tools to enhance   | 10:45 - 12:15  | Pegasus project<br>Moderator: Carla P.D. Fernanc   |
|   | clinical research and practise   | 12:15 - 12:45  | Lunch break  |
| 11:30 - 12:00   | Lunch break  | Session 4: Glo   | bal science and international netw   |
|   | Poster session   |  | Moderator: Lars T. Westlye   |
| 12:00 - 13:00   | Presentation of digital posters  | 12:45 - 13:15  | Dan Stein:<br>Global mental health and clini   |
| 13:00 - 13:10   | Coffee break   | 42.45 42.20  | neuroscience: Potential synerg   |
|   | Session 2: Treatment   | 13:15 - 13:30  | Q&A  |
|   | Modorator: Erik Johnson  |  | Linnen Maldina and Atting  |
| 13:10 - 13:30   | Moderator: Erik Johnsen<br>Erik Johnsen:<br>Emerging biological treatment strategies<br>in severe mental disorders: an overview  | 13:30 - 14:00  | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health seq<br>covid-19   |
| 13:10 - 13:30   | Moderator: Erik Johnsen<br>Erik Johnsen:<br>Emerging biological treatment strategies<br>in severe mental disorders: an overview<br>Catherine Harmer:   | 13:30 - 14:00<br>  | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health sequencies<br>covid-19<br>Q&A   |
| 13:10 - 13:30<br>   | Moderator: Erik Johnsen<br>Erik Johnsen:<br>Emerging biological treatment strategies<br>in severe mental disorders: an overview<br>Catherine Harmer:<br>Can we integrate our understanding<br>of pharmacological and psychological<br>treatments in depression?  | 13:30 - 14:00<br>14:00 - 14:15                                   | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health seq<br>covid-19<br>Q&A<br>Closing session:<br>Moderator: Ole Andreassen   |
| 13:10 - 13:30<br>13:30 - 14:00<br>13:30 - 14:00   | Moderator: Erik Johnsen<br>Erik Johnsen:<br>Emerging biological treatment strategies<br>in severe mental disorders: an overview<br>Catherine Harmer:<br>Can we integrate our understanding<br>of pharmacological and psychological<br>treatments in depression?<br>Q&A   | 13:30 - 14:00<br>14:00 - 14:15                                   | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health seq<br>covid-19<br>Q&A<br>Closing session:<br>Moderator: Ole Andreassen<br>Peter Falkai:<br>Comments from the Scientific Ad   |
| 13:10 - 13:30<br>13:30 - 14:00<br>13:30 - 14:00<br>14:10 - 14:30  | Moderator: Erik Johnsen:         Erik Johnsen:         Emerging biological treatment strategies in severe mental disorders: an overview         Catherine Harmer:         Can we integrate our understanding of pharmacological and psychological treatments in depression?         Q&A         Mari Nerhus:         Targeting treatment with vitamin D  | 13:30 - 14:00<br>14:00 - 14:15<br>14:15 - 14:25                  | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health sequ<br>covid-19<br>Q&A<br>Closing session:<br>Moderator: Ole Andreassen<br>Peter Falkai:<br>Comments from the Scientific Ad<br>Committee, and announcemen<br>poster prizes.  |
| 13:10 - 13:30<br>13:30 - 14:00<br>13:30 - 14:00<br>14:10 - 14:30<br>14:30 - 14:45   | Moderator: Erik Johnsen:         Erik Johnsen:         Emerging biological treatment strategies in severe mental disorders: an overview         Catherine Harmer:         Can we integrate our understanding of pharmacological and psychological treatments in depression?         Q&A       Q&A         Data Nethus:         Targeting treatment with vitamin D supplementation in psychotic disorders         Coffee break  | 13:30 - 14:00<br>14:00 - 14:15<br>14:15 - 14:25<br>14:25 - 14:30 | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health seque<br>covid-19<br>Q&A<br>Closing session:<br>Moderator: Ole Andreassen<br>Peter Falkai:<br>Comments from the Scientific Ad<br>Committee, and announcemen<br>poster prizes.<br>Ole A. Andreassen:<br>Conclusive remarks and<br>closing of meeting |
| 13:10 - 13:30<br>13:30 - 14:00<br>13:30 - 14:00<br>14:10 - 14:30<br>14:30 - 14:45<br>14:45 - 15:05                            | Moderator: Erik Johnsen:         Emerging biological treatment strategies in severe mental disorders: an overview         Catherine Harmer:         Can we integrate our understanding of pharmacological and psychological treatments in depression?         Q&A         Mari Nerhus:         Targeting treatment with vitamin D supplementation in psychotic disorders         Coffee break         Novin Balafkan:         Mapping genes associated with heterogeneity in response to antipsychotics  | 13:30 - 14:00<br>14:00 - 14:15<br>14:15 - 14:25<br>14:25 - 14:30 | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health sequ<br>covid-19<br>Q&A<br>Closing session:<br>Moderator: Ole Andreassen<br>Peter Falkai:<br>Comments from the Scientific Ad<br>Committee, and announcemen<br>poster prizes.<br>Ole A. Andreassen:<br>Conclusive remarks and<br>closing of meeting  |
| 13:10 - 13:30<br>13:30 - 14:00<br>13:30 - 14:00<br>14:10 - 14:30<br>14:30 - 14:45<br>14:45 - 15:05<br>15:05 - 15:25           | Moderator: Erik Johnsen:         Erik Johnsen:         Emerging biological treatment strategies in severe mental disorders: an overview         Catherine Harmer:         Can we integrate our understanding of pharmacological and psychological treatments in depression?         Q&A         Q&A         Mari Nerhus:         Targeting treatment with vitamin D supplementation in psychotic disorders         Coffee break         Novin Balafkan:         Mapping genes associated with heterogeneity in response to antipsychotics         Marco Hirnstein:         Is non-invasive brain stimulation effective treatment against schizophrenia?  | 13:30 - 14:00<br>14:00 - 14:15<br>14:15 - 14:25<br>14:25 - 14:30 | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health seque<br>covid-19<br>Q&A<br>Closing session:<br>Moderator: Ole Andreassen<br>Peter Falkai:<br>Comments from the Scientific Ad<br>Committee, and announcemen<br>poster prizes.<br>Ole A. Andreassen:<br>Conclusive remarks and<br>closing of meeting |
| 13:10 - 13:30 $13:30 - 14:00$ $13:30 - 14:00$ $14:10 - 14:30$ $14:30 - 14:45$ $14:45 - 15:05$ $15:05 - 15:25$ $15:25 - 15:30$ | Moderator: Erik Johnsen:         Erik Johnsen:         Emerging biological treatment strategies in severe mental disorders: an overview         Catherine Harmer:         Can we integrate our understanding of pharmacological and psychological treatments in depression?         Q&A         Q&A         Mari Nerhus:         Targeting treatment with vitamin D supplementation in psychotic disorders         Coffee break         Novin Balafkan:         Mapping genes associated with heterogeneity in response to antipsychotics         Marco Hirnstein:         Is non-invasive brain stimulation effective treatment against schizophrenia?         Committee - Erik Johnsen:         Conclusive remarks day 1 | 13:30 - 14:00<br>14:00 - 14:15<br>14:15 - 14:25<br>14:25 - 14:30 | Unnur Valdimarsdóttir:<br>COVIDMENT: an international res<br>consortium on mental health seque<br>covid-19<br>Q&A<br>Closing session:<br>Moderator: Ole Andreassen<br>Peter Falkai:<br>Comments from the Scientific Ad<br>Committee, and announcemen<br>poster prizes.<br>Ole A. Andreassen:<br>Conclusive remarks and<br>closing of meeting |

| Session 3: Po  | blitics, society and clinical implications<br>Moderator: Marit Haram   |  |  |  |  |  |
|--|--|--|--|--|--|--|
| 09:10 - 09:40  | Ole Johan Borge:<br>Future mental health research funding<br>in Norway: priorities and opportunities                 |  |  |  |  |  |
| 09:40 - 09:55  | Q&A  |  |  |  |  |  |
| 09:55 - 10:15  | Andreas Ringen:<br>Research possibilities in the clinic  |  |  |  |  |  |
| 10:15 - 10:35  | Martin Tesli:<br>The socioeconomic environment and<br>mortality in schizophrenia                                     |  |  |  |  |  |
| 10:35 - 10:45  | Coffee break   |  |  |  |  |  |
| 10:45 - 12:15  | Social session - Escape room:<br>Pegasus project<br>Moderator: Carla P.D. Fernandes                                  |  |  |  |  |  |
| 12:15 - 12:45  | Lunch break  |  |  |  |  |  |
| Session 4: Global science and international networks<br>Moderator: Lars T. Westlye |  |  |  |  |  |  |
| 12:45 - 13:15  | Dan Stein:<br>Global mental health and clinical<br>neuroscience: Potential synergies                                 |  |  |  |  |  |
| 13:15 - 13:30  | Q&A  |  |  |  |  |  |
| 13:30 - 14:00  | Unnur Valdimarsdóttir:<br>COVIDMENT: an international research<br>consortium on mental health sequels of<br>covid-19 |  |  |  |  |  |
| 14:00 - 14:15  | Q&A  |  |  |  |  |  |
| 1  | Closing session:<br>Moderator: Ole Andreassen  |  |  |  |  |  |
| 14:15 - 14:25  | Peter Falkai:<br>Comments from the Scientific Advisory<br>Committee, and announcement of<br>poster prizes.           |  |  |  |  |  |
|  | Ole A. Andreassen:   |  |  |  |  |  |

## Annual Retreat 2021 Poster Session 16 September

Other posters that were presented at the retreat (See the winning posters on page 49)

Aihua Lin: Distributed meta-analysis of genomewide association data with multivariate omnibus statistical tool (Meta-MOSTest).

Alina Marie Sartorius: An annotated evolutionary timeline of the oxytocin signaling pathway.

Andreas Dahl: Poor EURO 2020 predictive ability in a sample of healthy NORMENT researchers.

Beathe Haatveit: Inter-individual heterogeneity in cognitive performance across multiple domains among patients with schizophrenia and bipolar spectrum disorder.

Christina Bell: Differences in PCL-R facet scores between violent individuals with and without psychosis.

Claudia Barth: Sex differences in hippocampal subfield volumes and relationship to testosterone measures in schizophrenia and bipolar disorder.

Dani Beck: Adipose tissue distribution from body MRI is associated with cross-sectional and longitudinal brain age in adults.

Esten Leonardsen: Deep learning models learn general and disease-relevant representations of the ageing brain based on T1-weighted MRI data.

Jonelle Villar: Overlooking time-of-blood draw may lead to false associations in omics studies.

Laura Wortinger: Birth asphyxia is associated with white matter microstructural differences in the posterior limb of the internal capsule of patients with schizophrenia and bipolar disorders.

Linn Norbom: Maturation of cortical microstructure and cognitive development in childhood and adolescence: A T1w/T2w ratio MRI study.

Maren F. Werner: Limited association between infections, autoimmune disease and genetic risk and immune activation in severe mental disorders.



Margrethe Collier Høegh: Affective lability and social functioning across psychosis spectrum disorders.

Martina J. Lund: Brain age prediction using fMRI network coupling in youths and associations with psychiatric symptoms.

Monica B. E. G. Ormerod: Compound immune indices associated with severe mental disorders and prognostic characteristics.

Nora Refsum Bakken: Childhood trajectories of temperament and mental health problems to emotional disorders in adolescence.

Petros Drosos: Trajectories and predictors of outcome in schizophrenia: the beneficial role of amisulpride.

Petter Jakobsen: Motor activity analyses distinguish manic and euthymic mood states in bipolar disorder.

Pierre Berthet: Normative modelling of longitudinal cortical thickness measures in TOP.

Renata Alisauskiene: The influence of substance use on the effectiveness of amisulpride, olanzapine and aripiprazole: A pragmatic, randomized study.

Rikka Kjelkenes: Mapping normative trajectories of cognitive performance and its relation to psychopathology and polygenic scores in youth.

Sara Fernández: Multimodal imaging markers of the polygenic risk for mental disorders in youth.

Shahram Bahrami: Distributed genetic architecture across the hippocampal formation implies common neuropathology across major brain disorders.

Thomas Wolfers: Normative analytics for family structures.

Tiril Pedersen Gurholt: Population-based body-brain mapping links brain morphology with anthropometrics and body composition.

Torgeir Moberget: The genetic architecture of human cerebellar morphology.



# PhD Dissertations in 2021

## 7 PhD students at NORMENT defended their doctoral thesis during 2021:



Ingrid Hartveit Svendsen: Basic self-disturbances in first

treated psychosis - A seven-year follow-up study. An exploration of stability, impact on recovery and sense of coherence. Supervisor: Ingrid Melle. Jan 18, 2021.



Lynn Marquardt: tDCS as treatment in neuro-psychiatric disorders. The underlying neuronal mechanisms of tDCS treatment of auditory verbal hallucinations. Supervisor: Marco

Hirnstein. Feb 4, 2021.



**Kirsten Wedervang-Resell:** Immune and metabolic markers in early-onset psychosis. Supervisor: Anne Margrethe Myhre. May 7, 2021.





Isabella Kusztrits: About psychotic-like experiences and auditory verbal hallucinations. Transdiagnostic investigations of neurobiological, cognitive, and emotional aspects of a continuous phenomenon. Supervisor: Marco Hirnstein. Mar 19, 2021

Jannicke Fjæra Laskemoen:

sen. Jan 22, 2021.

Sleep disturbances in schizophre-

nia spectrum and bipolar disor-

ders. Supervisor: Carmen Simon-



### Dani Beck:

Cardiometabolic health and the ageing brain: Using brain and body MRI to elucidate the body-brain axis in healthy adults. Supervisor: Lars Tjelta Westlye. Oct 5, 2021.



(2013-2016 dissertations can be found in the 2018 Annual Report)

### 2017

Kristina Skåtun: Abnormal brain connectivity in schizophrenia and bipolar disorder – a resting state functional MRI study, supervisor: Lars T. Westlye, January 19, 2017

Mari Nerhus: Migration and Vitamin D in psychotic disorders - A cross sectional study of clinical and cognitive correlates, supervisor: Ingrid Melle, March 3, 2017

Marit Haram: The relationship between oxytocin pathway genes and personality traits and psychosis characteristics, supervisor: Martin Tesli, June 1, 2017

Kjetil Nordbø Jørgensen: Understanding brain structure alterations in severe mental disorders: The influence of cigarette smoking, antipsychotic medication and weight gain, supervisor: Ingrid Agartz, June 20, 2017

Beathe Haatveit: Executive functioning in schizophrenia spectrum disorders: Methods of measurement and longitudinal course, supervisor: Torill Ueland, August 22, 2017

Lynn Mørch-Johnsen: Brain structure imaging of apathy and auditory hallucinations in psychotic disorders, supervisor: Ingrid Agartz, December 1, 2017

Tiril Østefjells: Metacognition in severe mental disorders, supervisor: Jan Ivar Røssberg, December 7, 2017

Levi Kvitland: Cannabis use in the early phase of bipolar disorder. A naturalistic longitudinal study of a first treatment sample, supervisor:Petter Andreas Ringen, December 8, 2017

### 2018

Ragni Mørch: Inflammatory pathways in severe mental disorder a transdiagnostic approach, supervisor: Ole A. Andreassen, May 15, 2018

Erlend Strand Gardsjord: Subjective quality of life in first episode psychosis - A 10-year follow-up study, supervisor: Jan Ivar Røssberg, September 20, 2018

Niladri Banerjee: An evolutionary epigenetics approach to schizophrenia, supervisor: Stephanie Le Hellard, September 28, 2018

Christine Demmo: Neurocognitive functioning, clinical course and functional outcome in the early phase of bipolar I disorder: A prospective longitudinal study, supervisor: Torill Ueland, October 25, 2018



### Linn Rødevand:

Cardiovascular disease risk across psychosocial and genetic factors in severe mental disorders. Supervisor: Ole Andreassen. Dec 3, 2021.

> 50 people have so far completed their PhDs at the Centre



### 2019

- Nathalia Zak: A longitudinal investigation of cortical plasticity and structure in bipolar disorder type II, supervisor: Torbjørn Elvsåshagen, May 13, 2019
- Trude Jahr Vedal: The side effect burden of antipsychotic drugs A naturalistic study with focus on metabolic disturbance, supervisor: Erik G. Jönsson, May 31, 2019
- Saurabh Srinivasan: A Polygenic Enrichment Approach to Human Evolution in Schizophrenia and Cognitive Function, supervisor: Ole A. Andreassen, June 13, 2019
- **Gerard Dwyer:** New approaches to the use of magnetic resonance spectroscopy for investigating the pathophysiol ogy of auditory -verbal hallucinations, supervisor: Renate Grüner, October 9, 2019
- Runar Elle Smelror: Cognitive and clinical characteristics in adolescent non-affective early-onset psychosis and healthy controls, supervisor: Ingrid Agartz, November 8, 2019
- Geneviève Richard: Identifying markers of brain health and plasticity: A neuroimaging and behavioral study of cognitive aging and cognitive training following stroke, supervisor: Lars T. Westlye, November 11, 2019
- Linn Norbom: The illumination of the developing brain, Using MRI signal intensity contrasts to probe microstructural brain maturation, and associations with psychopathology and cognition, supervisor: Christian K. Tamnes, November 28, 2019
- Farivar Fathian: C-reactive protein in schizophrenia-spectrum disorders; relationship to cognitive functions and medications, supervisor: Erik Johnsen, December 5, 2019
- Luigi Maglanoc: Elucidating depression heteroge neity using clinical, neuroimaging and genetic data, supervisor: Lars T. Westlye, December 6, 2019

### 2020

- Priyanthi Borgen Gjerde: Lipid effects during antipsychotic drug treatment and their relevance for clinical outcomes. Supervior: Vidar M. Steen, January 29, 2020
- Ibrahim Akkouh: Transcriptional Modeling of Severe Mental Illnesses. Supervisor: Srdjan Djurovic, May 6, 2020
- Eirik Kjelby: Depressive symptoms in psychotic disorders: Trajectories of depression and antidepressive effectiveness of antipsychotic medication. Supervisor: Erik Johnsen, October 16, 2020
- Tone Elise Gjøtterud Henriksen: Blue-blocking glasses as adjunctive treatment for bipolar mania - and exploration of motor activity patterns in serious mental disorders. Supervisor: Anders Lund. October 23, 2020.

# International Collaboration

The research at NORMENT requires close cooperation with leading research environments, both nationally and internationally. Researchers at the Centre collaborate with a large number of researchers abroad (see page 58), participate in a series of international networks and consortia (see page 59), and have several bilateral research programs with international institutions, mainly in Europe and the USA. During the years, our international collaborations have resulted in a number of important scientific findings. NORMENT also actively recruits excellent researchers from other countries through international advertisements and networking, and as a result the Centre staff now consist of people from 32 nationalities.

We participate in several working groups of the Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA) consortium. In 2021, Professor Ingrid Agartz chaired the Early Onset Psychosis Working Group, while Researcher Clauda Barth was co-chair. Professor Ole A. Andreassen and Researcher Ida Sønderby co-chaired the CNV Working Group, and Andreassen was also co-chair of the Bipolar Disorder Working Group. Researcher Dag Alnæs coordinated the ENIGMA activities at NORMENT. As part of this consortium in 2021, Ida Sønderby was leading author on two studies of copy number variants and their associations with cerebral and cognitive alterations in humans (Translational Psychiatry) and effects on brain structure and risk for psychiatric illness (Human Brain Mapping).

We also contributed to several other ENIGMA papers, including studies on longitudinal structural brain changes in bipolar disorder (Abé et al., Biological Psychiatry) and associations of structural magnetic resonance imaging measures with psychosis onset in individuals at clinical high risk for developing psychosis (ENIGMA Clinical High Risk for Psychosis Working Group et al., JAMA Psychiatry).

Another important international network is the Psychiatric Genomics Consortium (PGC). Professor Ole A. Andreassen continued chairing the PGC Bipolar Disorders Working Group in 2021 and headed a large genome-wide association study of more than 40,000 people with bipolar disorder (Nature Genetics). Researchers at the Centre were also involved in several other PGC papers published in 2021, including studies of polygenic score methods for psychiatric disorders (Ni et al., Biological Psychiatry), sex-dependent shared and nonshared genetic architecture across mood and psychotic disorders (Blokland et al., Biological Psychiatry), and genetic variants in Alzheimer's disease (Wightman et al. Nature Genetics, de Rojas et al., Nature Communications). In addition, NORMENT researchers contributed with analytical expertise and data to several working groups of the PGC.

### **Guest Researchers**

Two international guest researchers had part-time positions at NORMENT in 2021 and collaborated closely with researchers at the Centre. Professors Anders M. Dale and Tyler Seibert from the University of California San Diego, USA, contributed with knowledge and analyses, participated in project discussions, and were involved in planning of future studies with our researchers.

Fortunately, despite strict travel restrictions during the pandemic, one of our guest researchers was able to visit NORMENT in 2021. Professor Anders M. Dale paid a visit to the Centre in July and participated on a Statistical Genetics Seminar, and a series of project meetings. Professor Ole Andreassen and Researcher Oleksandr Frei visited San Diego in November 2021, and we also had extensive interactions on Zoom meetings.

### **Visits Abroad**

As part of our international collaboration, we emphasize the mobility of PhD students, postdoctoral fellows and senior scientists exchanged with a diversity of countries. Due to the ongoing pandemic, most of the conferences and seminars have been attended digitally, and the mobility of NORMENT employees continued on a low level in 2021. However, some were able to travel in the periods with less strict travel restrictions. Sadaf Ghorbani visited Kirsten Brennand's lab at Yale, USA, for six months from July 2021 to January 2022, to exchange research and learn new techniques. Novin Balafkan visited Karolinska Stem Cell Core Facility, Karolinska Institutet, Sweden, for one month in October 2021, to establish long-term collaboration and gain an overview of the process taking place at a stem cell core facility.

Other people also had shorter stays abroad, to discuss collaborative projects and participate in project meetings. Some examples are shown below:

Dag Alnæs visited the Lifespan Neural Dynamics Group (LNDG), Centre for Lifespan Psychology, Max Planck Institute for Human Development, Germany, in October.

Ole A. Andreassen had a project meeting with Professor Stefansson at DeCODE genetics in December.

Ole A. Andreassen and Oleksandr Frei visited our guest researcher Anders Dale at UCSD, USA in November, to join a recent methods development project in imaging genetics led by NORMENT collaborators at UCSD.

Stéphanie Le Hellard visited Professor Marion Leboyer at IMRB – Inserm U955, Paris, in July to establish a collaboration on cannabis studies.

Trine Vik Lagerberg and colleagues visited INSERM, Hopital Fernand-Widal, Paris as part of the ongoing INTPART project.

Lena Stabell visited Peter Hjort at the University of Southern Denmark, in December.

### **Visits from Abroad**

Another part of our international involvement is to host students from European countries for internships and training. Hannah Oppenheimer from the University of Constance, Germany, and Johanna Jetter from the University of Dresden, Germany, visited the Multimodal Imaging group as research interns in the BRAINMINT project from October 2020 to February 2021 and from August to October 2021, respectively. In November 2021, PhD students Anna Krogh Andreassen and Christina Bruun Knudsen from the Via 11-study at Aarhus University, Denmark, visited the Cognitive mechanisms and outcome group for one month. Clara Chretienneau a Master student supervised by Romain Icick (INSERM and Hopitaux de Paris, France), came to Bergen in August to work in the group of Stephanie Le Hellard for a month.

During a normal year, NORMENT would have received regular visits from international researchers coming for project meetings, collaborative discussions and to give guest lectures. Due to the pandemic, most of these visits have been transferred to regular meetings on Zoom or other digital platforms. However, PhD student Anne Emilie Stürup from the Psychiatric Center Copenhagen, Denmark, had a short stay with the Pharmacology and intervention group in Bergen in October, where she gave a lecture on "Treatment of psychosis without use of antipsychotic drugs."

Some digital guest lectures are mentioned below:

Professor Cathryn Lewis gave a keynote lecture titled "Discoveries in depression" during the CoMorMent Annual Meeting on January 25, 2021.

Vinod Kumar from the Max Planck Institute for Biological Cybernetics, Germany, gave a talk to the Multimodal imaging group meeting about the functional and structural organization of thalamus, on March 15.

Several international keynote speakers were invited to give talks during the event "Precision Psychiatry: Combining big data with stem cells" hosted by the 4MENT project during Oslo Life Science Conference 2021, on February 17. Dr. Andre Marquand from the Donders Institute for Brain, Cognition and Behaviour, gave a talk on how to use machine learning and big data neuroscience to move toward precision medicine. Associate Professor Emanuel Schwarz from Central Institute of Mental Health in Mannheim gave presentation on systems medicine and artificial intelligence, and Dr. Weihua Yue from Peking University, China gave talk about pharmacogenomic study of antipsychotic medicines treatment in patients with schizophrenia.



Andre Marquand giving a talk at the Life Science Conference



Cathryn Lewis giving a keynote lecture at the CoMorMent Annual Meeting.

### CoMorMent: Investigating comorbid mental illness and cardiovascular disease

The CoMorMent project is funded by the EU Horizon 2020 programme and investigates how and why mental illness interacts with cardiovascular disease. The project started in 2020 and is led and coordinated by NORMENT and the University of Oslo. Partners in the project are from Iceland (Islensk Erfdagreining EHF), Denmark (Region Hovedstaden), Sweden (Karolinska Institutet, Amra Medical AB), UK (University of Edinburgh), Estonia (Tartu Ulikool), and the USA (Multimodal Imaging Services Corporation, dba HealthLytix).

The project takes on a big data approach, using information from 1.8 million volunteers from across Northern Europe, with the aim to identify the genetic, brain and body markers that are common in both cardiovascular and mental health conditions, thus uncovering the mechanisms underlying the higher incidence of cardiovascular disease in people with mental disorders.

So far, the project has produced several interesting results. A genetic analysis has identified shared genetic factors between loneliness, severe mental disorders and cardiovascular disease risk factors, indicating that part of the mechanism underlying the co-morbidity may be influenced by genetic factors (Rødevand et al., Translational Psychiatry). Interestingly, some of these overlapping factors were biological processed related to the brain, the epigenetic and immune system.

A key tool of the project is the development of "distributed containers". This tool allows for analysis of data in the same way across countries without sharing of sensitive data. This protects the data security of the research participants while allowing for complex data analysis. Diagnosis data has been harmonized across countries, which is of importance since different diagnostic codes have been used in the different countries over the years. Preliminary analyses indicate the validity of the harmonization given a similar distribution of ICD-codes (diagnoses) in similar cohorts in different countries. The project has also established a pan-European Stakeholder Forum which gives input to the research and participates at annual meetings.

In the coming years, the project will focus on generating new knowledge about comorbid cardiovascular disease in mental illness. One aspect is to identify longitudinal development of mental disorders in relation to the increased risk of cardiovascular diseases. The project will continue until June 2024.

Read more: https://www.comorment.uio.no/





Screenshot from the Annual CoMorMent meeting, Jan 25, 2021.

<u>REALMENT: Using real-world big data from eHealth, biobanks and national registries, integrated with clinical</u> <u>trial data to improve outcome of severe mental disorders</u>

In 2021, a new EU project started up which is led and coordinated by NORMENT and University of Oslo. The REALMENT project is funded by the EU Horizon 2020 programme for 4 years and will investigate how real-world data can be used to improve the treatment of mental disorders.

Project partners are from Sweden (Karolinska Institutet), Denmark (Region Hovedstaden), Iceland (deCODE Genetics), Finland (University of Helsinki), Estonia (University of Tartu), Italy (University of Bari), UK (Cardiff University), the Netherlands (Vrije Universiteit, Stichting Buro ECNP), the USA (CorTechs Labs), Belgium (Janssen Pharmaceuticals), and Norway (Smerud Medical Research Int AS, DNV-GL). The main aim of the project is to optimize the treatment of mental disorders through novel precision medicine strategies based on current pharmaceutical options. REALMENT will achieve its objectives by exploiting population-scale real-world data in combination with randomized clinical trial (RCT) data available to the partners. Big data from populations (Nordic registries), cohorts (European biobanks), and eHealth samples (medical records), including whole genome genotypes, will be analyzed in an EU-wide sustainable infrastructure using artificial intelligence and machine learning to develop prediction and stratification tools (precision psychiatry). These algorithms will be validated in large RCT data and rephenotyping projects and implemented in a clinical management platform, which will be made available to provide decision support to clinicians to optimize therapeutic effects.

Read more: <u>https://www.realment.uio.no/</u>



### <u>R-LiNK: Response to Lithium Network</u>

R-LiNK is an EU funded project that started in 2018. The project is coordinated by INSERM, France, and is based on a collaboration between several countries and recruiting centres across Europe. These include France (Paris, Besancon), Italy (Milano, Brescia), Spain (Barcelona), Denmark (Copenhagen), Sweden (Gothenburg), Norway (Oslo, Bergen), United Kingdom (London, Newcastle), and Germany (Dresden, Frankfurt, Munich).

The main objective of the project is to identify the eligibility criteria for treatment with Lithium in people with bipolar 1 disorder in terms of response, safety and tolerability. R-LiNK proposes a pragmatic study of individuals with bipolar 1 disorder when Lithium treatment is initiated. The aim is to identify early biomarkers to stratify individuals with the disorder according to their response to Lithium assessed prospectively.

This entails detailed assessments before and after Lithium initiation, and a follow up of all participants two years from the date of inclusion. In addition, the participants are asked to monitor their medication adherence using an interactive package that allows for self-rating of mental state and offer reminders during the whole study period.

Due to strict inclusion criteria, the first Norwegian patient was included in the study in the spring of 2021. In total, Oslo and Bergen currently have seven participants who are followed in the study. Each partner will continue including participants until the summer of 2022.

Read more: https://rlink.eu.com/





Screenshot from the REALMENT kick-off meeting, June 22, 2021.



### **INTPART Projects**

Researchers at NORMENT are currently involved in three INTPART projects funded by the Research Council of Norway. INTPART is a research programme for International Partnerships for Excellent Education, Research and Innovation, and promotes the development of long-term relations between Norwegian higher education and research institutions and strong research groups and institutions in priority partner countries. As part of this programme, we have collaborations with researchers in South Africa (Cape Town), France (Paris), and USA (San Diego).

# INTPART South Africa: Integrating global mental health with brain imaging and genetics in mental illness research and education

This collaborative project including NORMENT and the University of Cape Town (UCT) started in 2018. The main purpose of the project is to combine and integrate mental health research across sites and to educate researchers in modern imaging, genetic tools and transcultural clinical expertise. Principal investigators are Professor Ole A. Andreassen at NORMENT and Professor Dan Stein, Head of the Brain Behaviour Unit at the University of Cape Town.

Due to the corona pandemic, all project activities were moved to digital platforms, including student supervision and data analysis. To enable access for NORMENT students to South African data and improve training of UCT students, travel funds were allocated to the development of a secure data storage system for the project in Cape Town. During the project period, NORMENT and UCT have collaborated successfully and established concrete research education and training projects. PhD student Mary Mufford is now in the final stages of her project and Master's student Meghan Campbell finished her project in 2021. Both will start in new research positions at UCT and continue their close collaboration with researchers at NORMENT.

# INTPART France: Improving clinical services in bipolar disorder through education and research on illness mechanisms

The project started in 2019 and builds on a long-term collaboration between researchers at NORMENT and INSERM/ University of Paris. The current project focuses on clinical aspects of bipolar disorder, and the main aims are to provide better integration of research and clinical services, investigate early illness phases while providing front-line treatment, using new digital tools in data collection and clinical intervention, and to investigate underlying illness mechanisms including circadian rhythms and lithium response. Principal investigators are Senior researcher Trine Vik Lagerberg at NORMENT and Professor Bruno Etain from INSERM and the University of Paris.

In 2021, Thomas D. Bjella, Margrethe Høegh, Stephanie Le Hellard, Trine Vik Lagerberg, Ingrid Melle and Stine Holmstul Olsen visited Professor Bruno Etain and colleagues for the yearly project meeting at INSERM, Hopital Fernand-Widal, in October.



Photos from the yearly project meeting at INSERM in France, Oct, 2021.

### INTPART USA: Simulating the multi-scale pathophysiology of mental illness

NORMENT has collaborated closely with researchers at the University of California, San Diego for several years. The current INTPART project started in 2019 and is an extension of this collaborative effort, now focusing on multidisciplinary neuroscience. The primary objective is to enhance the existing interdisciplinary synergy between sites, improve tools and approaches for understanding mental disease, and educate translational researchers to address questions that require integration of big data (genomics) with clinical measurements of function. This project is headed by the Simula Research Laboratory in Oslo and also includes the Centre for Integrative Neuroplasticity (CINPLA) at the University of Oslo.

In 2021, Professor Anders M. Dale visited NORMENT in July, and Professor Ole Andreassen and Researcher Oleksandr Frei visited San Diego in November. The scientific activities in the project is high, with a large number of scientists involved, and more than 30 co-authored publications in 2021.

### **COVID-19 Projects**

The outbreak of the corona virus in early 2020 suddenly changed the lives of people all over the world. Almost two years later, we know that this long-lasting pandemic has had profound effects on both people and societies. However, we still have limited knowledge about long-term consequences of lockdowns, closed schools and workplaces, social distancing and isolation. Here, research is of high importance, and during 2021 NORMENT researchers have increasingly been involved in projects related to mental health and the pandemic. Some of these projects are described below.

### **COVIDMENT: The pandemic in Nordic countries**

The COVIDMENT project is a Nordic collaboration between Iceland, Sweden, Norway, Denmark and Estonia. The aim of the project is to investigate the role of pre-existing psychiatric disorders in risk and severity of a COVID-19 infection, and how COVID-19 infection affects mental health. Through comparisons of the different countries' handling of the pandemic, the researchers will investigate the short- and long-term effects of the pandemic on psychiatric illness trajectories.

### BryDeg2020: How does the pandemic affect people in Norway?

The Norwegian study BryDeg2020 led by the University of Bergen investigates how the COVID-19 pandemic affects coping and development of mental illness amongst adults, with a special focus on students. The goal is to gain increased knowledge about the factors underlying development of mental illness.



### COPE psychosis-bipolar: Psychotic disorders and corona

The COPE psychosis-bipolar study headed by the Early Detection in Psychosis Unit at Oslo University Hospital (TIPS Sør-Øst) investigates how people with psychosis or bipolar disorder are coping during the pandemic, and how the health care services can provide the best possible help during such crises.

### **Publications**

NORMENT researchers also contributed to several scientific publications related to the COVID-19 pandemic:

Hagen et al.: Mental health symptoms during the first months of the COVID-19 outbreak in Norway: A cross-sectional survey study (Scand J Public Health).

Heilbronner et al.: Interplay between the genetics of personality traits, severe psychiatric disorders and COVID-19 host genetics in the susceptibility to SARS-CoV-2 infection (BJPsych Open).

Monereo-Sánchez et al.: Diphtheria and tetanus vaccination history is associated with lower odds of COVID-19 Hospitalization (Front Immunol).

Reininghaus et al.: Outcomes associated with different vaccines in individuals with bipolar disorder and impact on the current COVID-19 pandemic- a systematic review (Eur Neuropsychopharmacol).

Unnarsdóttir et al.: COVIDMENT: COVID-19 cohorts on mental health across six nations (Int J Epidemiology).



### International Collaborators

### **Nordic Countries**

Denmark

- Anders Børglum, Professor, University of Aarhus, Aarhus
- Christian Gerlach, Professor, University of Southern Denmark, Odense
- Maria Faurholt-Jepsen, Associate Professor, University of Copenhagen
- Randi Starrfelt, Professor, University of Copenhagen
- Thomas Werge, Professor, iPSYCH and Mental Health Centre Sct. Hans, Copenhagen

### Iceland

- Hreinn Stefansson, Head of CNS Department, deCODE genetics, Reykjavik
- Kari Stefansson, CEO deCODE Genetics, Reykjavik
- Unnur Valdimarsdottir, University of Iceland, Karolinska Institutet, Sweden

### Sweden

- Anna Falk, Assoc. Professor, Karolinska Institutet, Stockholm
- Göran Engberg, Professor, Karolinska Institutet, Stockholm
- Hannes Bohman, Uppsala University
- Henrik Zetterberg, University of Gothenburg
- Kaj Blennow, Professor, University of Gothenburg
- Lars Farde, Professor, Karolinska Institutet, Stockholm
- Lars Nyberg, Professor, University of Umeå
- Mathias Lundberg, Uppsala University
- Mikael Landén, Professor, University of Gothenburg
- Patrick F. Sullivan, Professor, Karolinska Institutet, Stockholm
   Simon Cervenka, Assoc. Professor, Karolinska Institutet,
- Stockholm
  Sophie Erhardt, Professor, Karolinska Institutet, Stockholm
- Susanna Radovic, Assoc. Professor, University of Gothenburg

### Finland

 Aarno Palotie, Professor, Research Director, Institute for Molecular Medicine Finland, Helsinki

### ....

Europe

### Austria

- Maria Rettenbacher, Assoc. Professor, Medizinische Universität Innsbruck, Innsbruck
- W. Wolfgang Fleischhacker, Professor, Medizinische Universität Innsbruck

### Estonia

- Lili Milani, University of Tartu, Estonian Genome Center
- France
- Bruno Etain, Senior Scientist, Hôpital Henri Mondor-Chenevier, Creteil
- Chantal Henry, Professor, Hôpital Henri Mondor-Chenevier, Creteil
- Frank Bellivier, Professor, Université Denis Diderot, Paris
- Romain Icick, MD, PhD, Institut Pasteur, Paris, France
- Marion Leboyer, IMRB Inserm U955, NeuroPsychiatrie Translationnelle, Faculté de Santé de Créteil, Créteil
- Michel Thiebaut de Schotten, Associate Professor, Bordeaux Neurocampus, Bordeaux

### Germany

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 Andreas Meyer-Lindenberg, Professor, University Medical Centre Mannheim

- Douglas Garrett, Senior Researcher, Max Planck Institute for Human Development, Berlin
- Emanuel Schwarz, Research Associate, Central Institute of Mental Health, Mannheim
- Falk Kiefer, Professor, Central Institute of Mental Health, Mannheim
- Franziska Degenhardt, Principal Investigator, Kliniken und Institut der Universität Duisburg-Essen
- Marcella Rietschel, Professor, Central Institute of Mental Health, Mannheim
- Markus Nöthen, Professor, University of Bonn
- Michael Peitz, Professor, University of Bonn
- Peter Falkai, Dept of Psychiatry and Psychotherapy, LMU Munich
- Tania Lincoln, Professor, Hamborg University
   Thomas G. Schültze, Institute of Psychiatric Phenomics and Genomics, LMU Munich
- Vadim V. Nikulin, Principal Investigator, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig

### Italy

- Alessandro Bertolino, Professor, University of Bari
- Armida Mucci, Assoc. Professor, University of Naples
   Francesco Benedetti, Director, San Raffaele Scientific
- Institute, Milan
- Mirko Manchio, Ass Prof, Section of Psychiatry, Department of Medical Sciences and Public Health, University of Cagliari
- Patrizia Capolongo, Professor, University of Roma
- Silvana Galderisi, Professor, University of Naples

### Netherlands

- Andre Aleman, Professor, Groningen UMC
- Andre Marquand, Donders Institute
- Danielle Posthuma, Professor, Vrije Universiteit, Amsterdam
   Dirk J. A. Smit, Amsterdam UMC
- Dirk Schubert, Professor, Utrecht University Medical Center
- Iris Sommer, Professor, Utrecth University Medical Center
- Marie-Josè van Tol, Senior Scientist, University of Groningen
- Vivi Heine, Professor, Vrije Universiteit, Amsterdam

### Spain

- Eduard Vieta, Professor, Hospital Clinic, Institute of Neuroscience, University of Barcelona, Barcelona, Catalonia
- Mazahir Hasan, Research Professor, Achucarro Basque Center for Neuroscience, Bilbao
- Miguel Lopez, Senior Research Scientist, University of Santiago de Compostela

### Switzerland

- Ahmad Abu-Akel, Professor, University of Lausanne
- Narly Golestani, Professor, University of Geneva
- Stefan Borgwardt, Professor, University of Basel
- Stefan Kaiser, Professor, University of Geneva
- Sven Cichon, Professor, University of Basel

### United Kingdom

- Adrian J. Harwood, Professor, Cardiff University
- Allan Young, Institute of Psychiatry, Psychology & Neuroscience, King's College London
- Andrew MacIntosh, Professor, University of Edinburgh
- Angela Vincent, Professor Emeritus, University of Oxford
- Clara Strauss, Honorary Senior Lecturer, Sussex University, Brighton
- Eilis Hannon, Complex Disease Epigenetics Group, University of Exeter
- Guy Goodwin, Professor em, University of Oxford
- Gwenaëlle Douaud, Assoc. Professor, University of Oxford

- Ian Apperly, Professor, University of Birmingham
- Jonathan Mill, Complex Disease Epigenetics Group, University of Exeter
- James Walters, Professor, Cardiff University
- Michael O'Donovan, Professor, Cardiff University
- Stephen Smith, Professor, Oxford University

### USA

- Anders M. Dale, Professor, UCSD, San Diego
- Anna Devor, Associate Professor, UCSD, San Diego
   Elizabeth Bromley, Associate Professor, Semel Institute for
- Elizabeth Bromley, Associate Professor, seme institute for Neuroscience and Human Behavior, UCLA, Los Angeles
   Hauke Bartsch, USCD, San Diego

Judith M. Ford, Professor, Laboratory of Clinical and Cognitive

Kathleen Merikangas, Professor, National Institute of Mental

Kerry Ressler, Professor, McLean Hospital, Harvard Medical

Kristen Brennand, Associate Professor, Division of Molecular

Niamh Mullins, Associate Professor, Ichan School of Medicine

Ofer Pasternak, Associate Professor, Harvard Medical School,

Patrick Sullivan, Professor, University of North Carolina of

Rene Kahn, Professor, Icahn School of Medicine at Mount

Tetyana Zayats, Analytic and Translational Genetics Unit,

Wesley Thompson, Associate Professor, UCSD, San Diego

Sintia Belangero, Department of Morphology and Genetics,

Lakshmi Yatham, Professor, Department of Psychiatry,

Sheilagh Hodgkins, professor, University of Montreal

Alexander Melerzanov, Professor, Director of Medical

of the city of Moscow Research and Clinical Center for

Evgeny Burnaev, Professor, Research Center in Artificial

Maya Kulygina, Senior Researcher, V. Serbsky National

Research Centre of Psychiatry and Narcology, Moscow

Intelligence, Skolkovo Institute of Science and Technology,

Lev Brylev, Professor, Bujanov Moscow City Clinical Hospital

Oleg Papsuev, MD, PhD, V. Serbsky National Research Centre

Stephen Hart, Professor, Simon Fraser University, Burnaby

Systems Development, Artificial Intelligence Center, Moscow

Alla Guekht, Professor, State budgetary healthcare institution

Dmitry P. Vetrov - Bayesian Methods Research Group, Higher

University of British Columbia, Vancouver

Institute of Physics and Technology

of Psychiatry and Narcology, Moscow

Dan Stein, Professor, University of Cape Town

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Neuropsychiatry

Moscow

South Africa

Robert H. Yolken, Professor, Johns Hopkins School of

Tyler Seibert, Associate Professor, UCSD, San Diego

William Horan, Senior Scientist, UCLA, Los Angeles

Chi-Hua Chen, Associate Professor, UCSD, San Diego

Michael McCarthy, Associate Professor, UCSD, San Diego

John Kelsoe, Professor, UCSD, San Diego

Neuroscience, UCSF, San Francisco

Health, Bethesda

School, Boston

Boston

**Other Countries** 

Brasil

Canada

Russia

Psychiatry, Yale University

at Mount Sinai, New York

Chapel Hill, Chapel Hill

Sinai, New York

Medicine, New York

Steven Dilsaver, El Centro

Federal University of São Paulo

- Jordan Smoller, Professor, Harvard Medical School, Boston
- Joseph Ventura, Professor, UCLA, Los Angeles

Kent Kiehl, Professor, University of New Mexico

Melvin McInnis, Professor, University of Michigan

Paul Thompson, Professor, UCLA, Los Angeles

Susan McGurk, Professor, Boston University

Massachussets General Hospital, Boston

## **International Projects and Consortia**

- Bergen Global Mental Health Research Group
- BRAINCHART: Normative brain charting for predicting and stratifying psychosis
- <u>CHARGE Cohorts for Heart and Aging Research in Genomic</u> <u>Epidemiology</u>
- <u>COGENT Cognitive Genomics Consortium</u>
- <u>COMMITMENT COMorbidity Modeling via Integrative</u> <u>Transfer machine-learning in MENTal illness</u>
- <u>CoMorMent Predicting comorbid cardiovascular disease</u> in individuals with mental disorder by decoding disease mechanisms (EU Horizon 2020)
- <u>COST-MINDDS- Maximising Impact of Research in</u> <u>NeuroDevelopmental DisorderS</u>
- <u>ECNP Bipolar Disorder European College of</u> <u>Neuropsychopharmacology Bipolar Disorders Network</u> Ole A. Andreassen chairs the Bipolar Disorder Network
- <u>ECNP Schizophrenia European College of</u> <u>Neuropsychopharmacology Schizophrenia Network</u>
- EnGage . Enhancing Psychiatric Genetic Counselling, Testing and Training in Europe – COST Action CA17120
- ENIGMA Enhancing Neuro Imaging Genetics Through Meta Analysis Ingrid Agartz chairs the Early Onset Psychosis Working Group, Ole A. Andreassen co-chairs the Bipolar and CNV Working Groups, Ida E. Sønderby co-chairs the CNV Working Group
- EURICND European IPSC Consortium for Neuropsychiatric Disorders: Srdjan Djurovic chairs the consortium
- <u>EuroNES European Negative Symptoms Research Network</u>
- <u>GEMRIC The Global ECT-MRI Research Collaboration</u> Leif Oltedal coordinates the collaboration
- GenECTic Genomics of ECT-international consortium
- <u>HVN Hearing Voices Network</u>
- ICHR International Consortium on Hallucination Research
- IMAGEMEND Imaging Genetics for Mental Disorders
- <u>KaSP Karolinska Schizophrenia Project</u>
- <u>MINDDS Maximising Research Impact in</u> <u>Neurodevelopmental Disorders</u>
- PGBD Pharmacogenomics of Bipolar Disorder
- <u>PGC Psychiatric Genomics Consortium</u> Ole A. Andreassen chairs the Bipolar Disorder Working Group
- STRATA-G Schizophrenia: Treatment Resistance and Therapeutic Advances - Genetics
- <u>TRYGGVE 2 Nordic collaboration for sensitive data</u>

# Hvilken betydning har miljøfakto



# **Dissemination and Communication**

Dissemination is an important part of research. At NORMENT, we have a continuous focus on communicating our findings, not only to other researchers through publications in scientific journals and presentations at scientific conferences and meetings, but also to users and their families, health personnel, and the general public.

The Covid-19 pandemic continued to affect our dissemination activities, particularly due to cancelled international congresses. However, we managed to keep up the scientific production and present our research at several virtual conferences and meetings, as well as giving talks for health personnel and organizing digital events for the public. A selection of our dissemination activities in 2021 are listed on the following pages.

We actively use our website to share news and events, and researchers at the Centre contribute with texts about their research ("Månedens forsker") to reach out to a broader audience. Twitter is used to share news about publications, meetings, thesis defences, and other information related to science and mental disorders. At the end of 2021, NORMENT had about 950 followers on Twitter (increased from 800 in 2020).

We have also been on Facebook since March 2019. Our Facebook page is mainly targeted towards users, health personnel and the general public, and is mainly administrated by our User Representative. We actively use Facebook to share news and events from the Centre. More than 1200 people are now following us on Facebook (increased from 800 in 2020).

The NORMENT newsletter was launched in 2020, and is Other (41) targeted towards health personnel, research participants and the general public. During 2021, we distributed Conferences with NORMENT participation in 2021 guarterly newsletters to our 280 subscribers, with (67 oral presentations) information about research news, events and activities at the Centre, focusing on the applicability of our research. ECSR: European Consortium for Sociological Research The newsletter also includes presentations of each research WCPG: World Congress of Psychiatric Genetics group, a summary of their findings, and in what way the EPA: European Congress of Psychiatry research may be of importance for people with severe SOBP: Society of Biological Psychiatry mental disorders. SIRS: Schizophrenia International Research Society Conference ECNP: European College of Neuropsychopharmacology

- **185** Publications in scientific journals

International scientific presentations 86 (67 oral presentations, 19 posters)

- National scientific presentations 24 (20 oral presentations, 4 posters)

**58** Oral presentations for user organizations and health personnel



Oral presentations and other activities for the 26 general public



**39** News articles, interviews and feature articles in the media

Public events (see the following pages)

- ECSR (9)
- WCPG (5)
- EPA (5)
- SOBP (3)
- SIRS (2)
- ECNP (2)



## **Scientific Conferences and Meetings**

### Selected International Oral Presentations

**Aas, Monica:** GxE interactions in schizophrenia and bipolar disorders - an update from epidemiological studies", speaker and chair, Schizophrenia International Research Society conference (SIRS), digital, April 17-23, 2021.

**Aas, Monica:** Childhood adversity and the comorbidity between mood and general medical disorders: from associations to mechanisms, 21st World Congress of Psychiatry, digital, October 18-21, 2021.

Agartz, Ingrid: Birth asphyxia: Is there an area of prevention? Workshop at European Psychiatric Association (EPA), April, 2021.

Andreassen, Ole: COVID-19 the Scandinavian perspective, in symposium East Meets West: How did Psychiatric/ Mental Health Services Deal with the COVID-19 Pandemic? 29th European Congress of Psychiatry (EPA), April 11, 2021.

Andreassen, Ole: Bipolar Disorder: New Biological Insight and Potential Clinical Relevance From Large-Scale Genetic Studies, Society of Biological Psychiatry's 2021 Virtual Meeting, April 29 – May 1, 2021.

Andreassen, Ole: ENIGMA and the PGC: Converging Discoveries From Psychiatric and Neuroimaging Genomics, April 29 - May 1, 2021

Andreassen, Ole: The Psychiatric Genomics Consortium: Recent findings from large-scale genetic studies of bipolar disorder, 15th World Congress of Biological Psychiatry (WFSBP), June 2, 2021.

Andreassen, Ole: Dissecting genetic overlap between mental disorders and traits, plenary lectur, European College of Neuropsychopharmacology (ECNP), Lisbon, Portugal, October 4, 2021.

**Barth, Claudia:** Sex Differences in Hippocampal Subfield Volumes and Relationship to Testosterone Measures in Schizophrenia and Bipolar Disorders, European College of Neuropsychopharmacology (ECNP), Session Type: Poster Jam, Lisbon, Portugal, October 2-5, 2021.

**Cheng, Weiqiu:** Extensive polygenic overlap between major psychiatric disorders and brain morphology, World Congress of Psychiatric Genetics (WCPG) annual conference, virtual, October 12, 2021.

**de Lange, Ann-Marie:** Women's brain health; History, relevance, and future prospects, keynote speaker at the Annual Congress of the Swiss Neurological Society, Interlaken, Switzerland, November 18, 2021.

**Frei, Oleksandr:** <u>Polygenic overlap analysis with MiXeR</u>, World Congress of Psychiatric Genetics (WCPG) annual conference, virtual meeting, October 15, 2021 **Flaaten, Camilla Bärthel:** Long-term cognitive development in schizophrenia, Nordic Meeting in Neuropsychology, Copenhagen, Denmark, August 26, 2021

**Haatveit, Beathe:** Exploring the relationship between brain structure and symptom severity in psychotic disorders, 8th European Conference on Schizophrenia Research (ECSR), digital, September 24, 2021.

Haukvik, Unn Kristin: Chair of the session: Neuroimaging psychopathology in schizophrenia, European conference on schizophrenia research (ECSR), Berlin, online, April 9, 2021.

Jakobsen, Petter: The effects of light and light change on affective disorders, 29th European Conference of Psychiatry, virtual, April 11, 2021.

Johnsen, Erik: Amisulpride, aripiprazole, and olanzapine in patients with schizophrenia-spectrum disorders (BeSt InTro): a pragmatic, rater-blind, semi-randomized trial, SCNP, virtual meeting, June 3, 2021.

**Kaufmann, Tobias:** Polygenic Architecture of the Brain Functional Connectome and Overlap with Psychiatric Disorders, World Congress Psychiatry Genetics, online, October 12, 2021

Lagerberg, Trine Vik: Symposium: Trajectories of substance misuse and affective relapse in the early course of bipolar disorder, ISBD conference, virtual, May 15, 2021.

**Le Hellard, Stéphanie:** Epigenetic associations with Environmental Risk Factors for Mental Disorders, European Psychiatric Association, digital, April 12, 2021.

Lu, Li: Mental distress before and during the COVID-19 pandemic: latent class trajectory analyses from the Norwegian MoBa cohort, 2021 virtual workshop on the Research Response to COVID-19 in the Nordic Countries, November 4, 2021. (https://meetings.nshg-pm.org/2021covid19/)

**Melle, Ingrid:** Debate: Should Schizoaffective Disorder be Diagnosed Cross-Sectionally (ICD-11) instead of Longitudinally (DSM-5)? European Psychiatric Association 29th European Congress, Virtual, April 12, 2021.

**Melle, Ingrid:** Symposium presentation: The influence of childhood interpersonal trauma on premorbid adjustment, social cognition and outcome in psychosis, 8th ECSR, Virtual, September 25, 2021.



**Moberget, Torgeir:** The cerebellum and schizophrenia, The 11th International Symposium of the <u>Society for Research</u> on the Cerebellum and Ataxias: From J.E. Purkynë to the future, virtual, June 18-19, 2021

**Mørch-Johnsen, Lynn:** Thalamic nuclei volumes and their associations to psychotic symptomatology in schizophrenia and bipolar disorder, The 8th European Conference on Schizophrenia Research, digital symposium, September 24, 2021.

**O'Connell, Kevin:** Characterizing the Genetic Architecture of Bipolar Disorder in Ancestrally Diverse Clinical and Population Samples, World Congress of Psychiatric Genetics, Online, October 2021.

**Ottesen, Akiah:** Childhood trauma, antipsychotic medication, and symptom remission in first-episode psychosis, ECSR, virtual meeting, September 25, 2021.

Roelfs, Daniel: <u>Shared Genetic Determinants Between the</u> <u>Brain Functional Connectome and Psychiatric Disorders</u>, World Congress for Psychiatry Genetics, virtual, October 13, 2021

- CONCLUSION
- X Genetic overlap between the brain functional connectome and psychiatric conditions
- Link shared genetic loci back to biological processes implicated in psychiatric condition
- dentified a number of synaptic processes associated with shared loci





**Spindola, Leticia:** Exploration of brain-heritable methylation in schizophrenia cases and controls, PGC SCZ Meeting, Virtual Meeting, September 7, 2021.

**Sønderby, Ida Elken:** ENIGMA-CNV and other initiatives to understand the impact of rare copy number variants on brain structure and other measures, Society of Biological Psychiatry conference, online, April 30, 2021.

**Tamnes, Christian:** Linking brain structural and microstructural development to cognition and mental health, invited presentation for the ACHRI Child Health & Wellness Seminar, University of Calgary, digital, November 2021.

**Tesli, Natalia:** White matter matters: unraveling violence in psychosis and psychopathy, European Conference on Schizophrenia Research, Berlin, Germany (virtual conference), September 24, 2021.

**Ueland, Torill:** Cognitive remediation in the early phase of schizophrenia: results from an RCT, Nordic Meeting in Neuropsychology, Copenhagen, August 26, 2021.

**van der Meer, Dennis:** Making the MOSTest of genetics, Society of Biological Psychiatry Conference, virtual, April 29, 2021. **Vaskinn, Anja:** Cognitive clusters across schizophrenia and bipolar disorder, 14th Nordic Meeting in Neuropsychology, Copenhagen, Denmark, August 25, 2021.

**Vaskinn, Anja:** Childhood trauma and social cognition. European Congress on Schizophrenia Research, Berlin, Germany/digital, September 25, 2021.

**Wold, Kristin Fjelnseth:** Treatment resistance in first episode psychosis, ECSR 2021, Berlin, Germany, September 25, 2021.

**Widing, Line:** Premorbid characteristics of patients with DSM-IV Psychotic disorder NOS, 8th European Conference on Schizophrenia Research (ECSR) Virtual Conference, Berlin, Germany, September 25, 2021.

**Wortinger, Laura A.:** Birth Asphyxia and Its Implications for Neuropsychology and Brain Volume in Schizophrenia, EPA, virtual, April 10 -13, 2021.



**Åsbø, Gina:** Clinical Recovery in Schizophrenia and Bipolar Spectrum at 10-Year follow-Up: Challenging the Existing Definitions, SIRS, Online, April 19, 2021.

### **Selected International Poster Presentations**

**Aas, Monica:** Physical Activity and Childhood Trauma Experiences in Patients with Schizophrenia or Bipolar Disorders, Schizophrenia International research Society (SIRS), E-poster, April 17-23, 2021.

**Barth, Claudia:** Investigating white matter microstructure in adolescent early onset psychosis via ENIGMA Consortium, Society of Biological Psychiatry (SOBP), E-poster, April 29 - May 1, 2021.

**Frei, Oleksandr:** Improved quantification of gene set heritability and fold enrichments in schizophrenia using GSA-MiXeR, WCPG, E-poster, USA, October 14, 2021.

**Hindley, Guy:** Investigating the Shared Genetic Determinants of Migraine and Mental Disorders Beyond Genetic Correlation, WCPG 2021, E-poster, October 11-15, 2021.

**Hjell, Gabriela:** Interleukin-1 family signaling related to agitation in severe mental disorders, Society of Biological Psychiatry 2021 Annual Meeting, E-poster, April 30, 2021.

**Høegh, Margrethe:** Affective lability and social functioning in psychosis spectrum disorders, International Society for Bipolar Disorders Global Virtual Conference, E-poster, May 13-15th, 2021.

Jakobsen, Petter: Motor Activity Analyses Distinguish Manic and Euthymic Mood States in Bipolar Disorder, the 23rd Annual Conference of the International Society for Bipolar Disorders, E-poster, May 7, 2021.

**Rødevand, Linn:** Characterizing the shared genetic architecture of schizophrenia and cardiovascular disease risk factors, Nordic Society of Human Genetics & Precision Medicine, E-poster, November 8-9, 2021.

**Sartorius, Alina:** Evolution and annotation of the oxytocin signaling pathway, International Society of Psychoneuroendocrinology Annual Conference, E-poster, September 8, 2021.

**Spindola, Leticia**: Exploration of brain-heritable methylation in schizophrenia cases and controls, Epigenomics of Common Diseases, E-poster, November 19, 2021.

**Tesli, Natalia:** White matter matters: unraveling violence in psychosis and psychopathy, Society of Biological Psychiatry annual meeting; San Diego, USA, E-poster, April 30, 2021.

**Villar, Jonelle:** Does time-of-blood draw impact cell-derived data in studies of schizophrenia? World Congress of Psychiatric Genetics, USA, October 14, 2021

Winterton, Adriano: The oxytocin signalling gene pathway contributes to the association between loneliness and cardiometabolic health, International Society of Psychoneuroendocrinology (ISPNE), E-poster, September 7 - 9, 2021.

**Wortinger, Laura A:** Birth Asphyxia is Associated with White Matter Microstructural Differences in the Posterior Limb of the Internal Capsule of Patients with Schizophrenia and Bipolar Disorders, SIRS, E-poster, April 17-21, 2021.

### **Selected National Oral Presentations**

Andreassen, Ole: MoBa Genetics, Stiftelsen Kristian Gerhard Jebsen: Høstsamlingen 2021, Hurdalsjøen, October 27, 2021.

Andreassen, Ole: Genetic factors in Health Surveys, NOPE Annual Meeting, Bergen, November 3, 2021.

Bahrami, Shahram: DDI/DemGene meeting, Oslo, November 11-12, 2021.

**Hjell, Gabriela:** Cardiovascular health in severe mental disorders, Annual meeting of the Department of Behavioural Medicine, University of Oslo, October 13, 2021.

Kroken, Rune: Dimensions conference, December 3, 2021.

Løkhammer, Solveig: Childhood trauma in severe mental disorders: effects at the epigenetic level, NRSN national neuroscience symposium, Bergen, July 1, 2021.

**Simonsen, Carmen:** Experience with employing a coresearcher in a research project, Service-user involvement in research, Lillehammer, November 9-10, 2021.

**Stabell, Lena:** Antipsychotic effectiveness focusing on insight, the 15th Annual Research Presentations by the Research School in Clinical Medicine, Bergen, January 28, 2021.

**Stavrum, Anne-Kristin:** Epigenetic study of Environmental Risk Factors for Mental Disorders, Neuroscience Symposium, Bergen, June 29 - July 1, 2021.

**Svendsen, Ingrid Hartveit:** Selvforstyrrelser hos mennesker med en psykoselidelser, Fag- og forskningsdagene for sykepleietjenesten HSØ Norway, September 22, 2021. Videopresentasjon: Selvforstyrrelser hos mennesker med en psykoselidelse

**Sønderby, Ida Elken:** How large population studies can complement translational research, Stiftelsen Kristian Gerhard Jebsen: Høstsamlingen 2021, October 27, 2021.

van der Meer, Dennis: Applying genomics to gain insight into the human brain and mental disorders, Norwegian Research School in Neuroscience National Symposium, Virtual, June 30, 2021,

**Vaskinn, Anja:** Social cognition in severe mental disorders, Annual meeting of the Norwegian Neuropsychological Society, Oslo, November 18, 2021.

Ødegaard, Ketil Joachim: Transcranial magnetic stimulation, digital conference on treatment of depression, April 15, 2021.

### **Selected National Poster Presentations**

**Bakken, Nora Refsum:** Childhood trajectories of temperament and mental health traits to emotional disorders in adolescence, Frampeik, Bergen, October 16, 2021.

**Holen, Børge:** Opioid use disorder share genetic architecture with schizophrenia, bipolar disorder, and major depressive disorder, 7th Annual NORBIS Conference, Sola strandhotell, Stavanger, October 27, 2021.

**Strømme, Maria Fagerbakke:** Mortality and non-use of antipsychotic drugs after acute admission in schizophrenia: A prospective total-cohort study, Forskningens dag, October 4, 2021.

**Villar, Jonelle:** Does time-of-blood draw impact cell-derived data in studies of schizophrenia? Bioinformatics in Bergen, Bergen, August 19, 2021.

### **Patient Organizations and Health Personnel**

### Selected Presentations

Aminoff, Sofie Ragnhild: Mestringskurs for pasienter og pårørende i regi av Bipolarforeningen, Scandic St Olavs Plass, Oslo, Norge, June 15, 2021.

Andreassen, Ole: Grand Rounds Dept Psychiatry, Mount Sinai School of Medicine, NYC, USA, January 12, 2021.

**Busch-Christensen, Cecilie:** Mestringskurs bipolar lidelse, the Norwegian Bipolar Association, Hotel Scandic St. Olavs plass, Oslo, June 15-16, 2021.

**Fischer-Vieler, Thomas:** Factors in clinical violence risk assessment, Internal staff education programme at Psychiatric outpatient clinic, Hallingdal sjukestugu, December 1, 2021.

Haukvik, Unn Kristin: Hjerneanatomi ved vold og psykose, Department of psychosis treatment, Gaustad Hospital, May 7, 2021.

**Holen, Børge:** Precision medicine in psychiatry: Prediction of antipsychotic drug response, orientation meeting, Gaustad, digital, June 10, 2021.

**Hjell, Gabriela:** How to combine research and psychiatric clinical training, weekly seminar for psychiatrists at Østfold Hospital, digital, February 18, 2021.

**Ihler, Henrik Myhre:** Cannabis and negative symptoms in first episode psychosis, Nydalen DPS, Norway, September 2021.

**Kjelkenes, Rikka:** Hvordan utvikler hjernen seg fra barndom til voksen alder, Medlemsseminar Utdanningsforbundet Bærum, Sundvollen Hotell, November 12, 2021.

Johnsen, Erik: Antipsychotics, Grunnkurs LIS, virtual meeting, Norway, June 2, 2021.

Jakobsen, Petter: Bipolar lidelse og psykomotorisk aktivitet, Forskningens Dag, Division of Psychiatry, Haukeland University Hospital, Bergen, October 7, 2021.

Jørgensen, Kjetil: Teaching lecture for psychiatric hospital personell, Telemark Hospital, Skien, September 22, 2021.

**Kjelby, Eirik:** Sekundære psykoser, education meeting, Psykiatrisk klinikk, Haukeland university hospital, September 7, 2021.

**Kroken, Rune:** Nytt om antipsykotisk behandling, Fagmøte SUS, Stavanger, June 9, 2021.

Lagerberg, Trine Vik: MinDag – et digitalt verktøy for monitorering av alvorlig psykisk lidelse, seminar for Nasjonalt nettverk for psykoedukasjon ved bipolar lidelse, January 14, 2021. **Nerhus, Mari:** Plan D - a randomized controled trial of vitamin D supplementation in psychotic disorder, Ahus, September 28, 29, October 26, November 2,4 and December 14, 2021.

**Ottesen, Akiah:** Innvandring, traume og psykose, Blakstad LIS undervisning, March 16 and 23, 2021.

**Pentz, Atle:** Why study EEG in psychiatry, Information meeting Blakstad sykehus, August 10, 2021.

**Smeland, Olav:** Hvordan kan genetikken endre psykiatrien, Grunnkurs i voksenpsykiatri, Britannia Hotel, Trondheim, September 17, 2021.

**Steen, Nils Eiel:** Recent trends in severe mental disorders research – genetics and immunology, Digital educational meeting, Section for psychotic disorders treatment, Oslo University Hospital Trust, Oslo, June 7, 2021.

**Steen, Vidar M.:** Course in formal genetics (11 lectures), digital, November 8-9, 2021.

**Strømme, Maria Fagerbakke:** Mortalitet og bruk av antipsykotika hos pasienter med schizofreni, Fredagsmøtet Haukeland Universitetssykehus, Bergen, September, 2021.

**Sønderby, Ida Elken:** Kopitals variasjoner – forskning på store datasett gir ny innsikt i hjernestruktur og heterogenitet, Avdeling for neurohabilitering, OUS, Ullevål, Norge, October 13, 2021.

Tamnes, Christian K: Ungdomshjernen, invited presentation for pediatricians, Oslo, September, 2021.

**Ueland, Torill:** Course in cognitive remediation, Søndre Oslo DPS, October 9, 2021.

### **General Public**

**Selected Presentations and Activities** 

**Beck, Dani:** Appeared on the <u>Profoundly Pointless podcast</u>, March, 2021.

**Bjella, Thomas Doug:** Digital utvikling i forskning på mentale lidelser, presentation and panel discussion, EHiN-webinar; Psykisk helse i vår digitale tidsalder, Oslo, May 15, 2021.

**Elvsåshagen, Torbjørn:** Hjernepodden episode "Om traumer», Norwegian Brain Council, June, 2021.

Haukvik, Unn Kristin: Psykopoden Podcast, Faculty of Medicine, University of Oslo.

**Quintana, Daniel:** Everything Hertz podcast (<u>everythinghertz.com</u>). Episodes released twice a month discussing research practices.

Szabo, Attila: <u>Regenerative medicine news under the</u> <u>microscope</u>, scientific blog, Signals blog, November 04, 2021.

# lvordan kan forskning bidra til bedre andling av alvorlige psykiske lidelse



## **Public Events**

## Schizofreni: Hvilken betydning har miljøfaktorer?

On March 4, NORMENT arranged a webinar titled "Schizofreni: Hvilken betydning har miljøfaktorer?" The aim of the event was to share our knowledge on the role of environmental factors in the development of schizophrenia, and how they can influence illness trajectories.

The webinar covered topics such as early trauma (Monica Aas), immigration and migration (Akiah Ottesen), vitamin D and diet (Mari Nerhus), substance use (Henrik Myhre Ihler), and epigenetics (Stephanie Le Hellard). The event was led by Associate Professor Nils Eiel Steen, and ended with a panel discussion based on questions from the audience.



### Hvordan kan forskning bidra til bedre behandling av alvorlige psykiske lidelser?

On November 25, the Centre organized a webinar titled "Hvordan kan forskning bidra til bedre behandling av alvorlige psykiske lidelser?" The aim of the event was to show how our research can contribute to the development of better treatment of severe mental disorders.

The webinar included talks on personalized medicine (Ole Andreassen), treatment with and without medication (Erik Johnsen), conversational therapy (Jan-Ivar Røssberg) and digital treatment solutions (Trine Vik Lagerberg). The event was led by Associate Professor Unn Haukvik, and ended with a panel discussion based on questions from the audience.



### **BipolarWebinar**

During 2021, NORMENT has also been proud co-organizer of the webinar series "BipolarWebinar" arranged by the Norwegian Bipolar Association. The Association received funding from the Dam Foundation through the Norwegian Council for Mental Health to organize a series of six webinars about bipolar disorder and themes such as corona and loneliness, family relations, and work. Our User Representative, Cecilie Busch-Christensen, participated in the project group.

Several of our researchers contributed with talks on topics such as bipolar disorder in general (Sofie Ragnhild Aminoff, Trine Vik Lagerberg), causes of bipolar disorder (Olav Smeland), bipolar disorder and loneliness (Ole Andreassen), work and bipolar disorder (Cecilie Busch-Christensen, Torill Ueland), and corona and bipolar disorder (Carmen Simonsen).





Lokalt Lokalt Chordoni Innerriks Utenriks Trafikkeri direkte

Økt risiko for å dø: – Dette bør pasientene vite før de kutter ut medisinene

Når mennesker med schizofreni kutter ut medisiner, har de dobbel så høy risiko for å dø, viser stor pasientstudie fra Helse Bergen.



Nytt håp for bedre behandling av Alzheimers. Men da må behandlingen starte tidlig.

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Aftennoften







Ny norsk studie: Dette øker risikoen for bipolar lidelse KCCEB Norsk forkare har i en eter internasjonal studie undersekt gener som ka

Norske forskere har i en ster internasjonal studie undersøkt gener som kan øka risikeen for bipolar lidelse. Det kan åpne for nye behandlingsmetoder, sier

### Media Coverage

Andreassen, Ole: <u>There is a genetic link between</u> <u>intelligence and mood disorders</u>, news article, Inverse, January 20, 2021

Andreassen, Ole: <u>Får pris for demensforskning</u>, news article, Budstikka, February 1, 2021.

Andreassen, Ole: <u>Politimannen Stig (52) fikk brutal beskjed:</u> <u>– Det er som et spøkelse har tatt bolig i min kropp</u>, TV2 Nyheter, February 2, 2021.

Andreassen, Ole: <u>Demensforskning</u>, TV2 God Morgen Norge, February 3, 2021.

Andreassen, Ole: Ensomhet kan endre hjernen din, news article, NRK.no, February 2, 2021.

Andreassen, Ole: <u>Test kan vise om du kommer til å bli</u> <u>dement eller ikke</u>: - Ikke ferdig ennå, Avisa Oslo, February 9, 2021.

Andreassen, Ole: <u>Nytt håp for bedre behandling av</u> <u>Alzheimers. Men da må behandlingen starte tidlig</u>, feature, Aftenposten, February 9, 2021.

Andreassen, Ole: Lege om ketamin: Gir oppsiktsvekkende resultat mot selvmordstanker, news article, NRK.no, February 25, 2021.

Andreassen, Ole: <u>Målet er å øke livskvaliteten</u>, news article, Alt om din helse, March 30, 2021.

Andreassen, Ole: <u>Gentester: Dette må du tenke på før du</u> bestiller, news article, VG.no, April 5, 2021.

Andreassen, Ole: <u>Partydop mot posttraumatisk stress</u>, news article, Aftenposten A-Magasinet, April 16, 2021.

Andreassen, Ole and Smeland, Olav: <u>Ny norsk studie:</u> <u>Dette øker risikoen for bipolar lidelse</u>, news article, VG+, May 19, 2021.

Barth, Claudia: <u>How do hormonal transition periods impact</u> <u>female mental health?</u> Interview, FemTech, December, 2021.

Dahl, Andreas, Lofthus, Ingvild and Voldsbekk, Irene: Det er på tide med mer forskning på kvinnehjernen, chronicle, Morgenbladet, March 17, 2021.

de Lange, Ann-Marie: <u>BBC news documentary film 'A</u> <u>Mother's Brain'</u>, TV appearance, October 2021.

de Lange, Ann-Marie: <u>Research highlight - Inspire the</u> <u>Mind</u>, blogpost by Dr Pawluski, September, 2021.

de Lange, Ann-Marie: <u>Mommy Brain Revisited: the</u> <u>neuroscience of parenting</u>, podcast guest, August, 2021. de Lange, Ann-Marie, Kjelkenes, Rikka: <u>Graviditet kan gi</u> <u>kvinnehjernen ekstra beskyttelse</u>, news article, Forskning. no, March 8, 2021.

**Engen, Haakon:** <u>Resiliens - om å håndtere en påkjenning</u>, news article, NHI, February 17, 2021.

Flaathen, Camilla Bartell, Wold, Kristin Fjelnseth, and Åsbø, Gina: <u>Schizofreni gir dobbel risiko</u>, short op-ed, Klassekampen, April 10, 2021.

Lagerberg, Trine Vik: Lene (31): – Vi bruker å si at mamma har en tankesykdom, God Morgen Norge, TV2, April 7, 2021.

Lagerberg, Trine Vik: <u>Spørretime om bipolar lidelse</u>, EKKO, NRK Radio, May 4, 2021.

Lagerberg, Trine Vik: <u>Helsesektoren trenger frirom til</u> innovasjon, feature, Dagens Medisin, October 15, 2021.

Quintana, Daniel: <u>En løgn kan reise verden rundt på</u> <u>få timer</u>, magazine article, Magasinet Forskningsetikk, October, 2021.

**Simonsen, Carmen:** <u>Stigma fører til diskriminering</u>, news article, Erfaringskompetanse.no, January 11, 2021.

Smeland, Olav: Om gener og mentale lidelser med forsker Olav Smeland, podcast, Pia og Psyken, June 19, 2021,

**Smeland, Olav:** Ny norsk studie: Dette øker risikoen for bipolar lidelse, news article, VG+, May 19, 2021.

**Steen, Nils Eiel:** <u>Alvorlige psykiske lidelser rammer hele</u> <u>kroppen</u>, interview, Sykepleien, August, 2021.

**Strømme, Maria Fagerbakke:** Økt risiko for å dø: – Dette bør pasientene vite før de kutter ut medisinene, news article, Bergens Tidende, October 24, 2021.

Tamnes, Christian K: <u>Nøkkelen til menneskets suksess som</u> art, news article, Fri Tanke, April 22, 2021.

Tamnes, Christian K: <u>Ungdomshjernen er ikke utviklet nok</u> <u>til å ta store valg, mener forsker</u>, news article, NRK.no, February 19, 2021.

**Tesli, Natalia:** <u>En undergruppe av psykotiske pasienter har</u> <u>stor risiko for å bli voldelige, tror forskere</u>, news article, Forskning.no, November 1, 2021.

**Vaskinn, Anja:** <u>Tvang fører neppe til flere drap</u>, feature, Aftenposten, October 27, 2021.

Vaskinn, Anja: <u>En misforståelse om drap, vold og psykose,</u> <u>op-ed</u>, Aftenposten, November 7, 2021.

# Societal Impact

NORMENT has contributed to a series of scientific discoveries providing new insight into underlying mechanisms and treatments of severe mental illness. Our research also has the potential for a significant impact on society when it comes to clinical application, reducing stigma, and the development of innovative tools.

### **Clinical Utility**

By understanding more about how mental disorders develop, the Centre aims at contributing to early detection and prevention of illness and increasing the quality of treatment. Several scientific findings from the Centre have clinical relevance and can be applied for clinical purposes in the short term.

Researchers at the Centre have documented differences in the effectiveness of antipsychotic medications (Johnsen et al., 2020), effect on symptoms such as hallucinations (Sinkeviciute et al., 2021), sex differences (Hoekstra et al., 2021), and impact of substance use on treatment with antipsychotics (Alisauskiene et al., 2021). We have a specific focus on patients who do not respond to current treatments, investigating potential mechanisms (Werner et al., 2020) and developing advanced models to study non-response (Osete et al., 2021). We also study how psychotropic drugs impact outcome in schizophrenia, and use of antipsychotics seem to reduce risk of all-cause mortality (Strømme et al., 2021). These findings are important for the choice of treatment and can be used in clinical settings to improve pharmacological treatment.

Lipid disturbances are significant adverse effects of antipsychotics, and changes in lipid levels seem related to clinical improvements (Gjerde et al., 2020) and important metabolism hormones. This is linked to our findings of a high prevalence of comorbid cardiovascular disease in patients, which has not reduced during the last decade as seen in the rest of the population (Rødevand et al., 2019). These findings are important for understanding the high risk of somatic illnesses in psychotic disorders.

Similarly, the importance of the immune system in severe mental disorders is reflected in our research, including our genetic and metabolomics studies. We have shown a link between infections and vulnerability for mental illness (Werner et al., 2022) and found inverse associations between markers of inflammation and cognition in schizophrenia (Fathian et al., 2018). Based on this, the Centre is involved in a placebo-controlled randomized clinical trial with an add-on anti-inflammatory drug in early psychosis (Nasib et al., 2020), with large potential for improving the treatment of psychosis. Cognitive dysfunction is a significant problem in severe mental disorders, and our research focuses on the development of cognitive function over time, indicating primary stability but with significant heterogeneity (Vaskinn et al., 2020).

NORMENT researchers are also involved in intervention studies for cognitive difficulties in severe mental disorders, and have shown beneficial effects of cognitive training (Lystad et al., 2017) as well as social cognitive training (Vaskinn et al., 2019). We have also meta-analysed the cognitive enhancement effects of different pharmaceutical compounds (Sinkeviciute et al., 2018).

Further, our research has important implications for clinical diagnosis and clinical assessment. We have identified several factors that affect illness course and outcomes, including traumatic experiences (Ottesen et al., 2021), substance use (Ihler et al., 2021), sleep disturbances (Laskemoen et al., 2020), amotivational syndromes (Lyngstad et al., 2020) and affective lability (Høegh et al., 2022).

In addition, supporting eHealth and developing and testing digital tools are prioritized research areas for NORMENT. Our projects related to apps for clinical monitoring of patients have the potential for improving illness management and early intervention. These research tools can be further developed and integrated into the clinic to monitor variations in symptoms and behavior. eHealth can in general improve health care, reduce costs, and increase the focus on user needs and preferences.

Finally, the Centre has been involved in several important discoveries related to genes and brain function, that have provided increased insight into disease mechanisms. These findings can serve as a platform for new research to develop better early intervention and more targeted treatment in the long term. Knowledge about the variation of individual patients within diagnostic categories is the basis for the development of more individualized treatment, i.e. precision medicine.

### Dissemination

There is still large knowledge gaps concerning severe mental disorders in society (Takizawa et al., 2021), with associated misinformation and stigma (Simonsen et al., 2019). To make the new knowledge generated from our research available to the lay audience and thus counteract stigma, we have a continuous focus on dissemination activities through social media, newsletters, and public events (see <u>page 63</u>). Through our webinars, we have reached out to many people, including patients, family members, and health personnel. We have received positive feedback on these events, with constructive comments and questions to be followed up on in future seminars. This shows the need for updated knowledge in society and the importance of being present and visible to get in contact with the users of our research. Altogether, our dissemination activities reflect our aim to be a provider of knowledge about severe mental disorders that can help break down stigma in society.

### Innovation

NORMENT has also provided tools for prediction and stratification (genetics, imaging) which can lead to new knowledge that may improve clinical treatment in the longer term. These include novel statistical tools developed in collaboration with researchers at the University of California San Diego, such as "MOSTest" (van der Meer et al., 2021). Gaining more knowledge about mechanisms and developing diagnostic tools for stratification and outcome prediction will lead to better treatment planning for psychotic disorders and will thus be both directly and indirectly of value to society.

As part of our eNORMENT strategy, we have several projects based on new promising eHealth technology. A good example is the smartphone app called "MinDag" ("My Day"), which has been developed at NORMENT and is now applied in research. The app enables self-reports on sleep, daily activities, mood and psychotic symptoms, and substance use over time. Participants also use an activity tracker (actigraph) to record activity level and exposure to light.

We also have a collaboration with the Centre for Research-Based Innovation on Mobile Mental Health (INTROMAT). This project follows patients with bipolar disorders with smartphone technology allowing self-reports and passive measures of activity and sleep patterns to predict the emergence of new affective episodes. The projects may give new insights into the course of severe mental illness and detecting early signs of relapse to improve treatment.

For references, see publications on pages <u>82</u> and <u>88</u>.









# Facts about NORMENT



# **32** different nationalities are represented at NORMENT





# Funding



Researchers 17%

Core researchers 4% Guest researchers 1%

User representatives 1%

Administrative personnel 3%







# **NORMENT Staff**

| Last name         | First name      | Position                               | Research group leader |
|-------------------|-----------------|--|-----------------------|
| Agartz            | Ingrid          | Core researcher                        | Ingrid Agartz         |
| Akkouh            | Ibrahim         | Postdoc                                | Srdjan Djurovic       |
| Alnæs             | Dag             | Researcher                             | Lars T. Westlye       |
| Aminoff           | Sofie Ragnhild  | Researcher                             | Trine Vik Lagerberg   |
| Andreassen        | Ole A.          | Director & Core researcher             | Ole A. Andreassen     |
| Andreou           | Dimitrious      | Researcher                             | Ingrid Agartz         |
| Andresen          | Lavinia         | Engineer                               | Srdjan Djurovic       |
| Aspesletten*      | Maria           | Scientific assistant                   | Torill Ueland         |
| Audunsdottir      | Kristin         | PhD student                            | Lars T. Westlye       |
| Bahrami           | Sharam          | Researcher                             | Ole A. Andreassen     |
| Bakken            | Eivind          | Research nurse                         | Nils Eiel Steen       |
| Bakken            | Nora Refsum     | Medical student                        | Ole A. Andreassen     |
| Balafkan          | Novin           | Postdoc                                | Erik Johnsen          |
| Barrett           | Elisabeth Ann   | Researcher                             | Trine Vik Lagerberg   |
| Barth             | Claudia         | Researcher                             | Ingrid Agartz         |
| Bartz-Johannessen | Christoffer     | Biostatistician                        | Erik Johnsen          |
| Beck              | Dani            | Postdoc                                | Lars T. Westlye       |
| Bell              | Christina       | PhD student                            | Unn K. Haukvik        |
| Beresniewicz      | Justyna         | PhD student                            | Renate Grüner         |
| Berle             | Jan Øystein     | Associate professor                    | Erik Johnsen          |
| Berthet           | Pierre          | Postdoc                                | Lars T. Westlye       |
| Birkenæs          | Viktoria        | Neuropsychological assesment personnel | Ingrid Melle          |
| Bjarke            | Jill            | Administrative personell               | Erik Johnsen          |
| Bjella            | Thomas Doug     | Database manager                       | Database              |
| Bjerkaas-Kjeldal  | Kristine        | Research technician                    | Srdjan Djurovic       |
| Bless             | Josef           | Postdoc                                | Renate Grüner         |
| Blindheim         | Anne Alnes      | User representative                    | Erik Johnsen          |
| Brandt            | Christine Lycke | Administrative manager                 | Administration        |
| Brown             | Daniel          | Scientific assistant                   | Lars T. Westlye       |
| Bruun             | Sandra          | Master student                         | Torill Ueland         |
| Bukhari           | Shervin         | Research technician                    | Lars T. Westlye       |
| Busch-Christensen | Cecilie         | User representative                    | Administration        |
| Büchmann          | Camilla         | PhD student                            | Trine Vik Lagerberg   |
| Bärthel Flaaten   | Camilla         | PhD student                            | Torill Ueland         |
| Bøen              | Rune            | PhD student                            | Srdjan Djurovic       |
| Cheng             | Weiqiu          | Postdoc                                | Ole A. Andreassen     |
| Christensen*      | Karin Louise    | Scientific assistant                   | Lars T. Westlye       |
| Christoffersen*   | Cecilie         | Scientific assistant                   | Ingrid Melle          |
| Chu*              | Yunhan          | Researcher                             | Ole A. Andreassen     |

Last name First name Position Craig-Craven Alexander Engineer Dahl Andreas Phd student Davies Richard Postdoc de Lange Ann-Marie Postdoc Dieset Affiliated Ingrid Djurovic Srdjan Core researc Drosos Petros PhD student Dwyer Gerard Postdoc Elsvåshagen Torbjørn Researcher Engen Haakon Researcher Engen Magnus Johan PhD student Engh John Abel Affiliated Fasmer Ole Bernt Professor Fathian Farivar Researcher Fernandez Postdoc Sara Fisher-Vieler Thomas PhD student Frei Oleksander Researcher Frei\* Research tec Evgeniia Frid Leila Marie Research nu Erik Rimestad Frogner Researcher Cecilie Klem Scientific ass Funderud\* Affiliated Færden Ann Ghorbani Sadaf Postdoc PhD student Gjerde Kristian Varden Gjestad Rolf Research teo Granerud Guro PhD student Grüner Renate Group leade Gundersen Line Research nu Gurholt **Tiril Pedersen** Postdoc Marie Head engine Hagen Haram\* Marit Postdoc Hassan Muhammed Sumair Engineer Haugen Egil Anders Psychiatric s Haukvik Unn Kristin Group leader Helleland Administrati Torbjørn Herfindal-Engh Marina Monteverde Administrativ Hilland\* Eva Postdoc PhD student Hindley Guy Hirnstein Marco Researcher Hjell Gabriella PhD student Hjelmtvedt Torkild Research nu Engineer Holdhus Rita Holen PhD student Børge

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\* = Ended their position in 2021

\* = Ended their position in 2021

|                             | Research group leader |
|-----------------------------|-----------------------|
|                             | Renate Grüner         |
|                             | Lars T. Westlye       |
|                             | Stèphanie Le Hellard  |
|                             | Lars T. Westlye       |
|                             | Nils Eiel Steen       |
| her                         | Srdjan Djurovic       |
|                             | Erik Johnsen          |
|                             | Renate Grüner         |
|                             | Erik G. Jönsson       |
|                             | Lars T. Westlye       |
|                             | Torill Ueland         |
|                             | Nils Eiel Steen       |
|                             | Ketil J. Ødegaard     |
|                             | Erik Johnsen          |
|                             | Lars T. Westlye       |
|                             | Unn K. Haukvik        |
|                             | Ole A. Andreassen     |
| hnician                     | Srdjan Djurovic       |
| rse                         | Ketil J. Ødegaard     |
|                             | Lars T. Westlye       |
| istant                      | Torill Ueland         |
|                             | Ingrid Melle          |
|                             | Erik Johnsen          |
|                             | Erik Johnsen          |
| hnician                     | Erik Johnsen          |
|                             | Erik Jönsson          |
| r                           | Renate Grüner         |
| rse                         | Nils Eiel Steen       |
|                             | Lars T. Westlye       |
| er                          | Vidar M. Steen        |
|                             | Nils Eiel Steen       |
|                             | Vidar M. Steen        |
| ocial educator              | Erik Johnsen          |
| r                           | Unn K. Haukvik        |
| ve personell                | Administration        |
| ve personell/Research nurse | Administration        |
|                             | Ingrid Agartz         |
|                             | Ole A. Andreassen     |
|                             | Renate Grüner         |
|                             | Unn K. Haukvik        |
| rse                         | Ketil J. Ødegaard     |
|                             | Vidar M. Steen        |
|                             | Ole A. Andreassen     |

| Last name    | First name         | Position                               | Research group leader |
|--------------|--------------------|--|-----------------------|
| Holm         | Madelene           | PhD student                            | Lars T. Westlye       |
| Holmgren     | Asbjørn            | PhD student                            | Srdjan Djurovic       |
| Норе         | Sigrun             | Affiliated                             | Nils Eiel Steen       |
| Hoprekstad   | Gunnhild Eldhuset  | PhD student                            | Erik Johnsen          |
| Huflåtten    | Idun Bernadotte    | Neuropsychological assesment personnel | Trine Vik Lagerberg   |
| Hughes       | Timothy            | Researcher                             | Srdjan Djurovic       |
| Høegh        | Margrethe Collier  | PhD student                            | Trine Vik Lagerberg   |
| Haatveit     | Beathe             | Postdoc                                | Torill Ueland         |
| Ihler        | Henrik Myhre       | PhD student                            | Ingrid Melle          |
| Impellizzeri | Agata Antonia Rita | Senior engineer                        | Srdjan Djurovic       |
| Inderhaug    | Elin               | Bioengineer                            | Srdjan Djurovic       |
| Jaholkowski  | Piotr              | Postdoc                                | Ole A. Andreassen     |
| Jakobsen     | Petter             | PhD student                            | Ketil J. Ødegaard     |
| Johannessen  | Cecilie            | PhD student                            | Ingrid Agartz         |
| Johansen     | Ingrid Torp        | PhD student                            | Nils Eiel Steen       |
| Johansen     | Hogne Melle        | Scientific assistant                   | Database              |
| Johnsen      | Erik               | Core researcher                        | Erik Johnsen          |
| Jönsson      | Erik               | Group leader                           | Erik G. Jönsson       |
| Jørgensen    | Kjetil             | Researcher                             | Ingrid Agartz         |
| Karadag      | Naz                | PhD student                            | Ole A. Andreassen     |
| Karthikeyan  | Sandeep            | Head engineer                          | Ole A. Andreassen     |
| Kaufmann     | Tobias             | Researcher                             | Lars T. Westlye       |
| Kazimierczak | Katarzyna          | Research technician                    | Renate Grüner         |
| Kessler      | Ute                | Associate professor                    | Ketil J. Ødegaard     |
| Kim          | Milin              | PhD student                            | Lars T. Westlye       |
| Kippersund   | Ida                | Scientific assistant                   | Ingrid Agartz         |
| Kjelby       | Eirik              | Researcher                             | Erik Johnsen          |
| Kjelkenes    | Rikka              | PhD student                            | Lars T. Westlye       |
| Kondratska   | Olena              | Researcher                             | Srdjan Djurovic       |
| Koppe*       | Felix              | Scientific assistant                   | Torill Ueland         |
| Kristiansen  | Ingvil Julie       | Research nurse                         | Erik Johnsen          |
| Krogenes     | Marianne           | Research nurse                         | Ketil J. Ødegaard     |
| Kroken       | Rune               | Associate professor                    | Erik Johnsen          |
| Kruse        | Line               | Scientific assistant                   | Lars T. Westlye       |
| Kusztrits*   | Isabella           | PhD student                            | Renate Grüner         |
| Lagerberg    | Trine Vik          | Group leader                           | Trine Vik Lagerberg   |
| Lange        | Elisabeth          | PhD student                            | Ingrid Agartz         |
| Langeland    | Marianne           | Research nurse                         | Ketil J. Ødegaard     |
| Le Hellard   | Stèphanie          | Core researcher                        | Stèphanie Le Hellard  |
| Leonardsen   | Esten              | PhD student                            | Lars T. Westlye       |
| Lilleskare   | Lin                | Research nurse                         | Erik Johnsen          |
| Lin          | Aihua              | Postdoc                                | Ole A. Andreassen     |
| Ljung*       | Frida Mathilde     | Scientific assistant                   | Torbjørn Elsvåshagen  |

Last name First name Position Loftshus Ingvild Sandø Research teo Lu Li Postdoc Lund PhD student Martina Jonette Professor Lund Anders Lund-Heimark Hallvard Resident doo Lunding Synve Hoffart PhD student Lyngstad PhD student Siv Hege Professor Løberg Else-Marie Løchen Aili Scientific ass Løkhammer Solveig Medical stud Markl Therese Database cor Marquardt Lynn PhD student Melle Core researc Ingrid Researcher Moberget Torgeir Mohn Hanne Christine Neuropsycho Moretti Patricia Natalia Silva Postdoc Motazedi\* Ehsan Postdoc Anne M. Associate pro Myhre Mørch-Johnsen Researcher Lynn PhD student Mørkved Nina Nerhus Mari Postdoc PhD student Nerland Stener Neto Carla Engineer Norbom Linn Postdoc Nærland Terje Affiliated O'Connell Kevin Postdoc Olsen Stine Holmstul Clinical asses Olsen\* Axel Scientific ass Oltedal Leif Associate pro PhD student Ormerod Monica B. E. G. Osete Jordi Researcher Ottesen Akiah Researcher Parker Nadine Postdoc Pedersen Geir Researcher Pedersen Mads Lund Researcher Pentz Atle PhD student Polushina\* Tatiana Researcher Postdoc Puppo\* Francesca Quintana Daniel Researcher Rahman Postdoc Mohammad Zillur Reis de Assis Denis Postdoc Reponen Elina Johanna PhD student Richard Postdoc Geneviève

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\* = Ended their position in 2021

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|                               | Research group leader |
|-------------------------------|-----------------------|
| chnician                      | Lars T. Westlye       |
|                               | Ole A. Andreassen     |
|                               | Lars T. Westlye       |
|                               | Ketil J. Ødegaard     |
| ctor                          | Erik Johnsen          |
|                               | Nils Eiel Steen       |
|                               | Trine Vik Lagerberg   |
|                               | Erik Johnsen          |
| sistant                       | Lars T. Westlye       |
| dent                          | Stèphanie Le Hellard  |
| nsultant                      | Database              |
|                               | Renate Grüner         |
| her                           | Ingrid Melle          |
|                               | Lars T. Westlye       |
| ological assessment personnel | Torill Ueland         |
|                               | Vidar M. Steen        |
|                               | Ole A. Andreassen     |
| ofessor                       | Ingrid Agartz         |
|                               | Ingrid Agartz         |
|                               | Erik Johnsen          |
|                               | Trine Vik Lagerberg   |
|                               | Ingrid Agartz         |
|                               | Stèphanie Le Hellard  |
|                               | Lars T. Westlye       |
|                               | Ole A. Andreassen     |
|                               | Ole A. Andreassen     |
| ssment personnel              | Trine Vik Lagerberg   |
| sistant                       | Ole A. Andreassen     |
| ofessor                       | Ketil J. Ødegaard     |
|                               | Nils Eiel Steen       |
|                               | Srdjan Djurovic       |
|                               | Ingrid Melle          |
|                               | Ole A. Andreassen     |
|                               | Ingrid Melle          |
|                               | Lars T. Westlye       |
|                               | Erik G. Jönsson       |
|                               | Stèphanie Le Hellard  |
|                               | Srdjan Djurovic       |
|                               | Lars T. Westlye       |
|                               | Ole A. Andreassen     |
|                               | Srdjan Djurovic       |
|                               | Nils Eiel Steen       |
|                               | Lars T. Westlye       |

| Last name    | First name         | Position                      | Research group leader |
|--------------|--------------------|-------------------------------|-----------------------|
| Rise         | Henning Hoel       | Research coordinator          | Lars T. Westlye       |
| Roelfs       | Daniel             | PhD student                   | Lars T. Westlye       |
| Rokicki      | Jaroslav           | Researcher                    | Unn K. Haukvik        |
| Romm         | Kristin Lie        | Associate professor           | Ingrid Melle          |
| Rødevand     | Linn               | PhD student                   | Nils Eiel Steen       |
| Sahl*        | Andrè              | Clinical assistant            | Torill Ueland         |
| Sanders      | Anne-Marthe        | PhD student                   | Lars T. Westlye       |
| Sartorius    | Alina              | PhD student                   | Lars T. Westlye       |
| Schindler    | Louise             | PhD student                   | Lars T. Westlye       |
| Shadrin      | Alexey             | Researcher                    | Ole A. Andreassen     |
| Simonsen     | Carmen             | Researcher                    | Ingrid Melle          |
| Sinkeviciute | lgne               | PhD student                   | Erik Johnsen          |
| Slapø        | Nora               | PhD student                   | Erik G. Jönsson       |
| Smeland      | Olav               | Researcher                    | Ole A. Andreassen     |
| Smelror      | Runar Elle         | Postdoc                       | Ingrid Agartz         |
| Spindola     | Leticia            | Postdoc                       | Stèphanie Le Hellard  |
| Stabell      | Lena Antonsen      | Database consultant           | Erik Johnsen          |
| Stautland    | Andrea             | PhD student                   | Ketil J. Ødegaard     |
| Stavrum      | Anne-Kristin       | Researcher                    | Stèphanie Le Hellard  |
| Steen        | Nils Eiel          | Group leader                  | Nils Eiel Steen       |
| Steen        | Vidar M.           | Core researcher               | Vidar M. Steen        |
| Stokowy      | Tomasz             | Engineer                      | Vidar M. Steen        |
| Storli       | Ragnhild           | Administrative personell      | Administration        |
| Storvestre   | Guttorm Breivik    | PhD student                   | Unn K. Haukvik        |
| Strømme      | Maria F.           | PhD student                   | Erik Johnsen          |
| Svendsen     | Ingrid Harveit     | PhD student                   | Ingrid Melle          |
| Syrstad      | Vigdis Elin Giæver | PhD student                   | Ketil J. Ødegaard     |
| Szabo        | Attila             | Researcher                    | Srdjan Djurovic       |
| Sæther       | Linn Sofie         | PhD student                   | Torill Ueland         |
| Sødal*       | Hedda B.T.         | Clinical assessment personnel | Ingrid Agartz         |
| Sønderby     | Ida Elken          | Researcher                    | Srdjan Djurovic       |
| Tamnes       | Christian K.       | Professor                     | Lars T. Westlye       |
| Tesli        | Natalia            | PhD student                   | Unn K. Haukvik        |
| Tesli*       | Martin S.          | Affiliated                    | Ole A. Andreassen     |
| Thomassen    | Anne               | Clinical assesment personell  | Erik Johnsen          |
| Timpe        | Clara              | Research technician           | Lars T. Westlye       |
| Torsvik      | Anja               | Researcher                    | Vidar M. Steen        |
| Trentani     | Andrea             | Engineer                      | Vidar M. Steen        |
| Tønnesen     | Siren              | PhD student                   | Lars T. Westlye       |
| Ueland       | Torill             | Group leader                  | Torill Ueland         |
| Ueland       | Thor               | Affiliated                    | Nils Eiel Steen       |
| Ulrichsen    | Kristine           | PhD student                   | Lars T. Westlye       |
| Valstad*     | Mathias            | Researcher                    | ,<br>Frik G. Jönsson  |

| Last name         | First name             | Position                 | Research group leader |
|-------------------|------------------------|--------------------------|-----------------------|
| van der Meer      | Dennis                 | Researcher               | Lars T. Westlye       |
| Vandenberghe      | Matthieu               | Researcher               | Srdjan Djurovic       |
| Vaskinn           | Anja                   | Researcher               | Torill Ueland         |
| Vedde             | Ingeborg Helle         | Administrative personell | Administration        |
| Vik               | Ruth Kristine          | Research coordinator     | Ingrid Melle          |
| Villar            | Jonelle                | PhD student              | Stèphanie Le Hellard  |
| Voldsbekk         | Irene                  | PhD student              | Lars T. Westlye       |
| Værnes            | Tor Gunnar             | PhD student              | Trine Vik Lagerberg   |
| Wedervang-Resell* | Kirsten                | PhD student              | Ingrid Agartz         |
| Werner            | Maren Caroline Frogner | PhD student              | Ingrid Melle          |
| Westlye           | Lars T.                | Core researcher          | Lars T. Westlye       |
| Widing            | Line                   | PhD student              | Ingrid Melle          |
| Wiker             | Thea                   | PhD student              | Lars T. Westlye       |
| Winterton         | Adriano                | PhD student              | Lars T. Westlye       |
| Wirgenes          | Katrine Verena         | Researcher               | Ole A. Andreassen     |
| Wold              | Kristin Fjelnseth      | PhD student              | Ingrid Melle          |
| Woldeyouhannes    | Markos Tesfaye         | Postdoc                  | Ole A. Andreassen     |
| Wolfers           | Thomas                 | Postdoc                  | Lars T. Westlye       |
| Wortinger         | Laura A.               | Postdoc                  | Ingrid Agartz         |
| Ødegaard          | Ketil Joachim          | Group leader             | Ketil J. Ødegaard     |
| Øiestad           | Synne Stadheim         | Research coordinator     | Lars T. Westlye       |
| Aaberg            | Linn-Marie Elise       | Nurse                    | Erik Johnsen          |
| Aas               | Monica                 | Researcher               | Nils Eiel Steen       |
| Åsbø              | Gina                   | PhD student              | Ingrid Melle          |

\* = Ended their position in 2021

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NORMENT researchers published 185 scientific papers in 2021, of which 28 were published in scientific journals with an impact factor of above 10, including Biological Psychiatry, JAMA Psychiatry, Lancet Psychiatry, Molecular Psychiatry, Nature Communications, Nature Human Behaviour, Nature Genetics, Science Advances and World Psychiatry.

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