



**NORMENT**  
Norwegian Centre for  
Mental Disorders Research



# NORMENT

## Annual Report 2017



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## Scientific Highlights 2017

**Identified causes and predictors of premature death in first-episode schizophrenia spectrum disorders** (Melle et al., World Psychiatry)

**Discovered a fingerprint-like pattern in the brain that evolves during development and is sensitive to mental health** (Kaufmann et al., Nature Neuroscience)

**Identified genetic overlap between schizophrenia and cognitive functioning** (Smeland et al., JAMA Psychiatry)

**Reported that the cerebellum is among the most affected brain regions in schizophrenia** (Moberget et al., Molecular Psychiatry)

**Determined cortical brain abnormalities in bipolar disorder with an MRI analysis of 6503 individuals** (Hibar et al., Molecular Psychiatry)

## Leader's Comments



The first phase of NORMENT as a Centre of Excellence (CoE) is coming to an end. We have been through a year with midterm evaluation of the Centre and adjustment of our research plan. It is important for us as an innovative organization to always look for ways to improve and generate new ideas. Still, we must build on our strengths and maintain focus and resources on our main advantages, the synergy from the cross-disciplinary team at the Centre. This revision of our research programme has been a fruitful and innovative process, and it has enabled us to evaluate what we are doing at the Centre, focus on the most promising projects, and implement the necessary organizational changes.

In 2017 we continue with a strong scientific production. We have been involved in several high impact publications, and we have a series of papers in the best journals in our field. This shows how we have managed to attract excellent researchers and support them with an organization and infrastructure which lead to frontline science. The main discoveries are described in detail in other parts of this report, but here I would like to highlight researcher Tobias Kaufmann who not only published his results of brain imaging fingerprints predicting development of mental illness symptoms in Nature Neuroscience, but also successfully obtained the Young Research Talents grant from the Research Council of Norway. This is very motivating for everyone at the Centre, and shows how young researchers can build their future within the NORMENT framework. We will continue to support young talents in developing their careers.

Several of our publications have also attracted much interest beyond the academic field, with interviews and press releases in general news media. This has been facilitated by our dissemination group, who in short time has increased our focus on social media and information to lay people. Two user representatives have been employed at the Centre during 2017. They have helped us with the user perspective and have been very useful and integrated members of the research team.

Our initiative for modernization of our research tools, eNORMENT, has started to show results. We now have a mobile app that is operational, and most of our questionnaires and protocols are soon all electronic, with large gains in efficiency and accuracy in data collection.

We received excellent scores from our midterm evaluators, and we are now focusing on our next five year period as a Centre of Excellence, ending in 2023. This will be a highly exciting period. In the next few years we have a unique opportunity to make important discoveries in the field of severe mental illness. Our adjustment of the research plan includes more emphasis on stem cell research, as well as moving more towards clinical trials and interventions. Thus, from July 2018 we will have another partner, Haukeland University Hospital, and two new Core Researchers, Lars T. Westlye and Erik Johnsen. We welcome the new excellent scientists and look forward to their contribution to our team and improvement of the Centre.

It is a pleasure and privilege to be the Director of NORMENT with such an outstanding team of people!

A handwritten signature in blue ink, reading "Ole A. Andreassen".

Ole A. Andreassen  
Centre Director

## Prizes and Awards 2017



Researcher Tobias Kaufmann is receiving his paper prize at Oslo University Hospital



**Julien Laloyaux**

**Young Investigator Travel Award, 16th International Congress on Schizophrenia Research, San Diego, USA**

Title of oral presentation: Inducing hallucinations in participants from the general population: The role of negative emotions and cognitive resources



**Petter Andreas Ringen**

**Prize for outstanding paper, Oslo University Hospital, Norway**

Title of paper: Premorbid cannabis use is associated with more symptoms and poorer functioning in schizophrenia spectrum disorder (Psychological Medicine)



**Tobias Kaufmann**

**Prize for outstanding paper, Oslo University Hospital, Norway**

Title of paper: Delayed stabilization and individualization in connectome development are related to psychiatric disorders (Nature Neuroscience)

## 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 also integrated with the K.G. Jebsen Centre for Psychosis Research, funded by Stiftelsen Kristian Gerhard Jebsen.

The Centre is based on collaboration between the University of Oslo (host institution), the University of Bergen, and Oslo 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 2017, more than 160 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 mainly being carried out in eight research groups, led by Core Researchers (CR). The main research topics include Genetics, Antipsychotic Medication, Brain Imaging, and Outcome Predictors (factors that can be used to estimate illness course and outcome). 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 time-consuming clinical assessments, neuropsychological testing, 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.

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

- Been involved in discoveries of new gene variants associated with severe mental illness, including a large international study reporting 108 gene variants related to schizophrenia
- Gained new knowledge about the immune system and related genes in mental illness
- Developed novel and promising statistical tools to study mental disorders
- Provided evidence of how animal models can be used for studies of antipsychotic side effects
- Determined that complications before or during birth may affect brain development and play an important role in psychiatric illness
- Detected how brain connections evolve during development and are sensitive to 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

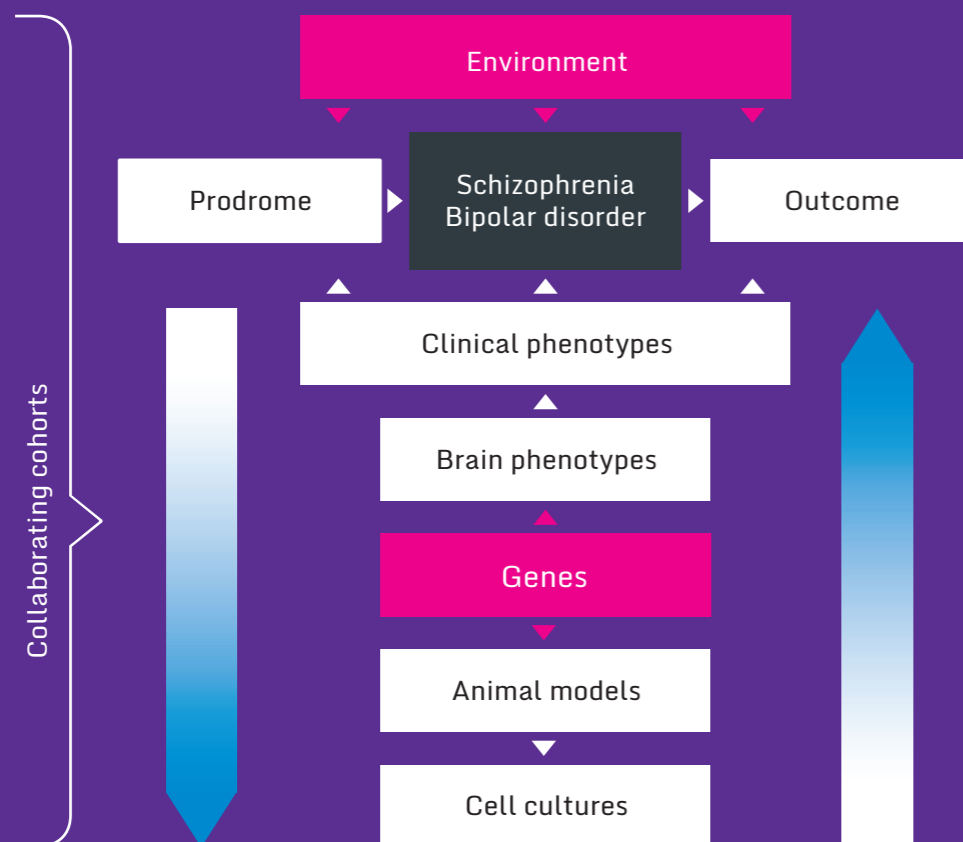
In the years to come, the research at NORMENT will particularly focus on immune factors and neuronal processes, based on the discoveries of new risk genes for schizophrenia and bipolar disorder. One promising new area of research is to use human stem cells developed from skin cells to investigate molecular and cellular mechanisms in mental illness. The Centre will also start more clinical trials and interventions to follow up new findings, and improve approaches for analysing large amounts of data (“big data”). Altogether, NORMENT aims to contribute substantially to a better understanding, care and treatment of severe mental disorders.

# Vision Statement

NORMENT's primary objective is to reveal underlying pathophysiological mechanisms of severe mental disorders such as schizophrenia and bipolar disorder, and to develop tools for stratification and outcome prediction. The main research topics at the Centre are **Genetics, Brain Imaging, Antipsychotic Medication, and Outcome Predictors**, which are reflected in the following scientific aims:

- Identify genetic factors for psychiatric disorders - common and rare variants
- Define new targets for antipsychotic medication to optimize the ratio of beneficial vs. adverse effects
- Determine brain imaging phenotypes linking genes to core clinical phenotypes
- Use genetic and environmental factors to predict disease progress and outcome

We profit 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 mechanisms which will be studied functionally in animal and cell culture models, applying a "vertical synergy" approach.



# Scientific Aims

## Identify Genetic Factors for Psychiatric Disorders – Common and Rare Variants

Family and twin studies have shown that schizophrenia and bipolar disorder have high heritability. Researchers at NORMENT have contributed to major breakthrough findings in international genome-wide association studies (GWAS) consortia and we have found evidence for new vulnerability genes for these disorders.

Preliminary results show that inherited changes in many genes (i.e. gene variants) and genomic regions are involved, but usually, each variant contributes to a relatively modest degree. Heritability is therefore still far from fully explained. In our research, we use combined approaches that include new genotyping methods to identify rare genetic variants. We also use new statistical methods for mapping multiple gene variants, in order to combine effect sizes and thus increase the power.

## Define New Targets for Antipsychotic Medication

Antipsychotic medication is the cornerstone in the treatment of schizophrenia, and has in recent years also been used for bipolar disorder. The medications are not equally effective for all patients, and have a limited effect on the core symptoms for approximately 20 % of those treated on psychosis indication.

Adverse effects are problematic and in some cases serious, involving metabolic and cardiovascular risk factors (weight gain, abnormal fat levels in the blood, diabetes etc.). Research at NORMENT has a particular focus on the immune system, lipid (fat) biosynthesis, and brain myelination processes. We use animal and other experimental models to enhance our knowledge about the mechanisms of action of antipsychotic medication. We aim to optimize antipsychotic treatment by increasing the desired effect of medication and reducing adverse effects.

## Identify Brain Imaging Phenotypes Linking Genes to Core Clinical Phenotypes

Advanced neuroimaging techniques including structural and functional magnetic resonance imaging (MRI) have revolutionized our understanding of the structural and functional makeup of the human brain.

We have contributed to the identification of structural brain abnormalities in schizophrenia, including volumetric alterations in fronto-temporal cortical areas and subcortical structures. Partly overlapping and partly diverging patterns have been found in bipolar disorder. Structural and functional brain phenotypes are highly

heritable, and current research at NORMENT aims to identify the genetic underpinnings of individual differences in the structural and functional organization of the human brain, and to disentangle the genetic and phenotypic associations with severe neuropsychiatric disorders.

## Use Genetic and Environmental Factors to Predict Disease Progress and Outcome

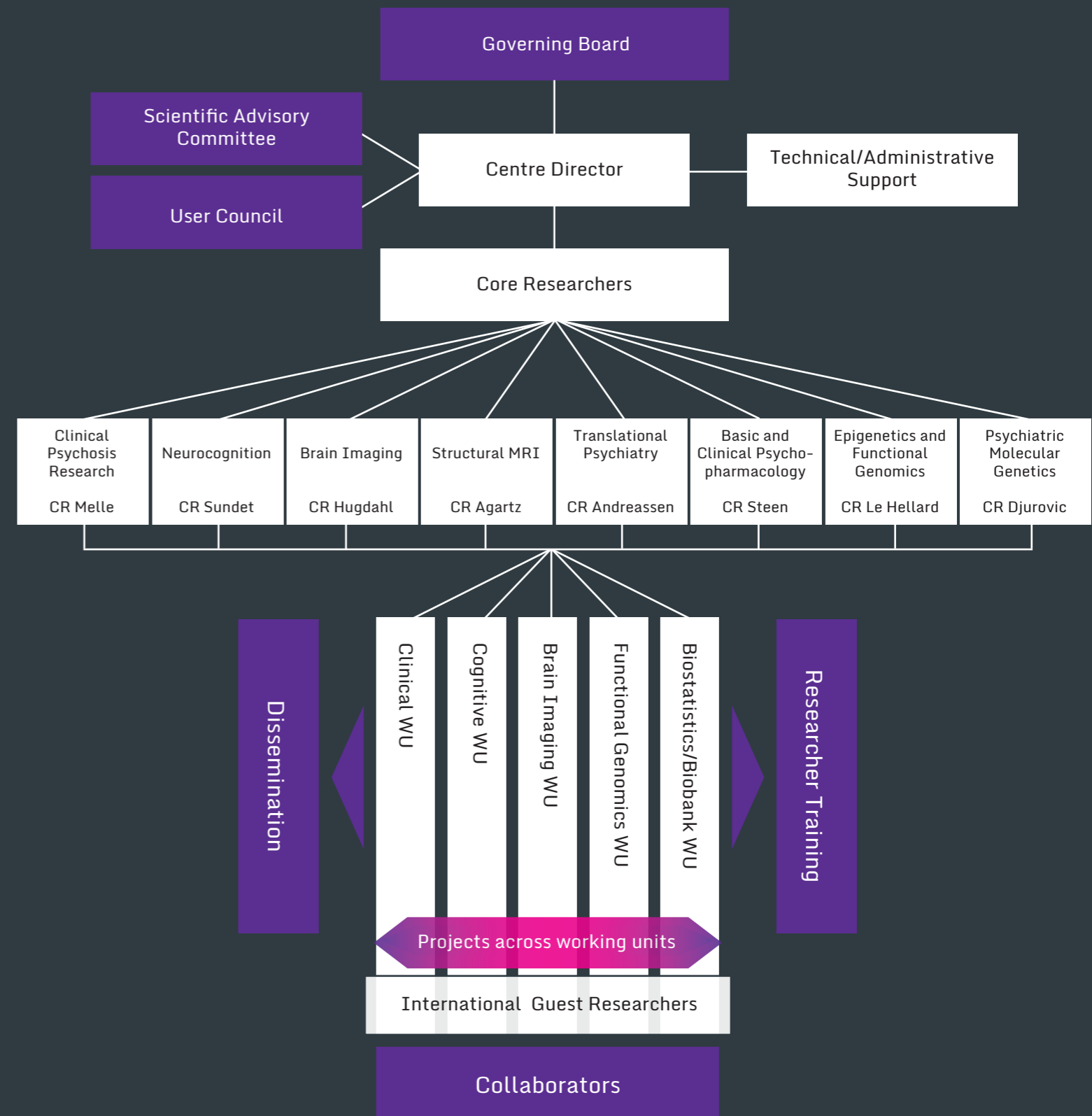
Some people with psychotic disorders recover completely while others develop chronic illness. Currently, we can only make general assumptions about the most likely prognosis for someone who develops a severe mental illness and are not able to predict the specific outcome for each individual patient. One of the main goals for NORMENT is to investigate how we can improve the understanding of course and outcome. Ultimately, the goal is to make personalized predictions for patients coming to their first treatment.

The main focus has been on investigating how specific environmental risk factors influence clinical, cognitive, and morphological characteristics either individually, or in interaction with other environmental and genetic risk factors. At present, we are studying the effects of early (childhood) traumatic events, cannabis use and migration, with additional studies of how the effects of trauma interact with the effects of cannabis use and migration.

We have also studied how trauma interacts with genetic factors on cognition and on structural changes in hippocampal subfields. To study the effects on course and outcome we also need well-described patient cohorts followed from their first treatment. Within the NORMENT centre we have established a first-treatment schizophrenia spectrum cohort and bipolar spectrum cohort in collaboration with Norwegian colleagues in the NORSMI network. The first part of the long-term follow-up will have a particular focus on functioning, cognition and negative symptoms.



## Organization of the Centre





## Governing Board

**Chair:**  
**Ivar Prydz Gladhaug\***

Professor  
Head of Institute  
Institute of Clinical Medicine  
University of Oslo



**Board member:**  
**Marit Bjartveit**

Clinic Manager  
Division of Mental Health  
and Addiction  
Oslo University Hospital



**Board member:**  
**Timothy Brennen**

Professor  
Research Dean  
Faculty of Social Sciences  
University of Oslo



**Board member:**  
**Inger Hilde Nordhus**

Professor  
Vice Dean for Research  
Faculty of Psychology  
University of Bergen



**Board member:**  
**Marit Bakke\*\***

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



\*Replaced Hilde Irene Nebb during 2017. \*\*Replaced Eyvind Rødahl during 2017.





# Scientific Advisory Committee

**Marcella Rietschel**  
Professor  
University of Mannheim



**Michael Foster Green**  
Professor  
University of California  
Los Angeles



**Terry Jernigan**  
Professor  
University of California  
San Diego



**Professor Marcella Rietschel** is Professor and Scientific Director of the Department of Genetic Epidemiology in Psychiatry at the Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Germany.

**Professor Michael Foster Green** is 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 Terry Jernigan** is 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.

**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 with SWOT analysis. Contribute by giving an annual lecture at postgraduate level.

## User Involvement

Lena-Maria Haugerud



Guro Smedsrud



Fabian Stang



### User Council

NORMENT's User Council represents the user community, and consists of individuals who have personal experience, competency and expertise related to mental health. The members of the User Council 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, 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 2017, the members of the User Council were:

**Lena-Maria Haugerud**, Psychiatric Auxiliary Nurse and founder of the National Association for Prevention of Self-Harm and Suicide

**Guro Smedsrud**, Master of Science in Biophysics and Medical Technology, and Leader of the Research Committee of the Norwegian Bipolar Association

**Fabian Stang**, Lawyer and Politician

In addition to the four quarterly meetings in 2017, the members of the User Council participated at the NORMENT Annual Retreat in September.

### User Representatives

NORMENT has employed part time User Representatives to further include the user perspective in the research. The User Representatives participate in daily activities at the Centre and bring the user perspective into group meetings, project planning, dissemination activities, and practical operation procedures. Further, the User Representatives are 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 act as a link to user organizations, such as the Norwegian Bipolar Association.

In 2017, the User Representatives were Marthe Hagen and Oda Antonsen.

## Working Units

While the research at NORMENT is organized into research groups headed by the eight Core Researchers, the daily infrastructure for collection, storage, and processing of scientific data is divided into five different Working Units (WU), as shown in the figure of the centre organization.

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 Working Units, since they are based on data collected from different groups and involve both clinical and other information about the participants. From mid-2018 there will be a change in names and organization of these units into Core Resource Units (CRU), with some adjustments in content.

The main responsibilities of the different Working Units are as follows:

**Clinical WU:** Inclusion and clinical assessments (diagnostic interviews, self-report questionnaires) of patients, as well as quality assurance of these assessments (reliability testing).

**Cognitive WU:** Neuropsychological testing (experimental tests, self-report questionnaires) of patients and healthy individuals, including measures such as attention, memory, and IQ.

**Brain Imaging WU:** Collection and processing of brain imaging data such as magnetic resonance imaging (MRI) and electroencephalography (EEG), to measure brain anatomy (structural MRI, DTI) and brain activity (functional MRI, EEG).

**Functional Genomics WU:** Processing of genetic data using molecular genetics methods, gene expression and DNA sequencing, as well as cultivation of human stem cells and use of animal models.

**Biostats/Biobank WU:** Large-scale genetic analysis using computational techniques, and analysis of large amounts of clinical, cognitive, imaging and genetic data, as well as storage of biological data in databases and registries.



## Technical and Administrative Support

In order to perform excellent research, the Centre is dependent on well-organized support functions that ensure a stable and efficient infrastructure. Such functions include technical and administrative support related to administrative documents and systems, development of procedures and protocols, organization of meetings and events, project budgets and economy, IT-support, internal and external communication, and coordination across research projects and units.

Several people have been involved in these support functions at the Centre in 2017:



Åshild M. Eftevåg  
Administrative manager



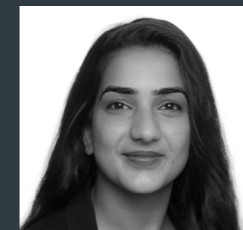
Trine Vik Lagerberg  
Head of Unit



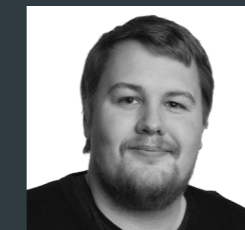
Ragnhild B. Storli  
Senior Executive Officer



Kate Frøland  
Senior Executive Officer



Asma Asghar  
Administrative Consultant



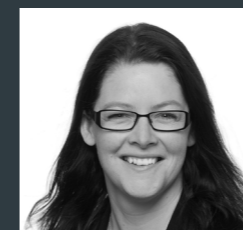
Tor J. Helleland  
Scientific Assistant



Thomas D. Bjella  
Head Engineer,  
Database



Therese Markl  
Scientific Consultant,  
Database



Ruth Kristine Vik  
Scientific Consultant,  
Database



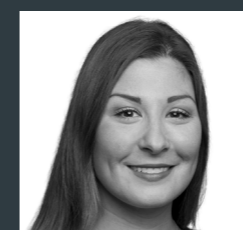
Lilliana Buer  
Scientific Assistant,  
Database



Eivind Bakken  
Study Nurse



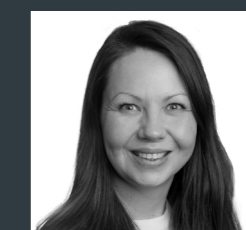
Line Gundersen  
Study Nurse



Caroline Huitfeldt  
Study Nurse



Christine Lycke Brandt  
Research Coordinator



Beathe A. Haatveit  
Research Coordinator



Martina J. Lund  
Scientific Assistant

## Core Researchers

The scientific leadership at NORMENT consists of eight Core Researchers with complementary expertise from different scientific fields. The research is organized into different research groups, each headed by a Core Researcher:

- |                             |  |
|-----------------------------|--|
| <b>Ingrid Melle</b>         | Professor at the University of Oslo and Oslo University Hospital, Head of the Clinical Psychosis Group               |
| <b>Kjetil Sundet</b>        | Professor at the University of Oslo, Head of the Neurocognition Group  |
| <b>Kenneth Hugdahl</b>      | Professor at the University of Bergen, Head of the Brain Imaging Group   |
| <b>Ingrid Agartz</b>        | Professor at the University of Oslo, Head of the Structural MRI Group  |
| <b>Ole A. Andreassen</b>    | Professor at the University of Oslo and Oslo University Hospital, Head of the Translational Psychiatry Group         |
| <b>Vidar M. Steen</b>       | Professor at the University of Bergen, Head of the Basic and Clinical Psychopharmacology Group                       |
| <b>Stéphanie Le Hellard</b> | Professor at the University of Bergen, Head of the Epigenetics and Functional Genomics Group                         |
| <b>Srdjan Djurovic</b>      | Professor at the Oslo University Hospital and University of Bergen, Head of the Psychiatric Molecular Genetics Group |



Front row, from the left: Ingrid Melle, Stéphanie Le Hellard, Ingrid Agartz  
Back row, from the left: Srdjan Djurovic, Kjetil Sundet, Ole A. Andreassen, Kenneth Hugdahl, Vidar M. Steen

# Clinical Psychosis Research

## Ingrid Melle



### Aims

An important goal is to increase our understanding of mechanisms underlying psychopathological phenomena and the concrete consequences of psychotic disorders, with particular emphasis on factors related to social dysfunction.

### Research Focus

The group has the main academic responsibility for clinical research at NORMENT. Our research focuses on the clinical phenomena, the early course and outcome of schizophrenia and bipolar disorder, and the clinical effects of environmental risk factors and genetics on course and outcome. Our research includes projects on the impact of early trauma, migration and substance use on the early course of schizophrenia and bipolar disorder. Current projects also focus on disorders of motivation, emotion processing and affect stability; and risk factors for suicidal thoughts and plans. We are expanding our protocol to include electronic data capture and have developed and piloted a smartphone application measuring affect lability and sleep disturbances. We are particularly focusing on how the early course of the treated disorder shapes long-term outcome, and are currently doing a ten-year follow-up of study participants recruited at first treatment. The study involves linkage to relevant Norwegian registry data.

### Main Projects

Predicting long-term outcome in schizophrenia and bipolar disorder with the following sub-studies:

- Risk factors for suicide and suicidal symptoms in psychotic disorders.
- Motivation and apathy in psychotic disorders.
- Substance use in psychotic disorders.
- Sleep disturbances in psychotic disorders.

### Achievements in 2017

Over the last year, group members have had central roles in showing that:

- Patients with psychotic disorders have disturbances in their vitamin D levels and that these disturbances are related to negative and cognitive symptoms (Nerhus et al., 2017).
- Severity of childhood trauma is associated with increased BMI and immune disturbances in the form of elevated C-reactive protein (Aas et al., 2017).
- Alcohol use disorders are related to more affective lability in bipolar disorder patients (Lagerberg et al., 2017).
- Stable symptomatic remission and early clinical recovery could be identified already after one year in treatment (Simonsen et al., 2017).
- Persons experiencing stable symptomatic remission had a more favorable development of subjective quality of life over the first ten years of treatment (Simonsen et al., 2017).

### Ambitions for 2018

- The clinical research group is large and includes several lines of research. Going into the second part of the CoE, the group will split into two groups, one focusing on developing new measures of clinical psychopathology and one focusing on the longitudinal development of the disorders. The formation of two well-functioning groups is a main goal for 2018.
- We are in process of developing a new clinical protocol that will integrate electronic data capture and the “MinDag” (“My Day”) smartphone app. The new protocol will be implemented in 2018.
- We are starting the second part of the long-term follow-up study which includes linkage to Norwegian patient registries.
- We are planning for a 20-year follow-up of our longest running cohort, the TIPS cohort.

### Central Publications 2017

Vitamin D deficiency associated with cognitive functioning in psychotic disorders (Nerhus et al., Journal of Clinical Psychiatry)

Alcohol use disorders are associated with increased affective lability in bipolar disorder (Lagerberg et al., Journal of Affective Disorders)

Early clinical recovery in first-episode psychosis: Symptomatic remission and its correlates at 1-year follow-up (Simonsen et al., Psychiatry Research)

### Core Researcher

Ingrid Melle

Professor  
University of Oslo and  
Oslo University Hospital

### Group Members Assessment Team Leader

Trine Vik Lagerberg  
Akiah O. Berg  
Bjarte Nystøyl  
Camilla B. Büchmann  
Carmen Simonsen  
Erlend S. Gardsjord  
Idun B. Huflåtten  
Ifeoma Onyeka

Jannicke F. Anderssen  
Levi Kvitland  
Margrethe C. Høegh  
Mari Todd-Kvam  
Mari Nerhus  
Marit Haram  
Monica Aas  
Ruth Kristine Vik  
Seyran Khalili  
Sherif Gohar  
Siv Hege Lyngstad

Sofie Aminoff  
Tale Moldestad  
Tiril Østefjells

### Associated Group Members

Ann Færden  
Elisabeth Haug  
Elizabeth A. Barrett  
Ingrid H. Svendsen  
Kristin L. Romm  
Petter Andreas Ringen

# Neurocognition

## Kjetil Sundet



### Aims

Cognitive functioning constitutes the behavioural fingerprint of brain functioning. Strengths and weaknesses in thinking, feeling and responding provide the backdrop for how people manage. Cognition is fuelled by the genetic make-up of the person whereas the neurodevelopmental output is formed in a constant interplay with psychosocial demands. People with psychosis differ in cognitive status and only a subgroup shows clear impairments. We aim to capture the variation in cognitive functioning to provide more valid diagnoses, better prognostic guidance and improved individualized intervention programmes. Structural and functional brain measures add to the validity of neurocognitive characterization as do clinical ratings of symptoms and functional capacity. We collaborate closely with the clinical and the brain imaging groups in the logistics of data collection to validly answer our research questions.

### Research Focus

The Neurocognitive Working Unit conducts neuropsychological assessment of all participants recruited to the study at all time-points (baseline and follow-ups). The research group's foci are to a) identify neurocognitive markers of subgroups to improve precise diagnoses, outcome and treatment; b) to monitor change and stability in neurocognitive functioning to better predict illness trajectories; c) to develop cognitive remediation programmes to improve behaviours not fully responding to medication and psychotherapy; d) to look for new measures of specific cognitive mechanisms governing global functions; and e) to search for measures of social cognition to better predict real-life functioning.

### Main Projects

- Cognitive Remediation studies focus on the effect of targeted training of neurocognitive and social cognitive functions, including work-related and social functioning measures.
- The 10-year follow-up study searches for markers of good outcome by identifying neurocognitive trajectories from baseline to follow-up in first episode psychosis.
- The ecoval study focuses on social processes combining naturalistic observation of real-world functioning with laboratory assessments and functional brain measures (ERPs).
- The Genetics of attention and effort study explores the functional integrity of the brain's effort network in schizophrenia, and the effect of psychosis susceptibility genes on cognitive mechanisms.
- The Neurocognitive Immune System study investigates how immune markers and their temporal pattern associate with cognitive measures.
- The Neurocognitive web-based study supplements the eNORMENT initiative, by implementing web-based assessment tools suited for large-scale studies of cognitive functioning.

### Achievements in 2017

- Included and assessed 170 patients and control participants in a 10-year follow-up study on neurocognitive predictors of functioning.
- Secured research collaboration for project on neurocognitive correlates of immune system pathology in a longitudinal perspective.
- Completed PhD on executive functioning in schizophrenia spectrum disorders.
- Reported overall stable neurocognitive functioning within group of first-treatment bipolar patients at 1-year follow-up, and improved neurocognitive functioning combined with better functional outcome in subgroup not experiencing relapse (Demmo et al., 2017).
- Documented that impaired social cognition (body language reading of emotion) in schizophrenia and bipolar disorder have functional consequences (Vaskinn et al., 2017).

### Ambitions for 2018

- Continue data collection of ongoing projects and assist PhD students (n=5) and post-docs to publish according to plan (PIs: Ueland, Vaskinn, Espeseth).
- Continue development of projects on neurocognitive correlates of immune system pathology in a longitudinal perspective (PI: Ueland) and video-ethnography and EEG in the ecoval study (PI: Vaskinn).
- Publish papers from Social cognition RCT study (PI: Vaskinn).
- Finalize translation and implementation of web-based neurocognitive tests (PI: Espeseth).
- Collaborate with the clinical group in developing new clinical and cognitive protocol to be implemented in 2018.
- Strengthen synergy profile of neurocognitive research in phase II of CoE.

### Central Publications 2017

Cognitive remediation and occupational outcome in schizophrenia spectrum disorders: A 2-year follow-up study (Lystad et al., Schizophrenia Research)

Neurocognitive functioning, clinical course and functional outcome in first-treatment bipolar I disorder patients with and without clinical relapse: A 1-year follow-up study (Demmo et al., Bipolar Disorders)

Impairment in emotion perception from body movements in individuals with bipolar I and bipolar II disorder is associated with functional capacity (Vaskinn et al., International Journal of Bipolar Disorder)

### Core Researcher

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# Brain Imaging

## Kenneth Hugdahl



### Aims

The aim is to understand the neurobiological and neurocognitive factors behind auditory hallucinations, and to contribute to develop new treatment and cognitive training methods.

### Research Focus

The research group uses a range of methods for structural and functional neuroimaging, together with neuropsychological methods of investigation. The research focus is to use cognitive, brain imaging, and neurochemistry methods and approaches to unravel the underlying neuronal changes that cause the perceptual experience of “hearing a voice”.

A special focus is on revealing the underlying neurochemistry of auditory hallucinations, and especially what is called “excitatory/inhibitory imbalance” in auditory hallucinations. With this is meant that auditory hallucinations may be the result of an imbalance in the brain between excitatory and inhibitory transmitters and that the relative balance/imbalance between these transmitters determines frequency and duration of hallucinatory episodes. For this purpose, the group has developed new sequences for MR spectroscopy to be able to measure excitatory (glutamatergic) versus inhibitory (GABAergic) transmitter levels in specific brain regions.

A further focus is on development of new sequences to measure transmitters simultaneously with changes in brain metabolism and activation in the same region in the brain. If this will turn out to be successful, it will represent a new way of understanding auditory hallucinations by focusing on the underlying neurochemistry, which in turn may lead to new pharmacological drugs for treatment.

### Main Projects

- ERC Advanced Grant project: Revealing the underlying neurocognitive and neurochemistry mechanisms behind the cyclic fluctuations seen in auditory hallucinations, and development of smartphone app technology for individualized sampling of symptom data online.
- FRIMEDBIO project: Using a multimodal imaging approach, with functional and structural MR imaging methods, to unravel the neurocognitive processes behind auditory hallucinations in schizophrenia.
- Helse-Vest project: Using fMRI, DTI and MRS to find underlying neurophysiological mechanisms for auditory hallucinations in schizophrenia.

### Achievements in 2017

- Formalized a model of levels of explanation as a basis for understanding auditory hallucinations (Bolken et al., 2017).
- Established convergence between functional and structural imaging data for auditory hallucinations in schizophrenia by showing how white matter tracts connect functional nodes in temporal and frontal lobes (Hugdahl, 2017).
- Showed that BOLD activation is possible to record simultaneously with data on glutamate and GABA (Brix et al., 2017).
- Improved on the symptom-app for online registration of symptoms related to auditory hallucinations in schizophrenia (Bless et al., in prep).
- Factor-analysed self-report questionnaire data from 450 patients related to emotional content of auditory hallucinations (Strauss et al., 2017).

### Ambitions for 2018

- Analyse previously acquired data on functional and structural MRI, with a focus on connectivity and white matter connections between activated nodes.
- Further improvement on simultaneous fMRI-MRS data acquisitions to establish vertical synergy between levels of explanation.
- Collect new data on patients with auditory hallucinations from a new cohort.

### Central Publications 2017

Auditory verbal hallucinations: neuroimaging and treatment (Bohlken et al., Psychological Medicine)

Within- and between-session reproducibility of GABA measurements with MR spectroscopy (Brix et al., Journal of Magnetic Resonance Imaging)

Auditory cortex characteristics in schizophrenia: Associations with auditory hallucinations (Mørch-Johnsen et al., Schizophrenia Bulletin)

### Core Researcher

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### Group Members

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# Structural MRI

## Ingrid Agartz



### Aims

To obtain knowledge on aetiology and pathophysiological mechanisms in severe mental disorders using brain imaging.

### Research Focus

The research focus is brain neuroanatomy studied with advanced magnetic resonance imaging (MRI) 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 use of medication. Advanced MR phenotypes are used (e.g. cortex thickness and area, myelin mapping, contrast, free-water-DTI) and development of new structural phenotypes is conducted.

We investigate large clinical cohorts of schizophrenia or bipolar disorders. In longitudinal follow-up designs we study the developmental brain trajectories. One subproject focuses on early-onset-psychosis and brain development over time in adolescents (Youth-TOP). We participate in international consortia (ENIGMA, IMAGEMEND) and coordinate two international collaborations on adolescent psychosis.

### Main Projects

- Investigation of how risk factors and biomarkers associated with disease impact on brain structure. Examples of such markers are infection or autoimmunity antibodies, early adversities in pre- or perinatal life (obstetric complications), or nutrients such as vitamin D and folate.
- Investigation of clinical symptoms such as persistent apathy, auditory hallucinations and sensory processing for associations with brain phenotypes. Evaluate influence of confounding variables.
- Brain change over lifetime: From longitudinal follow-up of adult and adolescent patient cohorts we examine the brain trajectories to help predict the future disease course.
- Early onset psychosis: A cohort of adolescents is followed over time (a multicentre study between the University of Oslo and Karolinska Institutet) for phenotypic characterization. We examine clinical and brain development, cardiovascular and metabolic factors. The aim is to increase knowledge about the causes of psychosis among youth and contribute to safer diagnosis, improved treatment and better preventive measures.
- Violence in severe mental disorders: We use advanced neuroimaging methods, registry data and thorough clinical characterization of psychotic and non-psychotic perpetrators of serious violent crimes to investigate the biological characteristics, social trajectories, and psychological core features of psychotic violence.

### Achievements in 2017

- In first-episode psychosis, antipsychotic medication demonstrates an effect on brain volume change over time independent of BMI change (Jørgensen et al., 2017).
- Alcohol use is associated with thinner cerebral cortex and larger ventricles in schizophrenia, bipolar disorder and healthy controls and can be an important confounder to brain imaging studies of other diseases (Lange et al., 2017).
- Auditory hallucinations in schizophrenia patients are related with thinner brain cortex, but not smaller surface area of the left Heschl's gyrus supporting the hypothesis that structural abnormalities of the auditory cortex underlie auditory hallucinations in schizophrenia (Mørch-Johnsen et al., 2017).
- Started the two-year follow-up of the adolescent psychosis study participants and coordinate an ENIGMA study for Youth-TOP (adolescents with early-onset psychosis).

### Ambitions for 2018

- Continue investigations of how risk factors (e.g. vitamin D or folate, antibodies from infection) or pharmacological treatment impact on brain structure or function in schizophrenia or bipolar disorder with use of advanced imaging phenotypes e.g. myelin mapping and free-water DTI.
- Initiating project evaluating brain myelination, sensory processing and psychopathology using MRI, EEG and clinical symptoms in the TOP sample (in collaboration with Erik Jönsson).
- Expand the study of violence in severe mental disorders to additional national sites (Unn K. Haukvik).
- Continue developing the adolescent psychosis cohort and data analysis.
- Launch late-onset psychosis TOP investigating patients from geriatric psychiatric clinics.

### Central Publications 2017

Alcohol use is associated with thinner cerebral cortex and larger ventricles in schizophrenia, bipolar disorder and healthy controls (Lange et al., Psychological Medicine)

Auditory cortex characteristics in schizophrenia: Associations with auditory hallucinations (Mørch-Johnsen et al., Schizophrenia Bulletin)

Brain volume change in first-episode psychosis: an effect of antipsychotic medication independent of BMI change (Jørgensen et al., Acta Psychiatrica Scandinavica)

### Core Researcher

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# Translational Psychiatry

## Ole A. Andreassen



### Aims

The group focuses on the relationship between genetic risk, environmental factors and biological variables, and how these are related to clinical disease forms and brain organic relationship in severe mental illness. The main focus is on genetic factors, since severe mental disorders have a high degree of heredity, and knowledge of the genetic structure is still sparse. There is also little knowledge about how genetic factors are related to environmental risk factors. Furthermore, the connection to different disease characteristics in patients, including clinical, cognitive and brain organic relationship is unknown. In charting such contexts, the goal is to gain more knowledge about disease mechanisms. Medications are an important part of treatment of diseases, and targets for the group are to gain more knowledge about how drugs work and interact with biological and mental factors.

### Research Focus

Discover new disease genes by severe mental disorders through participation in international consortia, with special interest for polygenic effects. Exploring disease genes and examine the context of clinical, cognitive and brain organic changes in well-described clinical material. This operation uses novel biostatistical methods and analysis. An important part of the activity is to study the mechanism of drugs. The focus is currently on the immune system; which genes affect this system, how it is related to psychological symptoms over time, and what role drugs play in this context. We also want to study the differences and similarities between disease groups, thus generating knowledge about what are disease-specific processes and what are phenotype-related processes.

### Main Projects

- **Polygenic architecture:** We use major international genetics studies along with new analysis tools to identify the polygenic contribution to disease development in bipolar disorder, schizophrenia and related disorders.
- **Genotype-phenotype mapping:** We identify the clinical and brain organic correlate genetic vulnerability factors in well described national and local cohorts of patients, and how this is related to the course.
- **Immune system:** We have a series of studies of genetic variants, serum markers, drugs and brain mechanisms related to different aspects of the immune system.
- **Psychosis across disorders:** We have several studies on developmental disorders and aging processes for finding common denominators for the development of psychosis.
- **Brain connectome:** We have several projects related to in vivo measures of connections in the brain, and how these are related to mental disorders and genetic architecture.

### Achievements in 2017

- Discovered a major individualization of functional brain networks during adolescence which is associated with later development of mental health (Kaufmann et al., 2017).
- Demonstrated cerebellar volume reductions across age ranges in schizophrenia providing evidence for a neurodevelopmental aetiology involving the cerebellum (Moberget et al., 2017).
- Identified genetic overlap between schizophrenia and cognitive functioning and brain structure volumes (Smeland et al., 2017).
- Identified genetic overlap between personality traits and a range of psychiatric disorders implicating new domains of psychopathology (Lo et al., 2017).
- Developed novel analytical tools for “Big Data” approaches to mental illness research.

### Ambitions for 2018

- Increasing our database from the large international consortia in imaging and genetics to inform causal processes in development of psychiatric disorders, leveraging novel analytical tools and the highly characterized NORMENT sample for pathophysiological studies.
- Initiate and increase activity in national population studies (MoBa) in collaborations with Nordic partners with registry and biobank data to detect gene and environment factors in severe mental disorders and develop precision medicine approaches.
- Strengthen the immunological focus by a large increase in immunologically characterized blood specimens and a closer collaboration with immunology expertise.
- Develop a BioPhysical Psychiatry synergy programme including EEG, imaging and stem cell research.

### Central Publications 2017

Delayed stabilization and individualization in connectome development are related to psychiatric disorders (Kaufmann et al., Nature Neuroscience)

Cerebellar volume and cerebellocerebral structural covariance in schizophrenia: a multisite mega-analysis of 983 patients and 1349 healthy controls (Moberget et al., Molecular Psychiatry)

Identification of genetic loci jointly influencing schizophrenia risk and the cognitive traits of verbal-numerical reasoning, reaction time, and general cognitive function (Smeland et al., JAMA Psychiatry)

Genome-wide analyses for personality traits identify six genomic loci and show correlations with psychiatric disorders (Lo et al., Nature Genetics)

Cortical abnormalities in bipolar disorder: an MRI analysis of 6503 individuals from the ENIGMA Bipolar Disorder Working Group (Hibar et al., Molecular Psychiatry)

### Core Researcher

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# Basic and Clinical Psychopharmacology

Vidar M. Steen



## Aims

The research group aims at identifying genetic and biological factors that are involved in therapeutic response and adverse effects during psychopharmacological treatment of psychotic disorders.

## Research Focus

The main focus of the research group is to explore and characterize how psychopharmacological drugs work in the treatment of schizophrenia and bipolar disorder, using a combination of clinical data, biomarker screening and functional studies in experimental models.

## Main Projects

- Screening for transcriptomic changes related to psychosis and psychopharmacological treatment, using both cross sectional and longitudinal clinical samples with matched controls.
- Examining the possible relationship between serum lipids and clinical outcome in patients treated with antipsychotic medication, including clinical samples with first episode psychosis and drug naive patients.
- Studying the metabolic effect of antipsychotic drugs in experimental models, including long-term exposure (> one year) in rat.
- Exploring the role of innate immunity in peripheral blood of patients with psychosis and matched controls.
- In addition, we participate in several projects to identify genetic risk factors for disease susceptibility and psychosis-relevant phenotypic traits.
- We are also responsible for running the Genomics Core Facility at the University of Bergen, to provide guidance and service on large scale genomic analyses.

## Achievements in 2017

- Completed the second phase of transcriptome profiling of schizophrenia, bipolar disorder and healthy controls (about 700 TOP samples).
- Identified changes in innate immunity biomarkers in patients with schizophrenia and bipolar disorder (unpublished data).
- Discovered associations between changes in serum lipid levels and cognitive performance in first episode psychosis (Gjerde et al., 2017).
- Participated in international consortia, to define the polygenic background of human brain structures, cognitive functions and neuropsychiatric phenotypes.
- Established methods and data analysis pipelines for NGS-based whole genome sequencing and RNA sequencing.

## Ambitions for 2018

- Perform RNA sequencing of about 500 peripheral blood samples (patients with schizophrenia and healthy controls) from the longitudinal Bergen Psychosis project 2 (BP2).
- Further characterize the genetic and biological mechanisms underlying activation of innate immunity markers in patients with psychosis, focusing on the effects of antipsychotic drugs.
- Study possible associations between brain imaging endophenotypes and serum lipid levels in patients with first episode psychosis treated with antipsychotic medication.

## Central Publications 2017

Increase in serum HDL level is associated with less negative symptoms after one year of antipsychotic treatment in first-episode psychosis (Gjerde et al., Schizophrenia Research)

Subchronic olanzapine exposure leads to increased expression of myelination-related genes in rat fronto-medial cortex (Erslund et al., Translational Psychiatry)

Genetic evidence for a role of the SREBP transcription system and lipid biosynthesis in schizophrenia and antipsychotic treatment (Steen et al., European Neuropsychopharmacology)

## Core Researcher

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# Epigenetics and Functional Genomics

Stéphanie Le Hellard



## Aims

Our main aim is to understand how the environment can influence the genetic susceptibility to develop psychiatric disorders by integrating environmental information with epigenetic and genetic information. We also maintain some activities in genetic studies for the identification of genes associated across psychiatric traits and related phenotypes.

## Research Focus

We particularly focus on schizophrenia and bipolar disorder. At the epigenetic level, we are characterising genome wide DNA methylation in patients and controls. We use mostly biostatistics and bioinformatics tools for the analysis of datasets. We integrate different levels of information in patients: Genetic, epigenetic, transcriptomics and environmental data. We are also developing cellular models to test the effect of environmental stressor on epigenomics and transcriptomics.

## Main Projects

- Epigenetic investigation of schizophrenia and bipolar disorder.
- Characterising epigenetic modifications across the life span.
- Characterising the molecular mechanisms of cannabis exposure risk in patients with psychosis.
- Characterising the molecular mechanisms of cannabis exposure risk in a cellular model.
- Identifying allelic heterogeneity at the gene level across mental disorders.
- Cognition and imaging genetics: We participate in several large consortium efforts and also have a few in house projects.

## Achievements in 2017

- Established a pipeline to characterise allelic heterogeneity (association at the gene level) across psychiatric traits and related phenotypes. We have then identified several genes which show such allelic heterogeneity (Polushina et al., 2017).
- Demonstrated that regions of recent evolution at the epigenome level are enriched for association in schizophrenia (Banerjee et al., unpublished data, available as preprint at: [www.biorxiv.org/content/early/2017/03/02/113175](http://www.biorxiv.org/content/early/2017/03/02/113175))
- Obtained genome wide DNA methylation typing in a sample of 1,000 individuals.
- Identified regions of potential differential methylation between cannabis users and non-users.

## Ambitions for 2018

- Publication of the regions of allelic heterogeneity.
- Publication of the regions of differential methylation in cannabis users.
- Genome wide DNA methylation typing in a total sample of 6,000 individuals from birth to adulthood.
- Establishing a model for the effect of cannabis in cells.

## Central Publications 2017

Analysis of the joint effect of SNPs to identify independent loci and allelic heterogeneity in schizophrenia GWAS data (Polushina et al., Translational Psychiatry)

A genetic association study of CSMD1 and CSMD2 with cognitive function (Athanasiu et al., Brain, Behavior, Immunity)

Identification of gene loci that overlap between schizophrenia and educational attainment (Le Hellard et al., Schizophrenia Bulletin)

## Core Researcher

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## Group Members

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# Psychiatric Molecular Genetics

## Srdjan Djurovic



### Aims

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.

### Research Focus

We have continued and developed support for the infrastructure, providing platform activities that include biobanking, database support, sample preparation, and quality control, as well as inclusion of samples for stem cells project and building up stem cells infrastructure. We have established the required competence and facilities for human induced pluripotent stem cell (iPSC) technology unit in our Centre allowing investigation of neuronal cells from participants. As of December 2017, fibroblasts have been collected from 70 participants. Validated iPSCs will be differentiated to neural progenitor cells (neural conversion) and regionalized neuronal subtypes, as well as astrocytes/ glial populations under standard in house methods. We also want to develop a psychopharmacological screening platform for psychiatric disorders using iPSC-derived neurons. Our efforts in identifying the polygenic basis of the human brain and neurodevelopmental disorders resulted in several translational studies published and we aim to further studies elucidating deep molecular phenotyping.

### Main Projects

- Human induced pluripotent stem cell (iPSC) technologies in psychiatric molecular genetics.
- Identification of the hidden heritability of severe mental disorders.
- Identifying the polygenic basis of the human brain and neurodevelopmental disorders .
- Prediction of longitudinal outcome and brain phenotype by polygenic scores.
- Identification of genetic loci associated with neurocognitive and MR phenotypes and plications for disease mechanisms in severe mental disorders.
- Biobanking, database, sample preparation, quality control.

### Achievements in 2017

- Inclusion of samples for stem cells project and building up stem cells infrastructure, and production and further characterization of induced pluripotent stem cells and induced neurons.
- Infrastructure/platform activities: Biobanking, database, sample prep, quality control.
- Identifying the polygenic basis of the human brain and neurodevelopmental disorders.
- New national and international collaborations established.
- Development and improvement of genetic prediction tools for disease course and outcome.

### Ambitions for 2018

- Continue inclusion for stem cells project and production and further characterization of induced pluripotent stem cells and induced neurons.
- Continue with disease modelling using stem cells.
- Continuation of translational projects.
- Explore how cortical network dynamics are related to genetics of psychotic disorders.
- Continuation of work at international collaboration.

### Central Publications 2017

**Genetic evidence for role of integration of fast and slow neurotransmission in schizophrenia** (Devor et al., Molecular Psychiatry)

**A genetic association study of CSMD1 and CSMD2 with cognitive function** (Athanasiu et al., Brain, Behavior, Immunity)

**Leveraging genome characteristics to improve gene discovery for putamen subcortical brain structure** (Chen et al., Scientific Reports)

### Core Researcher

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## Collaboration Across Research Groups

NORMENT is organized as an efficient cross-disciplinary research centre, where sharing of competence and infrastructure is a key principle. We have set aside about half of the Centre of Excellence grant to fund our core infrastructure, to enable easy access to state-of-the-art methodology, infrastructure for recruitment and assessment of participants, and database and biobank services. Most if not all research activities at the Centre depend on this tight integration and efficient use of resources across different research groups.

The “vertical synergy” approach that is used at the Centre (see page 10), requires a close collaboration between research groups and across scientific disciplines. 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 internal web pages. 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.

A few examples of publications based on synergy projects in 2017 are shown below:

Aas M, Melle I, Bettella F, Djurovic S, Le Hellard S, Bjella T, Ringen PA, Lagerberg TV, Smeland OB, Agartz I, Andreassen OA, Tesli M. Psychotic patients who used cannabis frequently before illness onset have higher genetic predisposition to schizophrenia than those who did not. *Psychological Medicine*.

Hoseth EZ, Ueland T, Dieset I, Birnbaum R, Shin JH, Kleinman JE, Hyde TM, Mørch RH, Hope S, Lekva T, Abraitte AJ, Michelsen AE, Melle I, Westlye LT, Ueland T, Djurovic S, Aukrust P, Weinberger DR, Andreassen OA. A study of TNF pathway activation in schizophrenia and bipolar disorder in plasma and brain tissue. *Schizophrenia Bulletin*.

Kaufmann T, Alnæs D, Brandt CL, Doan NT, Kauppi K, Bettella F, Lagerberg TV, Berg AO, Djurovic S, Agartz I, Melle I, Ueland T, Andreassen OA, Westlye LT. Task modulations and clinical manifestations in the brain functional connectome in 1615 fMRI datasets. *Neuroimage*.

Le Hellard S, Wang Y, Witoelar A, Zuber V, Bettella F, Hugdahl K, Espeseth T, Steen VM, Melle I, Desikan R, Schork AJ, Thompson WK, Dale AM, Djurovic S, Andreassen OA; Schizophrenia Working Group of the PGC. Identification of gene loci that overlap between schizophrenia and educational attainment. *Schizophrenia Bulletin*.

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

**Genetics:** Combine large amounts of genetic data with relevant environmental factors, and move this to experimental studies in human stem cells. This is a novel approach at the Centre which is likely to open new opportunities to examine disease mechanisms.

**Antipsychotic Medication:** Study specific immune and lipid (fat) mechanisms in clinical groups, and translate these to animal and stem cell studies to better understand the action of medication.

**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 Predictors:** 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.

Being a Centre of Excellence provides great opportunities to broaden and strengthen our cooperation, align research goals, and profit from of our complementary expertise and valuable infrastructure, as well as performing more cost-efficient research through strong leadership and an integrated approach. Further, there is a large degree of sharing of postdocs and support personnel across different groups, and several PhD students have been co-supervised by Core Researchers and members of different research groups at the Centre.



## Top Day 2017 NORMENT

June 8 - Ullevål, Oslo.

- 09.00 - 09.30 Ole A. Andreassen: Update and plans
- 09.30 - 09.55 Ingrid Melle: Activity and teams
- 09.55 - 10.20 Ragni H. Mørch: PhD summary: Inflammation in severe mental disorders
- 10.35 - 10.55 Linn C.B. Norbom: Grey-white matter intensity contrast, associations with age and risk of psychosis in youth
- 10.55 - 11.15 Nathalia Zak: Longitudinal studies of cortical plasticity and structure in bipolar disorder type II
- 11.15 - 11.35 Alice Popejoy: Oh Say, Can You See? Illuminating the Importance of Light Detection Genes in Humans
- 11.35 - 11.55 Genevieve Richard: Assessing treatment-induced neuroplasticity using multimodal MRI
- 11.55 - 12.45 Lunch
- 12.45 - 12.50 Chair: Trine Vik Lagerberg After Lunch Programme
- 12.50 - 13.10 Lynn Mørch-Johnsen: Brain structural correlates of auditory hallucinations in schizophrenia and bipolar disorder
- 13.20 - 13.40 Magnus Johan Engen: Cognitive dimensions and global functioning in relapsing and non-relapsing first episode psychosis patients
- 13.40 - 14.00 Trude Jahr Iversen: Metabolic side effects of antipsychotic drugs - focus on adiponectin and thyroid hormones
- 14.00 - 14.20 Siren Tønnesen: Predicting brain age in healthy controls, bipolar disorders and schizophrenia using multisite diffusion tensor imaging
- 14.35 - 15.00 Beathe Haatveit: PhD summary: Executive functioning in schizophrenia spectrum disorders: Methods of measurement and longitudinal course
- 15.00 - 15.25 Erlend S. Gardsjord: PhD summary: Subjective quality of life in first-episode-psychosis
- 15.25 - 15.50 Kjetil N. Jørgensen: PhD summary: Understanding brain structure alterations in severe mental disorders: The role of cigarette smoking, antipsychotic medication and weight gain

## Researcher Training

NORMENT offers a range of training and development opportunities for our PhD students, postgraduate researchers, and other research staff. About 45 PhD students and 40 postdoctoral fellows were working at or affiliated with the Centre in 2017. During the year, there have been various gatherings and meetings with the aim of contributing to a best possible researcher training. Scientific sharing and synergy across domains were important topics at these events, and is an underlying principle for all research activities at the Centre.

### PhD Education and Training of Young 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 at a national level. 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 2017, NORMENT organized weekly research meetings where PhD students and postdocs presented their projects, results and future plans across research groups and scientific disciplines. There were also weekly workshops in the fields of statistics, academic writing, and clinical supervision, as well as meetings organized by the different research groups at the Centre where PhD students and postdocs presented their research.

### TOP Day

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 2017, the TOP Day took place in Oslo on June 08. After a general introduction by centre director Ole A. Andreassen and deputy director Ingrid Melle, 12 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.



### Young Researchers Meeting

Another important event related to researcher training at the Centre is the Young Researchers Meeting. This was established in 2015 as a yearly one-day meeting for the PhD students, postdocs and other researchers that are early in their career. The meeting is fully planned by the young researchers themselves and is an arena to discuss topics that they consider important to their scientific development and career.

The Young Researchers Meeting in 2017 took place on November 07 at The Norwegian Academy of Science and Letters in Oslo, and 50 people attended the meeting. The topic of the meeting was “The diagnostic system of the future”, with a focus on psychotic disorders.

Different groups at the Centre presented relevant knowledge from their field, to provide both a clinical, cognitive, brain imaging, genetic, and biomarkers perspective on the topic. These were followed by group discussions and debates built on the framework of the “Maudsley debates”. The discussions resulted in many interesting perspectives and reflections on the use of diagnostic categories in psychiatry, to what extent our current knowledge about biological mechanisms of the disorders supports the diagnostic system, and how the future development of the diagnostic system might be.

### 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 2017, there were nine Synergy Meetings in total, each with 20-40 participants from different groups at the Centre. The meetings covered broad topics such as Genetics, Biostatistical Approaches, Registry Data, eNORMENT, Immunology, Psychopharmacology, Epigenetics, and Stem Cells.



### Annual Retreat

The Annual Retreat is the main event for everyone at the Centre, and is organized as a yearly two-day conference in an interactive and enthusiastic atmosphere. In 2017, the meeting took place on September 18-19 at Quality Hotel Expo at Fornebu outside Oslo. More than 130 people from Oslo and Bergen participated, in addition to members of our Scientific Advisory Committee, the User Council, and external researchers invited to give talks on specific topics of relevance for the work at NORMENT.

The main part of the programme consisted of plenary lectures given by researchers and postdocs at the Centre, where findings and ongoing projects were described. These lectures were divided into separate sections, such as Molecular Psychiatry, Immunology, Clinical and Psychological Perspectives, Lifespan Perspectives, and Neurocognitive and Imaging Biomarker Approaches, but still with a focus on the synergy between projects and topics.

Simon Kyaga from Karolinska Institutet in Sweden was invited to give a talk on creativity and psychopathology, while Ivar Ragne Jenssen from the Norwegian Broadcasting Corporation (NRK) talked about developmental processes and thinking in organizations, both of them contributing with some new and important perspectives of relevance for our research.

Project meetings were also a part of the retreat, in addition to a separate workshop focusing on dissemination and social media, reflecting that this topic is increasingly important at the Centre.

During the poster session at the end of the first day, master students and PhD students, as well as postdocs, got the opportunity to present new findings and discuss projects and ideas in a more informal setting. This year’s prize for best poster was awarded to postdoc Anja Torsvik working in Bergen, for her poster entitled “Global gene expression analysis in schizophrenia and bipolar disorders: activation of immune pathways”. With the prize also comes a grant of NOK 10,000 from the Dr. Einar Martens Foundation to be used on research.



Postdoc Anja Torsvik was awarded the poster prize at the Annual Retreat.

A number of other PhD students and postdocs also presented posters at the retreat:

**Akiah Ottesen Berg:** Vitamin D deficiency, VDR genetic polymorphisms, and brain volume in patients with psychosis.

**Alex Craig-Craven:** Initial Experiences with Functional MRS of GABA.

**Ann Færden:** Self report of apathy in first episode psychosis.

**Daniel Quintana:** Dose-dependent social-cognitive effects of intranasal oxytocin delivered with novel Breath Powered device in adults with autism spectrum disorder: A randomized placebo-controlled double-blind crossover trial

**Erlend Strand Gardsjord:** Are predictors of subjective quality of life stable over the course of a psychotic disorder.

**Ifeoma Onyeka:** Comorbidity of physical disorders among patients with severe mental illness with and without substance use: a systematic review.

**Ingrid Hartveit Svendsen:** Seven year follow-up of first episode psychosis: Prediction of diagnostic changes and stability in self-disturbances.

**Jannicke Fjæra Anderssen:** The effects of sleep disturbance in severe mental disorders.

**Monica Aas:** Childhood maltreatment severity is associated with elevated C-reactive protein and body mass index in adults with schizophrenia and bipolar diagnoses.

**Oleksandr Frei:** Bivariate Gaussian Mixture Model of GWAS (BGMG) detects polygenic overlap between complex traits beyond genetic correlation.

**Ragni Mørch:** Inflammatory markers are altered in severe mental disorders independent of comorbid cardiometabolic disease risk factors.

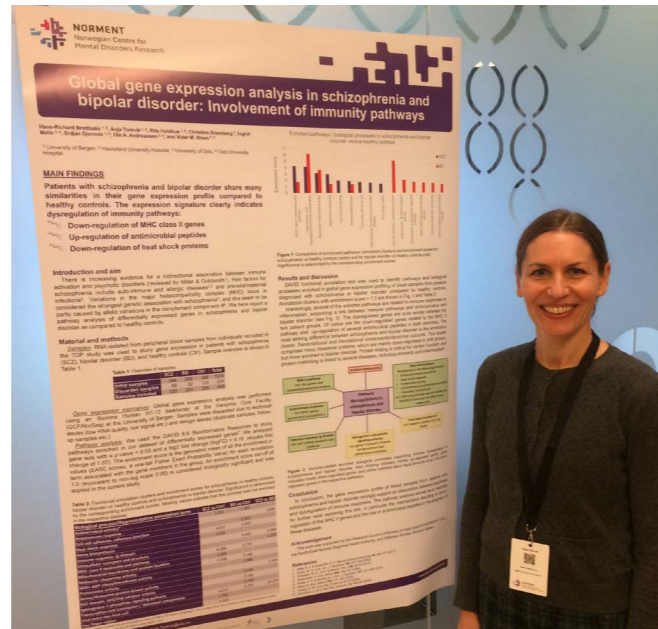
**Runar Smelror:** Disorganized Symptoms are Associated With Neurocognitive Impairment in Adolescent Schizophrenia: Measured With the MATRICS Cognitive Battery and the Wallwork/Fortgang PANSS 5-Factor Model.

**Siv Hege Lyngstad:** Enduring Depression and Apathy in First-episode Psychosis. Consequences for Outcome at 1 year Follow-up.

**Tatiana Polushina:** Allelic heterogeneity across psychotic disorders and related phenotypes.

**Trude Seselie Jahr Iversen:** Thyroid status in patients with psychotic disorders and contribution from use of antipsychotics - preliminary results.

**Wen Li:** Molecule-based analysis of genetic correlation among psychiatric disorders



## Annual Retreat 2017

September 18 - Day one

12.00 - 13.00	<b>Lunch</b>
13.00 - 13.30	Welcome address and status of NORMENT by Ole A. Andreassen
13.30 - 14.00	Simon Kyaga, senior consultant in Psychiatry, Karolinska Institutet: Creativity and Psychopathology
14.45 - 15.45	<b>Molecular Psychiatry</b> Moderator: Srdjan Djurovic
14.45 - 15.00	Alexey Shadrin: Unraveling the genetics complex traits using GWAS summary statistics
15.00 - 15.15	Jarek Rokicki: Gene expression patterns in the brain and relevance for psychiatry
15.15 - 15.30	Anne-Kristin Stavrum and Vidar M. Steen: Transcriptomics and Methyloicis resources, what we have so far, how to use the data and examples
15.30 - 15.45	Attila Szabo: Application of human induced neuronal stem cells to investigate the role of inflammatory factors in severe mental disorders
16.15 - 17.00	<b>Immunology</b> Moderator: Ingrid Dieset
16.15 - 16.30	Rune A. Kroken: First wave of cytokine analyses from the Best Intro Study with repeated measures
16.30 - 16.45	Eva Z. Hoseth: Immune and Wnt pathway in psychosis
16.45 - 17.00	Erik Johnsen: Norwegian Prednisolone in Early Psychosis Study, rationale and design
17.15 - 18.15	<b>Clinical and Psychological Perspectives</b> Moderator: Torill Ueland
17.15 - 17.30	Anja Vaskinn: Linking "neuro" to "psychology" in schizophrenia: A personalized investigation of electrophysiology, cognition and real-life behaviour
17.30 - 17.45	Julien Laloyaux: An experimental psychology approach to positive psychotic symptoms
17.45 - 18.00	Ingrid Melle: Is untreated bipolar disorder dangerous?
18.00 - 19.15	Tobias Kaufmann: Age patterns and sexual dimorphic brain features across a range of psychiatric disorders: A large scale investigation of 20,032 MRI scans
18.15 - 19.00	<b>Poster session and Aperitif: Doktor Einar Martens Legat Poster Prize 2017</b>
19.30	<b>Dinner</b>



September 19 - Day two

08.30 - 09.30	Ivar Ragne Jenssen, NRK: Fra seminarprat til praktisk handling
09.45 - 11.00	<b>Lifespan perspectives</b> Moderator: Ingrid Agartz
09.45 - 10.00	Else-Marie Løberg: Findings from clinical hallucinations data from the "Barn i Bergen" study
10.15 - 10.30	Nina Mørkved: Data on trauma and psychosis from the Bergen psychosis project 2 in the lifespan perspectives
10.30 - 10.45	Vera Lonning and Runar Smelror: YouthTOP - early results
10.45 - 11.00	Yunpeng Wang: Registry results
11.15 - 12.45	<b>Neurocognitive and Imaging Biomarker Approaches</b> Moderator: Kristiina Kompus
11.15 - 11.30	Verónica Expósito de Mäki-Marttunen: Cognitive control and the locus coeruleus-norepinephrine system
11.30 - 11.45	Unn Haukvik: Imaging psychotic violence
11.45 - 12.00	Tiril Pedersen Gurholt: Studies on folate, vitamin D and intracranial brain volume
12.00 - 12.15	Torgeir Moberget: A multi-sample study of cerebellar involvement in (severe) mental illness
12.15 - 12.30	Priyanthi B. Gjerde and Kjetil N. Jørgensen: Lipids, cortical thickness and gray/white matter intensity contrast across the psychosis spectrum
12.30 - 12.45	Ole A. Andreassen: Conclusive remarks
12.45 - 13.45	<b>Lunch</b>
13.45 - 15.15	<b>Parallel sessions</b>
	<b>Dissemination/Social media</b>
13.45 - 14.05	Christine Lycke Brandt: Dissemination and communication at NORMENT
14.05 - 14.25	Daniel S. Quintana: Using social media to disseminate your research and boost your scientific career
14.25 - 14.55	Petter Nesser: How terrorists and terrorist researchers exploit social media
14.55 - 15.15	Discussion: Purpose and methods of social media strategies
	<b>Project meetings Oslo-Bergen</b>
14.15 - 15.15	Immune function and inflammation
14.15 - 15.15	Genotyping the control pipeline



# PhD Dissertations

## 2013

**Dieset, Ingrid:** Endothelial and inflammation markers in schizophrenia and bipolar disorder, supervisor: Ole A. Andreassen, 28.11.2013

**Reckless, Greg:** A functional MRI investigation of the relationship between extrinsic motivation and decision-making: normal characteristics and possible dysfunction in schizophrenia. supervisor: Jimmy Jensen, 20.12.2013

**Wirgenes, Katrine:** Genetic factors in schizophrenia associated with endophenotypes, supervisor: Ole A. Andreassen, 04.12.2013

## 2014

**Barder, Helene:** Longitudinal neurocognitive trajectories in first-episode psychosis: Relationships between illness severity and cognitive course, supervisor: Kjetil Sundet, 23.06.2014

**Bratlien, Unni:** The relevance of premorbid and prodromal phases in psychotic disorders, supervisor: Merete Gløne Øie, 28.05.2014

**Elvsåshagen, Torbjørn:** A study of cortical structure and plasticity in bipolar II disorder, supervisor: Ulrik Fredrik Malt, 19.05.2014

**Falkenberg, Liv Eggset:** Neuronal underpinnings of healthy and dysfunctional cognitive control, supervisor: Kenneth Hugdahl, 05.12.2014

**Holmen, Aina:** Neurocognition in early-onset schizophrenia with a particular focus on executive function, supervisor: Bjørn Rishovd Rund, 23.01.2014

**Mattingsdal, Morten:** Functional profiling of single-nucleotide polymorphisms associated with bipolar disorder, supervisor: Ole A. Andreassen, 02.09.2014

**Mork, Erlend:** Self-harm in patients with schizophrenia: risk factors and clinical characteristics, supervisor: Lars Mehlum, 04.09.2014

## 2015

**Bless, Josef:** The smartphone as a research tool in psychology. Assessment of language lateralization and training of auditory attention, supervisor: Kenneth Hugdahl, 15.10.2015

**Fernandes, Carla P. D.:** A genetic study of schizophrenia and bipolar disorder - a cognitive endophenotype approach, supervisor: Stephanie Le Hellard, 05.03.2015

**Gjevik, Elen:** Psychiatric comorbidity in children with autism spectrum disorder - from genes to clinical characteristics. supervisor: Ole A. Andreassen, 27.05.2015

**Sönmez, Nasrettin:** Depressive symptoms and cognitive behavior therapy in first episode psychosis, supervisor: Jan Ivar Røssberg, 29.05.2015

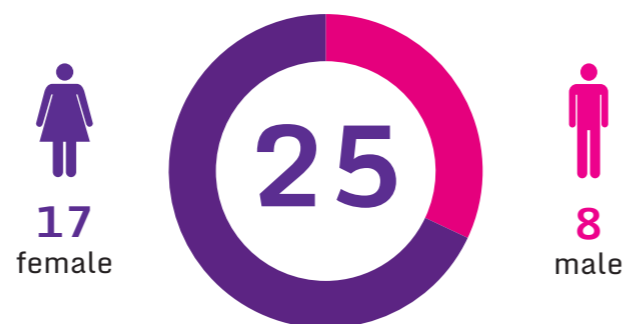
## 2016

**Bolstad, Ingeborg:** Effects of aripiprazole vs haloperidol on brain activity in healthy volunteers, supervisor: Jimmy Jensen, 08.03.2016

**Brandt, Christine Lycke:** Brain networks in psychotic disorders: A neuroimaging study of working memory related activation, connectivity and anatomy, supervisor: Lars Tjelta Westlye, 13.06.2016

**Lystad, June Ullevoldsæter:** Neurocognition, cognitive remediation and functional outcome in schizophrenia spectrum disorders, supervisor: Torill Ueland, 09.12.2016

25 PhD candidates have so far completed their PhDs at the Centre



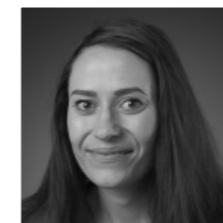
## 2017



**Kristina Skåtun:** Abnormal brain connectivity in schizophrenia and bipolar disorder - a resting state functional MRI study, supervisor: Lars T. Westlye, 19.01.2017



**Mari Nerhus:** Migration and Vitamin D in psychotic disorders - A cross sectional study of clinical and cognitive correlates, supervisor: Ingrid Melle, 03.03.2017



**Marit Haram:** The relationship between oxytocin pathway genes and personality traits and psychosis characteristics, supervisor: Martin Tesli, 01.06.2017



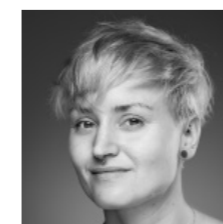
**Kjetil Nordbø Jørgensen:** Understanding brain structure alterations in severe mental disorders: The influence of cigarette smoking, anti-psychotic medication and weight gain, supervisor: Ingrid Agartz, 20.06.2017



**Beathe Almenning Haatveit:** Executive functioning in schizophrenia spectrum disorders: Methods of measurement and longitudinal course, supervisor: Torill Ueland, 22.08.2017



**Lynn Mørch-Johnsen:** Brain structure imaging of apathy and auditory hallucinations in psychotic disorders, supervisor: Ingrid Agartz, 01.12.2017



**Tiril Østefjells:** Metacognition in severe mental disorders, supervisor: Jan Ivar Røssberg, 07.12.2017



**Levi Kvitland:** Cannabis use in the early phase of bipolar disorder. A naturalistic longitudinal study of a first treatment sample, supervisor: Petter Andreas Ringen, 08.12.2017

# International Collaboration

The research at NORMENT requires close cooperation with leading research environments, both nationally and internationally. The researchers at the Centre collaborate with a large number of researchers abroad (see page 52), participate in a series of international networks and consortia (see page 53), and have several bilateral research programmes with international institutions, mainly in Europe and the USA.

These collaborations resulted in a number of important scientific findings in 2017, including the detection of a genetic overlap between schizophrenia and cognitive functioning (Smeland et al., JAMA Psychiatry), and the finding that the cerebellum is among the most affected brain regions in schizophrenia (Moberget et al., Molecular Psychiatry). As part of the Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA) consortium we contributed to findings of cortical brain abnormalities in bipolar disorder (Hibar et al., Molecular Psychiatry) and widespread alterations of brain fibre pathways in schizophrenia (Kelly et al., Molecular Psychiatry). Through the Psychiatric Genomics Consortium (PGC) we reported new genetic copy number variants in schizophrenia (Marshall et al., Nature Genetics).

NORMENT also actively recruits excellent researchers from other countries through international advertisements and networking, and as a result of this the Centre staff consisted of people from 29 nationalities in 2017.

## Visits Abroad

We also strive to strengthen the mobility of PhD, postdoc and senior scientists exchanged with a diversity of countries, and work to host students from other countries. In 2017, postdoc Olav Smeland and researchers Tobias Kaufmann and Yunpeng Wang were located abroad (Smeland in San Diego, USA; Kaufmann in Tübingen, Germany; Wang in Copenhagen, Denmark), while researcher Monica Aas had two two-months stays at Harvard University, Boston, USA.

Several researchers also had shorter stays abroad, to discuss collaborative projects and participate in project meetings. Some examples are shown here:

**Alexey Shadrin** visited Professor Anders M. Dale, University of California San Diego, USA, to discuss and work on collaborative projects.

**Ann Færden** visited Professor Valerie Krasnov, Moscow Research Institute of Psychiatry, Russia, for cooperation with psychiatry in Russia financed by the University of Oslo.

**Daniel Quintana** visited Postdoc Julian Koenig, Heidelberg University, Germany, for collaborative discussion and seminar presentation.

**Erik Jönsson** had weekly visits to the Centre for Psychiatric Research, Department of Clinical Neuroscience, Karolinska Institutet, Sweden, to work on collaborative projects, including HUBIN (Human Brain Informatics), SCAPS (Stockholm Child and Adolescent Psychosis Study), and KaSP (Karolinska Schizophrenia Project).

**Ingrid Agartz** had several visits to the Centre for Psychiatric Research, Department of Clinical Neuroscience, Karolinska Institutet, Sweden, for research meetings and data collection in HUBIN, SCAPS and KaSP projects.

**Kenneth Hugdahl** visited Professor Iris Sommer, Utrecht University Medical Center, Netherlands, to discuss collaborative projects.

**Kirsten Wedervang-Resell** visited the Mindlock Research Group, Department of Psychiatry, University of Oxford, UK, for article writing.

**Oleksandr Frei** visited the Center for Translational Imaging and Precision Medicine, University of California San Diego, USA, to collaborate on the project "Bivariate Gaussian Mixture Model of GWAS".

**Silje Skrede** visited Professor Miguel López, Research Center of Molecular Medicine and Chronic Diseases, University of Santiago de Compostela-Instituto de Investigación Sanitaria, Spain, to perform animal experiments.

**Torbjørn Elvsåshagen** visited the Section on Neural Plasticity, NIMH, USA, for general discussion concerning neuroplasticity in health and disease, and discussion of research findings.

## Visits From Abroad

In 2017, several international researchers were invited to give guest lectures at the Centre in relation to project meetings and discussions, and we had three master students visiting from other European countries.



Professor André Aleman giving a lecture at NORMENT

## Guest Lectures

**André Aleman**, University of Groningen, Netherlands: Noninvasive neurostimulation to target brain circuits underlying positive and negative symptoms in schizophrenia, Oslo

**Chi-Hua Chen**, University of California San Diego, USA: Genes, the brain and psychiatric disorders, Oslo

**Douglas Garrett**, Max Planck Institute, Berlin, Germany: Bring the noise: Variability as signal in the study of human aging and cognition, Oslo

**Gitte Moos Knudsen**, Copenhagen University Hospital, Denmark: The Neurobiology Research Unit at Rigshospitalet/Copenhagen University Hospital, Oslo

**Iris Sommer**, Utrecht University Medical Center, Netherlands: Top-down processing in hallucinations, Bergen

**Johanne Badcock**, University Western Australia, Australia: Loneliness and its relationship to mental and physical health across the psychosis spectrum, Bergen

**Thomas Wolfers**, University of Nijmegen, Netherlands: Normative modelling and pattern-recognition for meta-analyses, Oslo



Professor Gitte Moos Knudsen giving a lecture at NORMENT

## Student Internships

**Alessia Di Sero**, Centre for Mind/Brain Sciences, University of Trento, Italy: Master thesis in Cognitive Neuroscience, Structural MRI Group, 11 months

**Alice B. Popejoy**, Institute for Public Health Genetics, University of Washington, Seattle, USA: PhD student internship (RCN visiting student grant), Translational Psychiatry Group (Biostatistics), 6 months

**Daniel Roelfs**, Faculty of Medicine, Lund University, Sweden: Master student internship (Erasmus exchange), Translational Psychiatry Group (Electrophysiology), 6 months

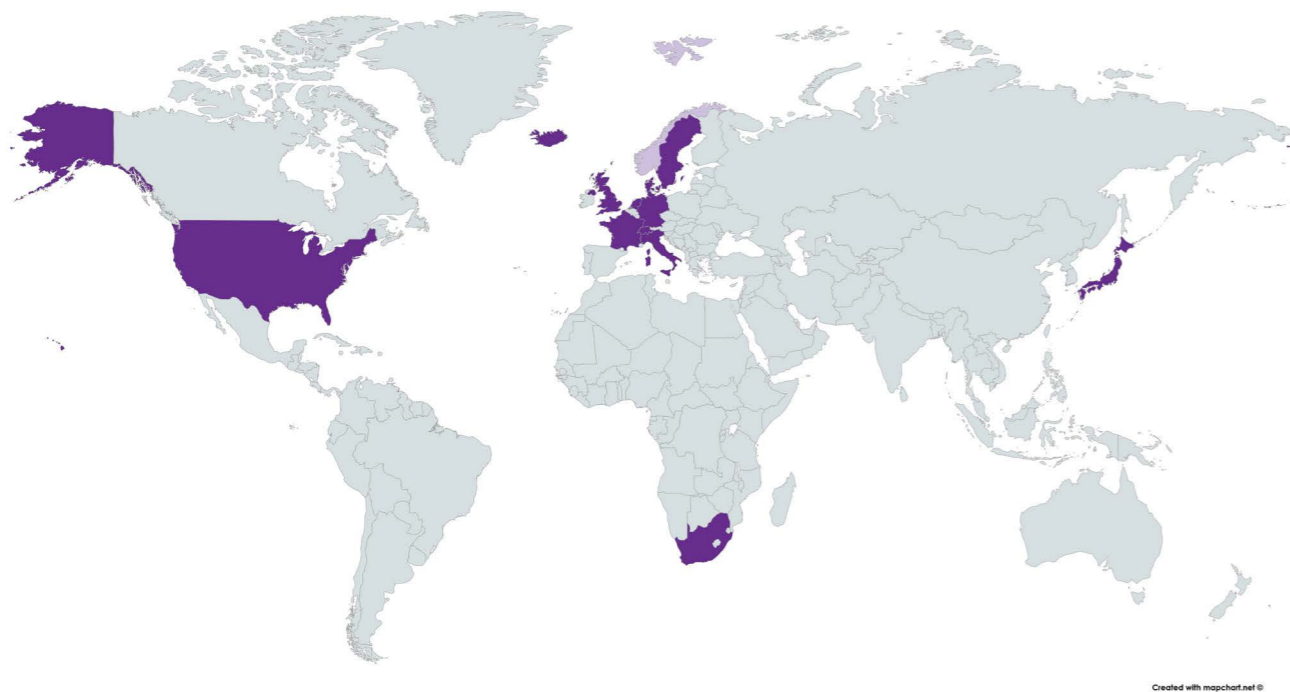
**Jessica Izzo**, Department of Psychology, University of Turin, Italy: Master student internship (Erasmus exchange), Translational Psychiatry Group (Multimodal MRI), 3 months

## Guest Researchers

Three international guest researchers, all from the University of California San Diego, USA, had part-time positions at NORMENT in 2017:

- **Professor Anders M. Dale**
- **Associate Professor Anna Devor**
- **Associate Professor Wesley Thompson**

The guest researchers paid several visits to research groups at NORMENT in 2017, to contribute with knowledge and analyses, discuss projects, and plan future studies with researchers at the Centre.



## International Collaborators

### Nordic Countries

#### Denmark

- **Christian Gerlach**, Professor, University of Southern Denmark, Odense
- **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

#### Sweden

- **Anna Falk**, Associate Professor, Karolinska Institutet, Stockholm
- **Göran Engberg**, Professor, Karolinska Institutet, Stockholm
- **Håkan Ahlström**, Professor, Akademiska Hospital, Uppsala
- **Lars Farde**, Professor, Karolinska Institutet, Stockholm
- **Mikael Landén**, Professor, University of Gothenburg
- **Patrick F. Sullivan**, Professor, Karolinska Institutet, Stockholm
- **Simon Cervenka**, Senior Lecturer, Karolinska Institutet, Stockholm
- **Sophie Erhardt**, Professor, Karolinska Institutet, Stockholm

### Europe

#### 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

#### Germany

- **Andreas Meyer-Lindenberg**, Professor, University Medical Centre Mannheim
- **Douglas Garrett**, Fellow, Max Planck Institute for Human Development, Berlin
- **Markus Nöthen**, Professor, University of Bonn
- **Per Hoffman**, Post doc, Life and Brain GmbH, Bonn
- **Rea-Rodriguez-Raecke**, Post doc, University of Aachen

#### Italy

- **Alessandro Bertolino**, Professor, University of Bari
- **Silvana Galderisi**, Professor, University of Naples

#### Netherlands

- **Andre Aleman**, Professor, Groningen University Medical Center
- **Danielle Posthuma**, Professor, Vrije Universiteit, Amsterdam
- **Iris Sommer**, Professor, Utrecht University Medical Center
- **Vivi Heine**, Professor, Vrije Universiteit, Amsterdam

### Switzerland

- **Ahmad Abu-Akel**, Professor, University of Lausanne
- **Narly Golestani**, Professor, University of Geneva
- **Sven Cichon**, Professor, University of Basel

### United Kingdom

- **Angela Vincent**, Professor Emeritus, University of Oxford, Oxford
- **Clara Strauss**, Honorary Senior Lecturer, Sussex University, Brighton
- **Michael O'Donovan**, Professor, Cardiff University, Cardiff
- **Stephen Smith**, Professor, Oxford University, Oxford

### USA

- **Anders M. Dale**, Professor, University of California San Diego
- **Anna Devor**, Associate Professor, University of California San Diego
- **John Kelsoe**, Professor, University of California San Diego
- **Jordan Smoller**, Professor, Harvard Medical School, Boston
- **Joseph Ventura**, Professor, University of California Los Angeles
- **Morris Bell**, Professor, Yale School of Medicine, New Haven
- **Ofer Pasternak**, Associate Professor, Harvard Medical School, Boston
- **Patrick Sullivan**, Professor, University of North Carolina of Chapel Hill
- **Paul Thompson**, Professor, University of Southern California, Los Angeles
- **Robert H. Yolken**, Professor, Johns Hopkins School of Medicine, New York
- **Wesley Thompson**, Associate Professor, University of California San Diego
- **William Horan**, Senior Scientist, University of California Los Angeles

### Other Countries

#### Japan

- **Gaku Okugawa**, Associate Professor, Kansai Medical University, Osaka

#### South Africa

- **Dan Stein**, Professor, University of Cape Town

## International Projects and Consortia

**Center for Traumatic Brain Injury (Center-TBI)**  
<https://www.center-tbi.eu/>

**Cognitive Genomics Consortium (COGENT)**  
<http://www.feinsteininstitute.org/2017/01/feinstein-institute-genetic-discovery-provides-new-insight-cognitive-disorders>

**Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE)**  
<http://www.chargeconsortium.com>

**European Negative Symptoms Research Network (EuroNES)**  
<http://eurones.eu>

**European College of Neuropsychopharmacology (ECNP) Bipolar Disorders Network**  
 (CR Andreassen chairs the ECNP Bipolar Network)  
<https://www.ecnp.eu/research-innovation/ECNP-networks/List-ECNP-Networks/Bipolar-Disorders.aspx>

**European College of Neuropsychopharmacology (ECNP) Schizophrenia Network**  
<https://www.ecnp.eu/research-innovation/ECNP-networks/List-ECNP-Networks/Schizophrenia.aspx>

**Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA)**  
 (CR Andreassen leads the ENIGMA Bipolar Working Group, and CR Agartz leads the ENIGMA Early Onset Psychosis Working Group)  
<http://enigma.ini.usc.edu>

**Imaging Genetics for Mental Disorders (IMAGEMEND)**  
<http://www.imagemend.eu>

**International Consortium on Hallucination Research (ICHR)**  
<https://hallucinationconsortium.org>

**Psychiatric Genomics Consortium (PGC)**  
 (CR Andreassen chairs the PGC Bipolar Disorder Working Group)  
<https://www.med.unc.edu/pgc>

**Psychiatric Diagnostic and Prevention Consortium (PsychDPC)**  
<http://www.psych-dpc.eu>

Norske og amerikanske forskere har  
 eit menneske vil utvikle demenssjukdomen Alzheimers. Det vil enno ta ein del tid før  
 testen kan takast i bruk her i landet.



**SFF NORMENT**  
 @SFFNORMENT  
 NORMENT: Norsk senter for forskning på mentale lidelser. K.G. Jebsen-senter for psykoseforskning. Norwegian Centre for Mental Disorders Research

Oslo, Norway  
 med.uio.no/norment/  
 Joined April 2016  
 58 Photos and videos

Tweets 265 Following 170 Followers 177 Likes 64

Tweets Tweets & replies Media

SFF NORMENT @SFFNORMENT · Nov 11  
 NORMENT-studie omtalt i @DagensMedisin #cannabis #gener #psykose @Monica\_Aas

**Høyere genetisk risiko for psykose blant cannabi...**  
 Ny studie kan tyde på at det er en genetisk sammenheng mellom bruk av cannabis og psykoseutvikling.  
 dagensmedisin.no

SFF NORMENT Retweeted  
 UNESCO @UNESCO · Nov 10  
 Science empowers people to develop the solutions they need, providing local answers to global challenges.

November 10 is World #ScienceDay for Peace & Development!

## Dissemination and Communication

NORMENT continuously works to communicate our research, not only to other researchers through publications in scientific journals and presentations at scientific conferences and meetings, but also to patient organizations, health personnel, and the general public. A selection of our dissemination activities are listed on the following pages.

During 2017, we have also used more resources on our website ([www.med.uio/norment](http://www.med.uio/norment)), as well as our Twitter account (<https://twitter.com/SFFNORMENT>).

The website has been updated with new information about the Centre, our research, and information for study participants. We also publish news articles on a regular basis (27 articles in 2017), and each month one of the PhD students or postdocs at the Centre present their research in a popular scientific way, to reach out to a broader audience.

Our Twitter account was created in 2016 and has been increasingly used in 2017 to share information about new publications, meetings, thesis defenses, and other information related to science and mental disorders. NORMENT posted about 130 tweets in 2017, and users saw the tweets more than 94.000 times.

**144** Publications in scientific journals

**77** International scientific presentations (45 oral presentations, 32 posters)

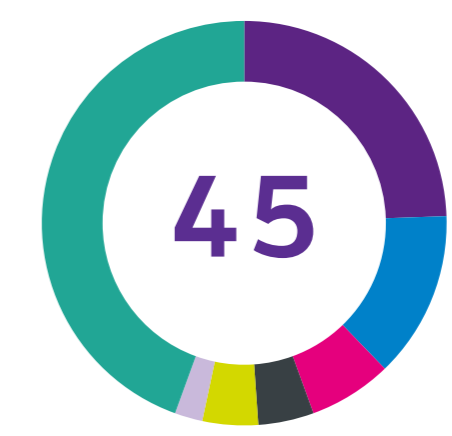
**79** National scientific presentations (57 oral presentations, 22 posters)

**80** Oral presentations for patient organizations and health personnel

**16** Oral presentations and other activities for the general public

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

- ECSR (11)
- EPA (6)
- ICHR (3)
- SCNP (2)
- SOBP (2)
- ICSR (1)
- Other (20)



Oral presentations at international scientific conferences

ECSR: European Conference on Schizophrenia Research, EPA: European Congress of Psychiatry, ICHR: International Consortium on Hallucination Research, SCNP: Scandinavian College of Neuro-psychopharmacology, SOBP: Society of Biological Psychiatry, ICSR: International Congress on Schizophrenia Research

## Scientific Conferences and Meetings

### Organization of Conferences

Research conference on mental health and addiction, arranged together with SERAF (Norwegian Centre for Addiction Research), Gardermoen, February 13-15, 2017.

<http://www.med.uio.no/norment/forskning/aktuelt/aktuelle-saker/2017/forskerkonferansen-2017.html>

### Selected International Oral Presentations

**Aas, Monica:** Childhood Trauma Across Psychopathology: Mediators and Outcome in Clinical Samples and Molecular Mechanistic Correlates, 25th European Congress of Psychiatry (EPA), Florence, Italy, April 01-04, 2017.

**Agartz, Ingrid:** Auditory hallucinations and auditory cortex in schizophrenia and bipolar disorder, 6th European Congress of Schizophrenia Research (ECSR), Berlin, Germany, September 15, 2017.

**Agartz, Ingrid:** ENIGMA-EOP (Early-Onset Psychosis), 25th European Congress of Psychiatry (EPA), Florence, Italy, April 03, 2017.

**Aminoff, Sofie Ragnhild:** Is affective lability in bipolar disorder associated with a bipolar disorder polygenic score, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 16, 2017.

**Andreassen, Ole A:** Imaging Genetics Biomarkers in Bipolar Disorder, European College of Neuropsychopharmacology (ECNP) Bipolar Network Meeting, March 28, 2017.

**Andreassen, Ole A:** Cortical and Subcortical Volumetric Abnormalities in Bipolar Disorder, 25th European Congress of Psychiatry (EPA), Florence, Italy, April 04, 2017.

**Andreassen, Ole A:** Polygenic architecture of mental illness. Recent discoveries and future potential, 47th Behavior Genetics Annual Meeting, Oslo, July 01, 2017.

**Andreassen, Ole A:** Update ENIGMA Bipolar disorders, Society of Biological Psychiatry (SOBP), San Diego, USA, May 20, 2017.

**Andreassen, Ole A:** Big data in psychiatric research - moving towards mechanisms, Karolinska Institute, SCMM, Stockholm, Sweden, August 21, 2017.

**Berg, Akiah:** Association found between current vitamin D levels and white matter volume in patients with psychosis and healthy controls, 6th European conference on schizophrenia research (ECSR), Berlin, Germany, September 16, 2017.

**Bless, Josef:** Digital therapies working group, International Consortium on Hallucination Research and Related Symptoms, Lille, France, November 06-08, 2017.

**Craig-Craven, Alexander Richard:** Initial Experiences with Functional MRS of GABA, 4th International Symposium on MRS of GABA, Leuven, Belgium, September 22, 2017.



Postdoc Akiah Berg giving an oral presentation at ECSR in Berlin

**Dunvoll, Guro:** Electroencephalography (EEG) recordings and equivalence class formation - A pilot study. Experimental Analysis of Behavior Group Conference, London, United Kingdom, April 2017.

**Elvsåshagen, Torbjørn:** Longitudinal and Cross-Sectional Investigations of LTP-Like Cortical Plasticity in Healthy Individuals and Subjects With Bipolar Disorder Type II, American College of Neuropharmacology (ACNP), Palm Springs, USA, December 06, 2017.

**Engen, Magnus Johan:** Cognitive dimensions and global functioning in relapsing and non-relapsing first episode psychosis patients: a 1-year follow-up study, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 16, 2017.

**Faerden, Ann:** First episode psychosis: Factors that influence burden and outcome", 6th Chair of symposium, 6th European conference on schizophrenia research (ECSR), Berlin, Germany, October 14, 2017.

**Gohar, Sherif:** Serum lipid levels and cytokines in relation to depressive symptomatology in psychotic disorders, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 14-16, 2017.

**Hugdahl, Kenneth:** Auditory hallucinations and imaging, International Congress on Neurobiology, Psychopharmacology and Treatment Guidance (ICNP), Greece, May, 2017.

**Hugdahl, Kenneth:** Functional neuroimaging and neurochemistry of auditory verbal hallucinations, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 14-16, 2017.

**Iversen, Trude Seselie Jahr:** A naturalistic study of antipsychotic-associated side effects, Scandinavian College of Neuropsychopharmacology (SCNP), Copenhagen, Denmark, April 26-28, 2017.

**Kusztrits, Isabella:** Update "QPE" validation Norway, 4th International Consortium Meeting on Hallucination Research, Lille, France, November 11, 2017.

**Lagerberg, Trine Vik:** The relationship between affective lability and substance use disorders in bipolar disorder, International Congress on Dual Disorders (ICDD), Madrid, Spain, March 23-26, 2017.

**Laloyaux, Julien:** Inducing hallucinations in participants from the general population: The role of negative emotions and cognitive resources, 16th International Congress on Schizophrenia Research (ICSR), San Diego, USA, March 24-28, 2017.

**Lonning, Vera:** Cortical brain abnormalities in early onset psychosis: results from the NORMENT EOP cohort, 25th European Congress of Psychiatry (EPA), Florence, Italy, April 03, 2017.

**Lyngstad, Siv Hege:** Enduring Depression and Apathy. Consequences for outcome in first-episode psychosis (FEP), 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 16, 2017.

**Melle, Ingrid:** Early changes in negative symptoms and long-term outcome in first-episode psychosis, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 16, 2017.

**Mørch, Ragni:** Inflammatory markers are altered in severe mental disorders independent of comorbid cardiometabolic disease risk factors, Scandinavian College of Neuropsychopharmacology (SCNP), Copenhagen, Denmark, April 26-28, 2017.

**Østefjells, Tiril:** Metacognition in severe mental disorders, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 16, 2017.

**Quintana, Daniel:** Dose-dependent Social-cognitive Effects of Intranasal Oxytocin Delivered with Novel Breath Powered Device in Adults with Autism Spectrum Disorder: A Randomized Placebo-controlled Double-blind Crossover Trial, Society of Biological Psychiatry (SOBP), San Diego, USA, May 19, 2017.

**Simonsen, Carmen:** Subjective experience of disability in first-episode psychosis at 1-year follow-up, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 16, 2017.

**Smeland, Olav:** Identification of genetic loci shared between schizophrenia and brain structure volumes, symposium on Leveraging Novel Statistical Methods and Big Data to Improve Imaging Genetics, 25th World Congress of Psychiatric Genetics (WCPG), Orlando, USA, October 14, 2017.

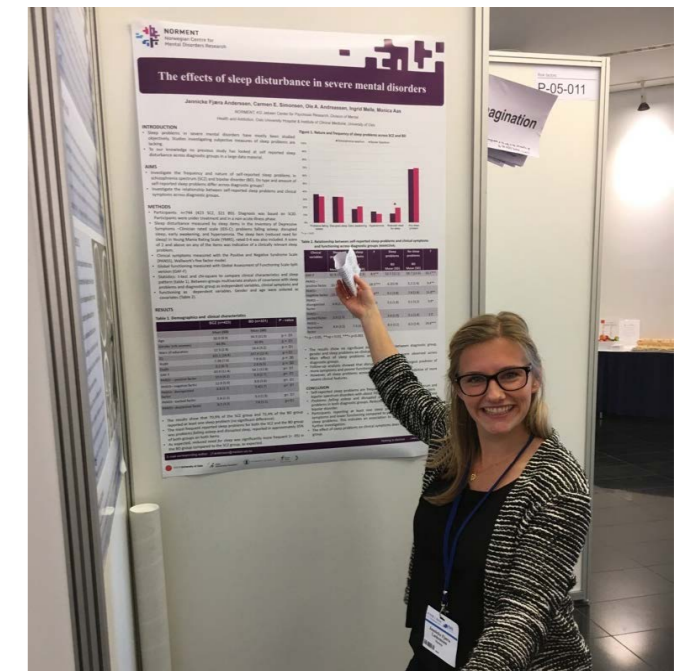
**Smelror, Runar:** Auditory Hallucinations in Early-Onset Psychosis: Associations with Heschl's gyrus, 25th European Congress of Psychiatry (EPA), Florence, Italy, April 01, 2017.

**Sønderby, Ida Elken:** Update, ENIGMA-CNV, ENIGMA Annual Retreat, San Diego, USA, May 16, 2017. Ueland, Torill: Cognitive Remediation in Early Phase Psychosis, Cognitive Remediation in Psychiatry, New York, USA, June 09, 2017.

**van der Meer, Dennis:** Predicting cortical thinning from genetic variation, Cognomics, Nijmegen, The Netherlands, September 08, 2017.

### Selected International Poster Presentations

**Anderssen, Jannicke Fjæra:** The effects of sleep disturbance in severe mental disorders, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 14 -16, 2017.



PhD student Jannicke F. Anderssen presenting her poster at ECSR in Berlin

**Beresniewicz, Justyna:** TBSS analysis of white matter alterations in schizophrenia patients vs. healthy controls, 4th International Consortium Meeting on Hallucination Research, Lille, France, November 06-08, 2017.

**Farivar, Fathian:** The C-reactive protein in schizophrenia-spectrum disorders, relationship to cognitive function in acute phase of psychosis with a longitudinal perspective in a pragmatic, randomized trial, 6th European Conference on Schizophrenia Research (ECSR), Berlin, Germany, September 12-14, 2017.

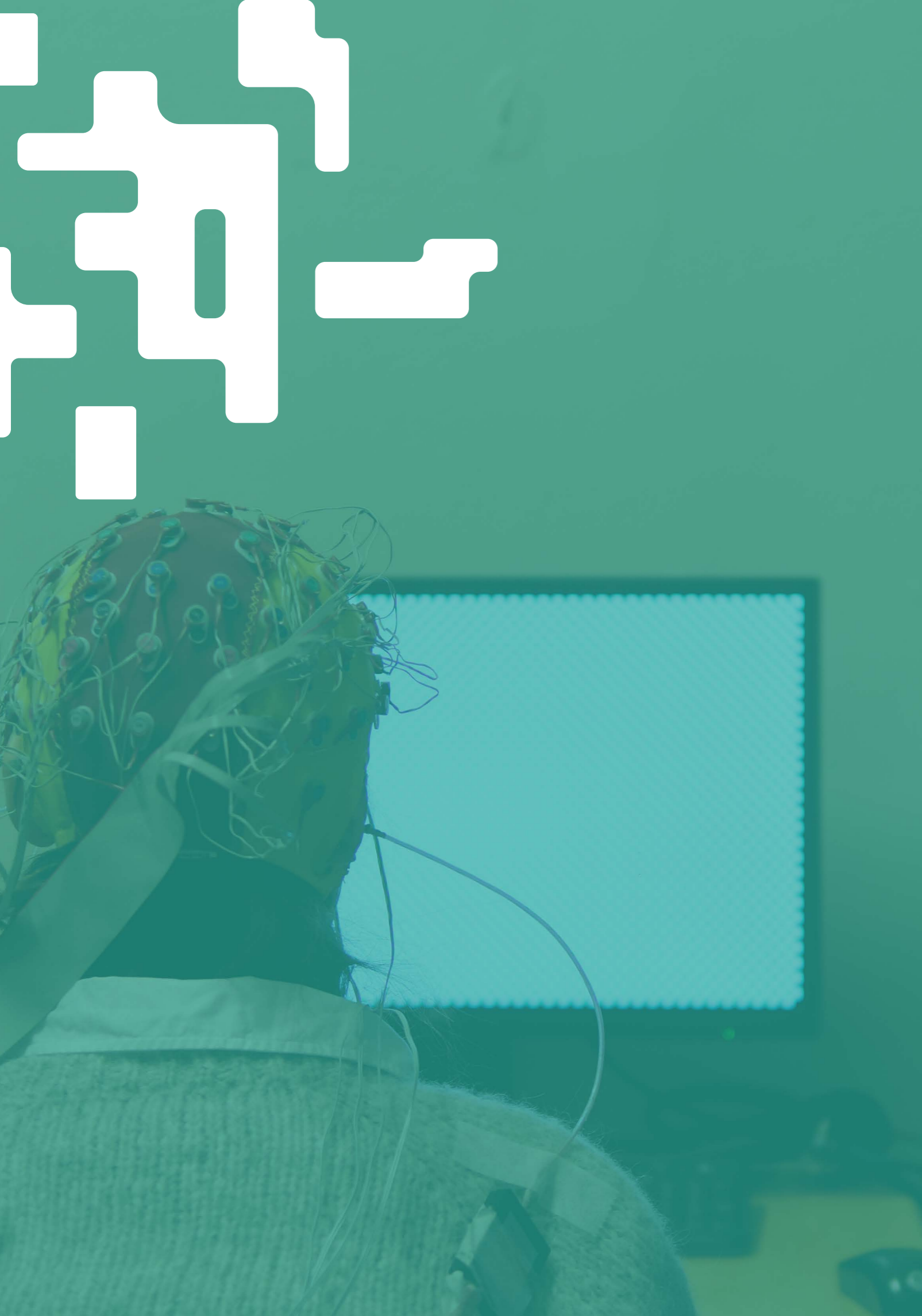
**Frei, Oleksandr:** Bivariate Gaussian Mixture Model of GWAS (BGMG) detects polygenic overlap between complex traits beyond genetic correlation, 25th World Congress of Psychiatric Genetics (WCPG), Orlando, USA, October 17, 2017.

**Gurholt, Tiril:** Age-Related Effect of Vitamin D on Hippocampus Volume in Schizophrenia and Bipolar Disorder, International Congress on Schizophrenia Research (ICSR), San Diego, USA, March 27, 2017. Halvorsen, Jens: Common Variants of Genes Involved in Synaptic Plasticity are Associated with Individual Variation in Visual Attention Capacities, Society for Neuroscience (SFN) Washington DC, USA, November 13, 2017.

**Hartberg, Cecilie:** Cortical thickness, cortical surface area and subcortical volumes in schizophrenia and bipolar disorder patients with cannabis use, European College of Neuropsychopharmacology (ECNP), Paris, France, September 04, 2017.







## Societal Impact and Innovation

Mental disorders such as schizophrenia and bipolar disorders are major challenges and costs for the European health care system and severely affect both the patients and their families. To cope with the future challenges, it is clear that a new generation of scientists and health care personnel is required in the area of mental disorders.

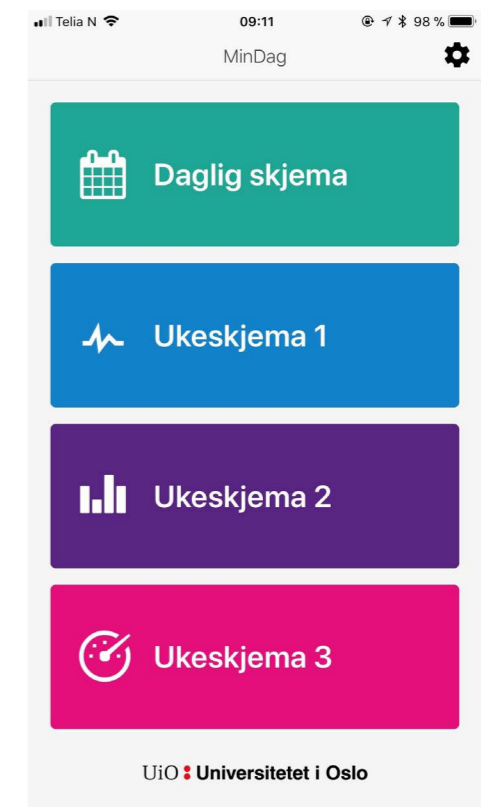
This shortage in skilled workers has been addressed in the European Commission where the knowledge needs of future PhD programmes have been further developed. Due to the long-time period from discovery to impact of health care, it is too early to identify concrete changes in the treatment of people with severe mental disorders based on the current results.

The training of many psychiatrists and psychologists at the Centre will have a large and lasting impact on future research in mental disorders in Norway. We observe that new knowledge is brought into clinical practice and also into the education of health care personnel.

The Centre has so far provided added value by developing tools for prediction and stratification (genetics, imaging) which can lead to new knowledge to improve clinical treatment. It is likely that new genetic findings in due time will be implemented in the diagnostics of psychotic disorders, as supplementary information for the clinical decisions. 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 directly and indirectly of huge value to society.

It is also important to note that the resources we have established so far (e.g., patient samples with rich phenotype information, biobanks and large-scale genotyping data) contribute to international consortia. Our data are also made available to collaborators as much as the ethical approval allows us. These procedures increase the value of our research investments.

We have been involved in two pending patent applications related to treatment of social dysfunction and biostatistical tools. In addition, as part of our eNORMENT strategy we have developed a smartphone app called “MinDag” (“My Day”). The primary function of the app is to allow for collection of data from study participants on areas such as sleep, mood, symptoms, and drug use over time. The overall goal with the “MinDag” project is to improve the understanding of interactions between lifestyle factors, environment, and symptoms. Having the participants track symptoms and other factors over time can also allow for new insight into early detection and diagnostics, as well as improve treatment and early signs of relapse. In the future, the aim is to develop a programme for research based on app technology and translate the app solutions to clinical use.

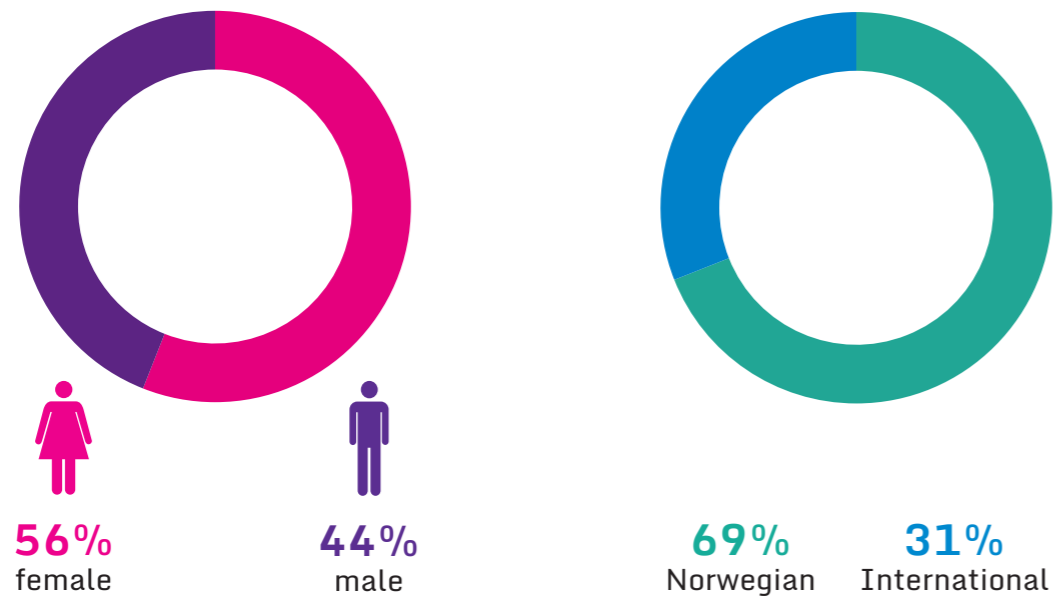


Screenshot from the “MinDag” app

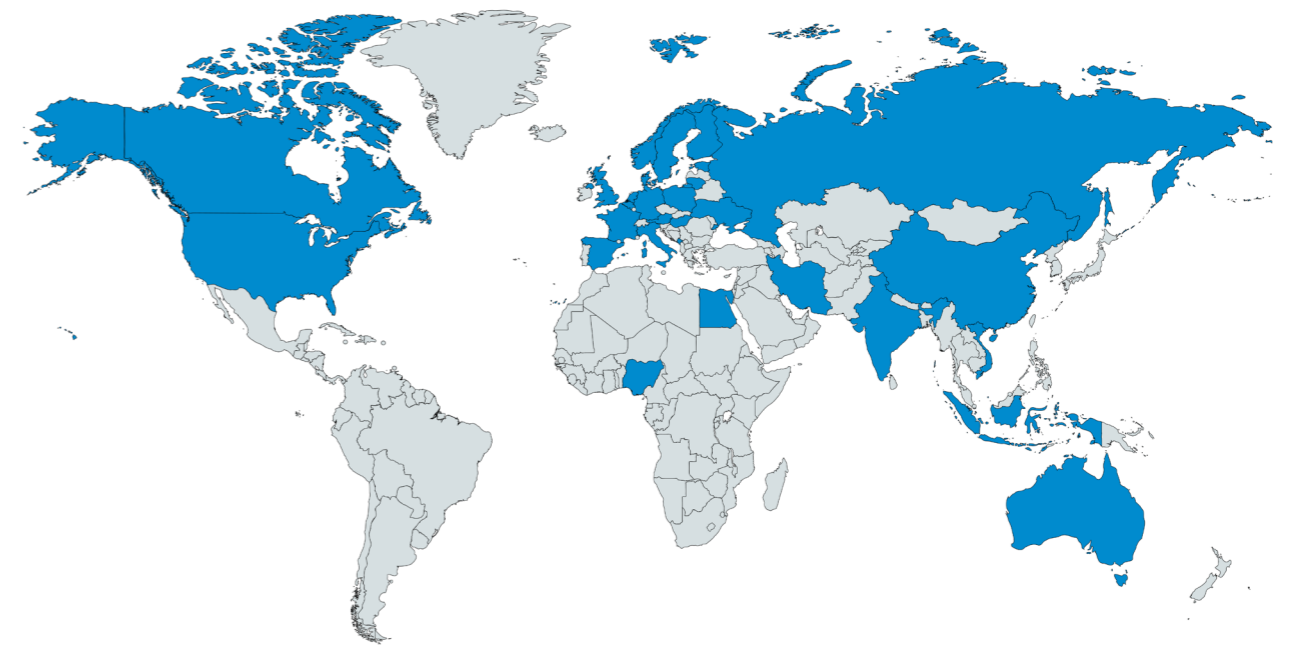
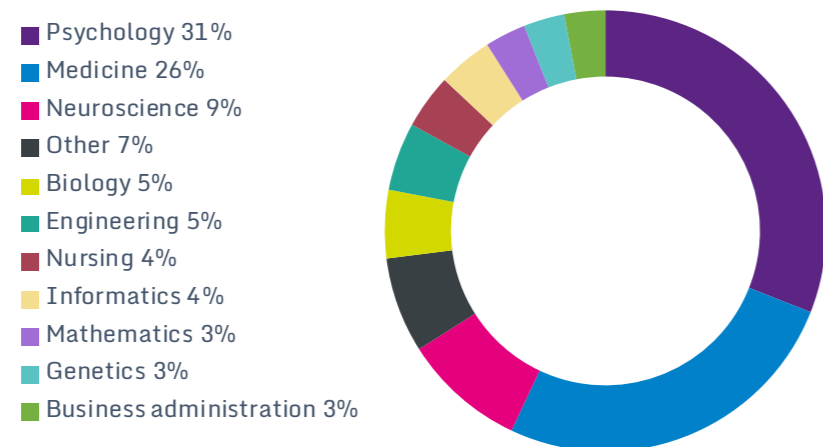


## Facts about NORMENT

### Employees

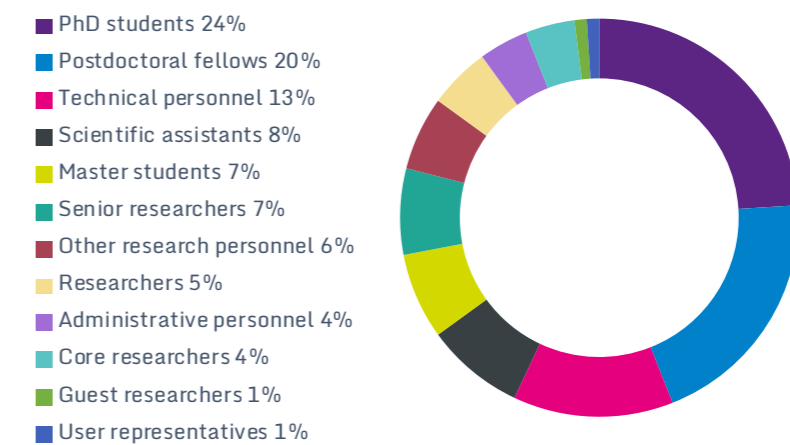


### Professional Backgrounds

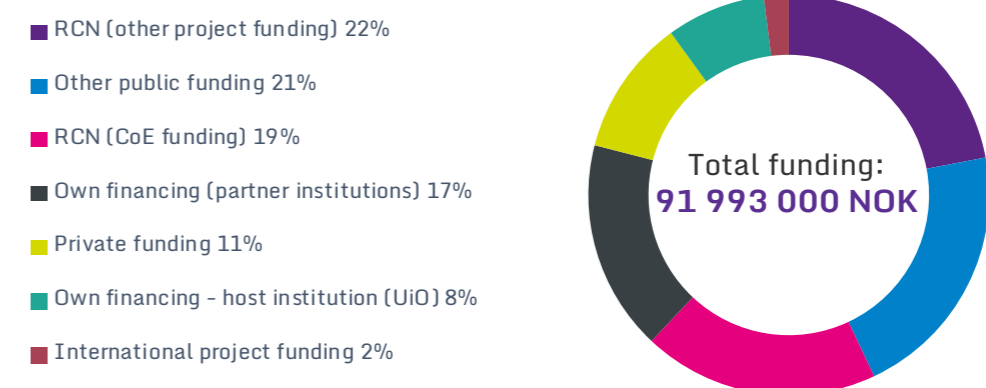


**29** different nationalities are represented at NORMENT

### Staff Positions



### Funding



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Adriano Winterton, NORMENT

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Christine Lycke Brandt  
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for their work on editing the Annual Report.



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