NORMENT
Norwegian Centre for
Mental Disorders Research

NORMENT
Annual Report 2016

UiO : University of Oslo

UNIVERSITY OF BERGEN

Oslo University Hospital

STIFTELSEN KGJ

Norwegian Centre of Excellence
The Research Council of Norway

Leader's Comments 5

Vision Statement 6

Scientific Aims 9

Governing Board 11

Highlights from the first 3.5 years 12

Selection of Prizes and Awards 13

Organization of the Centre 15

Scientific Advisory Committee 16

Core Researchers 17

Collaboration Across Research Groups 18

Research Groups:

- Translational Psychiatry Group 20
- Clinical Psychosis Research Group 22
- Neurocognition Group 24
- Psychopharmacology and Animal Studies Group 26
- Structural MRI Group 28
- Psychiatric Molecular Genetics Group 30
- Brain Imaging Group 32
- Epigenetics and Functional Genomics Group 34

Researcher Training 36

International Collaboration 42

Dissemination and Communication 44

Societal Impact and Innovation 48

NORMENT Staff 50

Publications 52

During the last year we have witnessed how novel discoveries and frontline research findings have evolved from translational cross-disciplinary projects

Leader's Comments

For NORMENT, 2016 has been an excellent year. We have been operational for 3.5 years, focusing our research on psychotic disorders, and we are starting to harvest from the investments in building the Centre and its transdisciplinary structure. We observe how the participating research groups profit from the competence and infrastructure within the Centre, and are able to leverage its large added value to better disclose the many secrets of schizophrenia and bipolar disorder.

During the last year we have witnessed how novel discoveries and frontline research findings have evolved from translational cross-disciplinary projects, to be published in high impact journals proving that the "vertical synergy" approach works in practice.

Further, 2016 has been an excellent year not only for scientific publications. We have also been successful in obtaining competitive funding. Both senior and more junior group leaders have received a series of grants. Especially, it is impressive how Core Researcher Kenneth Hugdahl managed to secure his second ERC Advanced Grant, the most prestigious research grant in Europe, on a project focused on auditory hallucinations. This is very motivating for everyone at the Centre, and it is really an excellent example for all of us. Congratulations Kenneth!

We have also been successful in hiring young, talented researchers. The recruitment of young scientists is important for the success of the Centre, and essential for future development of the research field. I welcome each of you, and hope you thrive and become valuable members of our team. We will continue to encourage our young scientists to develop their own projects and follow their ideas. The Young Researchers Meeting will be extended to more long term meeting seminars.

We have now a highly international team of experts across key research areas in psychiatry. However, in order for interactions and synergy to take place, we need an efficient Centre organisation to facilitate interactions and synergy between the different research groups. Project management, coordination, and administration across the Centre is becoming increasingly important, and here we have implemented our updated intranet system, meeting structure and communication strategy.

We are now preparing the research plan for the next five year period of the Centre. This has been a very creative and exciting process, building on the best of the existing programme, and improving and revising the research plan according to new developments in the field. Due to the breakthrough in discovering new risk genes, we will now focus our "vertical synergy" approach on immune factors and neuronal transmission. We will strengthen our functional research programme with iPSC (stem cell) methodology, and start more clinical trials and interventions to follow up our new findings. Further, we will improve our "Big Data" approaches, and develop our eNORMENT infrastructure for exploiting ICT technology.

We are all looking forward to further develop and improve the psychosis research within the NORMENT Centre at the highest international level, to contribute substantially to a better understanding, care and treatment of schizophrenia and bipolar disorder.

Ole A. Andreassen
Centre Director

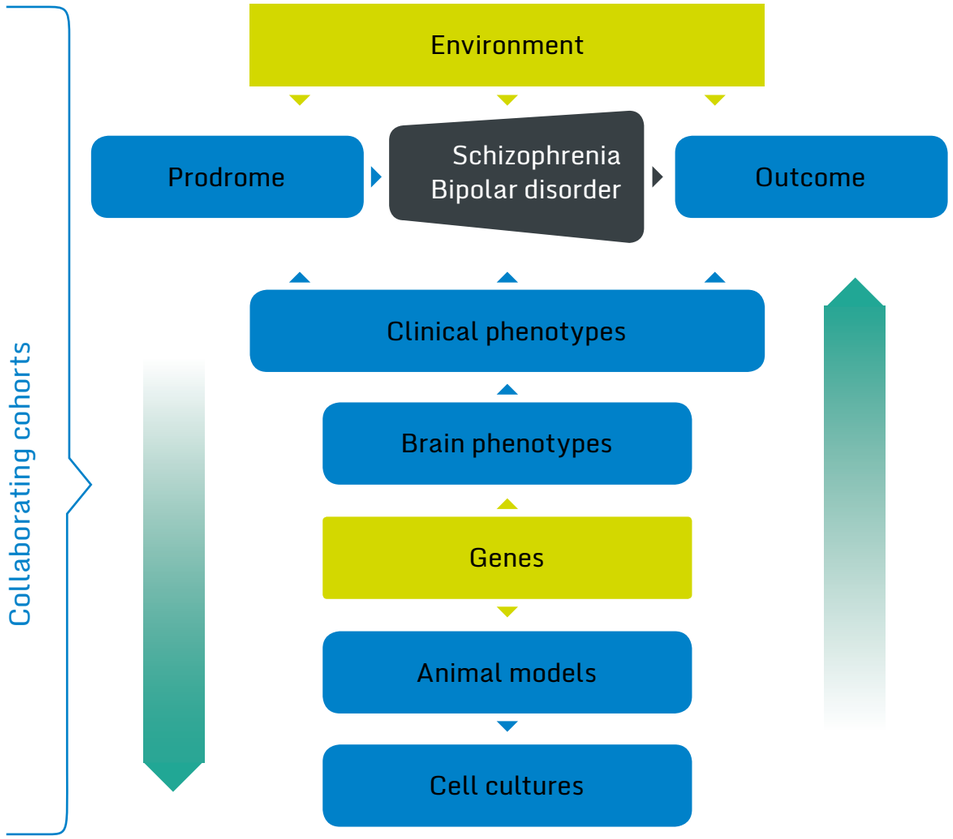
Vision Statement

NORMENT's primary objective is to reveal underlying pathophysiological mechanisms in schizophrenia and bipolar disorder and to develop tools for stratification and outcome prediction, using a "vertical synergy" approach, with the following subgoals:

- **Identify genetic variants or expression variation to reveal "missing heritability".**
- **Define new targets to optimize the ratio of beneficial vs. adverse effects of antipsychotics.**
- **Determine new brain imaging phenotypes linking genes and 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 will be 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 our "vertical synergy" approach.

NORMENT's Research Strategy: A "Vertical Synergy" Approach



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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 GWAS (genome-wide association studies) 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 the 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.

Predict Course and Outcome – Including Mortality

Some patients 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.

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Governing Board

Chair:
Hilde Irene Nebb

Professor
Deputy Dean of Research
Faculty of Medicine
University of Oslo

Board member:
Marit Bjartveit

Clinic Manager
Division of Mental Health and Addiction
Oslo University Hospital

Board member:
Tim 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:
Eyvind Rødahl

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

Highlights from the first 3.5 years

In general, we have been successful in obtaining many of our aims during the first 3.5 years as a Centre of Excellence. We have been involved in several monumental discoveries of new common disease gene variants associated with schizophrenia, bipolar disorder, and related and overlapping diseases and traits including cognitive function and suicidal behavior, many of them published in high impact journals (Nature, Nature Genetics, Lancet, Molecular Psychiatry). Especially, we contributed to the report of over 100 schizophrenia gene loci (Nature). We have also been involved in the first phase of the long-range-phasing approach focusing on cognitive disorders, and discovered unique very rare variants (Nature, New England Journal of Medicine). We have also developed novel statistical tools including LD based analysis, annotation enrichment and pleiotropy enrichment, and applied them to a series of psychiatric phenotypes, as well as other diseases (Nature Genetics, American Journal of Human Genetics, PLOS Genetics).

We have gained new knowledge about the immune abnormalities in clinical samples, and genes involved in these factors (MHC), including related immune genes and immune disorders. Applying gene expression data, we have discovered expression patterns related to immune risk gene variants and immune pathways. We also obtained new knowledge about underlying molecular mechanisms of the bipolar disorder risk gene ANK3 (Biological Psychiatry).

Further, we have provided evidence how animal models can be used for translational studies of antipsychotic side effects, and shown how schizophrenia risk genes related to the immune system induce abnormal behaviour and altered brain function when transferred to mouse models.

Using state-of-the-art brain imaging tools, we have determined how early environmental factors (obstetric complications) affect brain development, and may play a causative role in psychiatric disorders. As partners of the international ENIGMA consortium, we contributed significantly to the identification of several novel genetic loci for variation in human brain volumes (Nature). Nearly all Core Researchers (CR) at the Centre were involved, and many participated in new discoveries of region-specific genetic patterns using large-scale brain imaging genetics studies. We were successful in discovering gene variants associated with brain imaging markers, and hippocampal volume.

In a series of studies we have identified factors affecting outcome in patients with schizophrenia and bipolar disorders. Childhood trauma is prevalent and seems to have an effect on a wide range of factors, including age at onset and other clinical characteristics in psychosis. We have expanded this by showing that current psychosocial stressors are more prevalent in youth who later develop psychotic disorders. We have shown that also cannabis reduces the age at onset in bipolar disorder, with indications of both a dose-response effect and an additive effect with childhood trauma.

Several of our junior investigators have received prizes for best poster, best paper or best presentation at conferences. Further, CR Hugdahl received his second ERC Advanced Grant during this period, and guest researcher Anders M. Dale and CR Andreassen were elected to the Norwegian Academy of Science and Letters, and post doc Monica Aas as junior member. CR Hugdahl also received the Møbius Prize, the Norwegian Research Council's prize for outstanding research, and the Honorary Meltzer Award from (Biological Psychiatry) the University of Bergen.

NORMENT researchers have also been actively involved in the organization of international conferences within our field. Especially, five out of eight Core Researchers (Andreassen, Djurovic, Le Hellard, Melle and Steen) were members of the organizing committee at the World Congress of Psychiatric Genetics (WCPG) 2014 in Copenhagen. We have also contributed to the annual conferences of the Scandinavian College of Neuro-psychopharmacology (SCNP) and several national meetings.

Selection of Prizes and Awards

2014

Aas, Monica — NARSAD Young Investigator Grant, Brain & Behavior Research Foundation, New York, USA

Hugdahl, Kenneth — Møbius Prize, the Norwegian Research Council's prize for outstanding research, Norway

Hugdahl, Kenneth — Honorary Meltzer Award, University of Bergen, Norway

2015

Aas, Monica — Young Scientist Award, Scandinavian College of Neuropsychopharmacology (SCNP), Copenhagen, Denmark

Kaufmann, Tobias — Prize for outstanding paper, Oslo University Hospital, Norway
(Disintegration of sensorimotor brain networks in schizophrenia, Schizophrenia Bulletin)

2016

Andreassen, Ole A. — Prize for outstanding paper, Oslo University Hospital, Norway
(Subcortical volumetric abnormalities in bipolar disorder, Molecular Psychiatry)

Berg, Akiah Ottesen — Prize for outstanding paper, Oslo University Hospital, Norway
(Childhood trauma mediates the association between ethnic minority status and more severe hallucinations in psychotic disorder, Psychological Medicine)

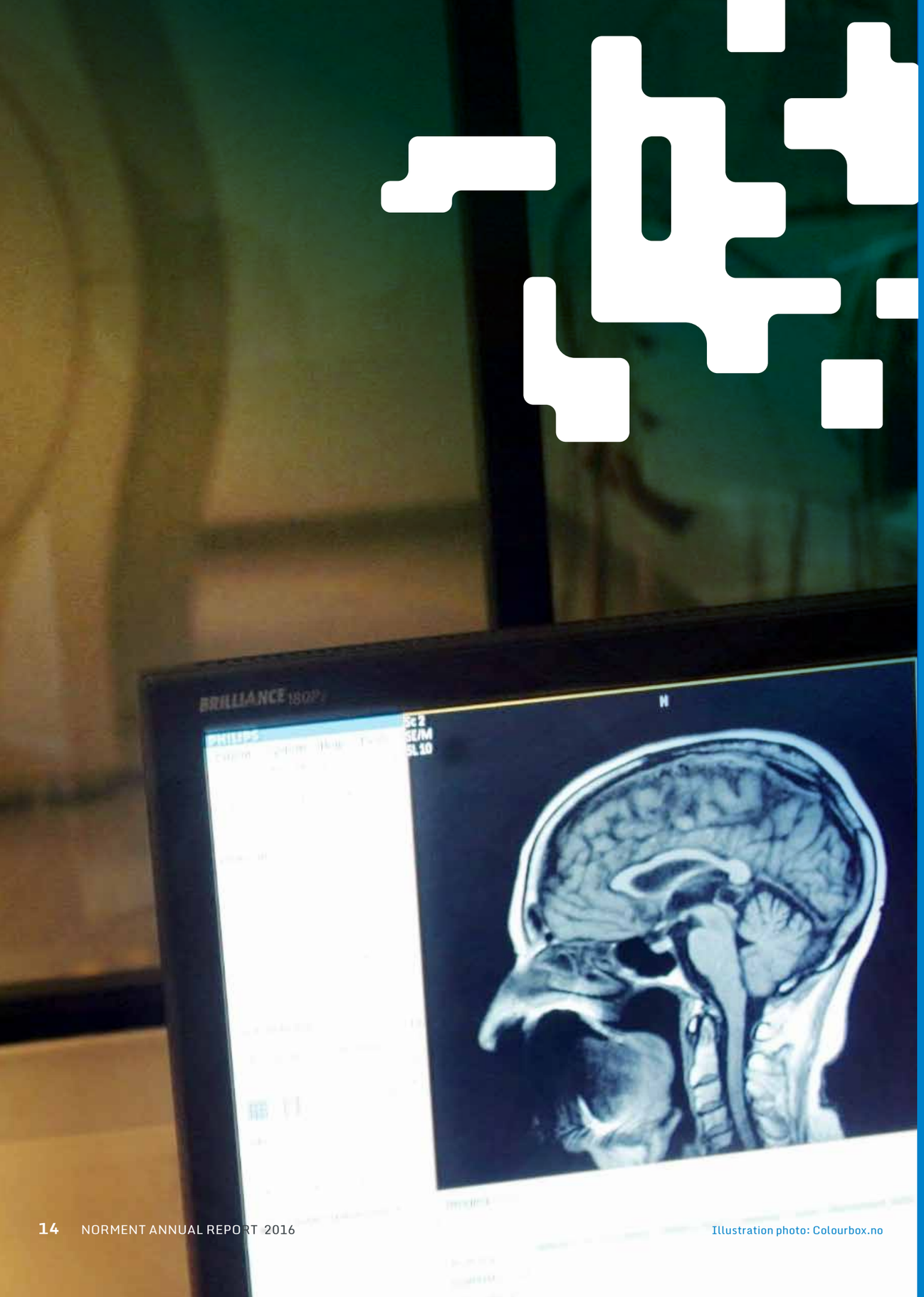
Moberget, Torgeir — Merit Abstract Award, Human Brain Mapping Conference, Geneva, Switzerland
(Cerebellar grey matter volume in schizophrenia - a multi-site study of 543 patients and 760 controls)

Quintana, Daniel — Rafaelsen Young Investigators Award, International College of Neuropsychopharmacology, Seoul, South Korea

Smeland, Olav B. — Poster prize, Scandinavian College of Neuropsychopharmacology, Århus, Denmark
(Genetic overlap between schizophrenia and subcortical brain volumes)

Skrede, Silje — Annual research prize, Norwegian Psychiatric Association, Trondheim, Norway
(Olanzpin aktiverer uttrykk av lipidgener - bare et problem?)

Post doc Nhat Trung Doan, group leader Lars T. Westlye, and professor Ole A. Andreassen, co-authors on the price-winning paper "Subcortical volumetric abnormalities in bipolar disorder"



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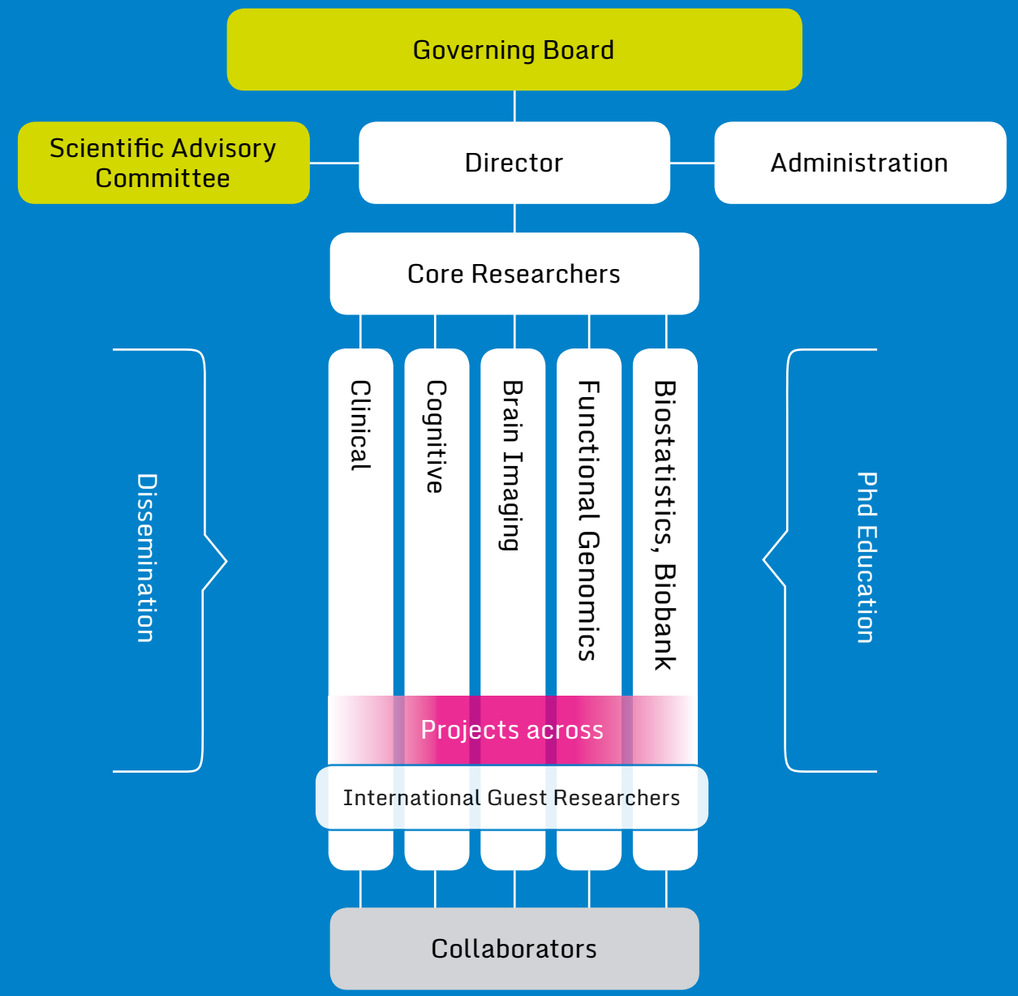
Organization of the Centre



Scientific Advisory Committee

NORMENT has established an Advisory Committee of external scientific researchers:

Professor Marcella Rietschel is Professor at the University of Mannheim and scientific director for the Department of Genetic Epidemiology at the Central Institute for Mental Health, situated in Mannheim, 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. 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 Neuroscience and director for the Center for Human Development, University of California San Diego - UCSD, as well as director for the Coordinating Center for the ADNI 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.

Core Researchers

NORMENT has organized its research into groups with complementary expertise.
Each research group is headed by one of NORMENT's eight Core Researchers (CR):

Ole A. Andreassen	Professor at the University of Oslo and Oslo University Hospital, director of NORMENT and head of the Translational Psychiatry Group
Ingrid Melle	Professor at the University of Oslo and Oslo University Hospital, head of the Clinical Psychosis Research Group
Kjetil Sundet	Professor at the University of Oslo, head of the Neurocognition Group
Vidar M. Steen	Professor at the University of Bergen, head of the Psychopharmacology and Animal Studies Group
Ingrid Agartz	Professor at the University of Oslo, head of the Structural MRI Group
Srdjan Djurovic	Professor at the Oslo University Hospital and University of Bergen, head of the Psychiatric Molecular Genetics Group
Kenneth Hugdahl	Professor at the University of Bergen, head of the Brain Imaging Group
Stephanie Le Hellard	Professor at the University of Bergen, head of the Epigenetics and Functional Genomics Group

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

Collaboration Across Research Groups

The Centre 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 the Centre of Excellence (CoE) grant to fund our core infrastructure, to enable easy access to state-of-the-art methodology, infrastructure for patient recruitment and assessment, and database and biobank service. This has transformed the research of the participating CRs to allow for frontline collaborative research projects. Thus, most if not all research activities at the Centre depend on this tight integration and efficient use of resources across different research groups.

The Centre has implemented a ”vertical synergy” approach, integrating research groups with a multi-disciplinary approach for fruitful enrichment across disciplines. Long-term funding enables longitudinal studies of large representative patient cohorts, combined with expensive large-scale genotyping, transcriptome profiling and imaging studies not otherwise possible.

There are specific added values related to the aims:

1. Gene variants and RNA: Enable collection of sufficiently large samples for comparison of gene variation versus gene expression on a global scale, preferably in patient-derived stem cells. The cost of deep sequencing is still declining and we will in part build upon our established collaboration with deCODE. It is likely that this approach may open new opportunities to examine the underlying disease mechanisms.

2. Immune and lipid mechanisms: Enable us to build a translational setup to take specific mechanisms from clinical samples (i.e. new RNA analysis) and move them into transgenic animal models and cell culture studies.

3. Brain imaging phenotypes: Enable access to technology and the ability to systematically study large numbers of patients, who will be genotyped and extensively clinically characterized – a sample which is unique internationally.

4. Outcome prediction: Enable us to determine the association between genes, environment and their effect on outcome trajectories in a sample of unprecedented size and characterization, which at the end of the funding period can lead to development of tools for prediction and identification.

The Centre has provided new 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 post docs and support personnel across different groups, and several PhD students have been co-supervised by CRs and members of different research groups at the Centre.

Collaborative projects

The Centre groups have worked with several large international collaborative projects, including the Psychiatric Genomics Consortium (PGC), the Cognitive Genomics Consortium (COGENT), the Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA) Network, the International Consortium on Hallucination Research, and the Imaging Genetics for Mental Disorders (ImageMend) Consortium. These collaborations have led to several publications in high impact scientific journals (Nature, Nature Genetics, American Journal of Human Genetics, Nature Communications, Molecular Psychiatry).
Further, we have a number of collaborative projects within the Centre, organized through the monthly Synergy Meetings and named Synergy Projects with project lists available at our intranet page. These are organized under different research topics, such as Polygenic Risk Score, Functional studies of risk genes, Transcriptome profiling and epigenetics, Immunology and psychosis, Lipids and myelination, Cannabis, and Imaging Genetics. Thus, we organize collaborative research projects with these transparent and integrated project overviews, to facilitate innovative approaches and efficient project progress.

Several findings related to clinical characteristics have been published, all building on tight collaboration between groups, involving biomarkers and polygenic risk models. Collaborative studies on cognitive traits have also been conducted, and we have published several translational studies focusing on the relationship between clinical and cognitive features, and genetic risk and immune factors related to cognitive function. This line of studies has also included imaging phenotypes.

In studies applying MRI technology, highlighted by Nature Genetics, Molecular Psychiatry and Schizophrenia Bulletin papers, we have identified key elements of brain structure and function underlying schizophrenia and bipolar disorders. Here, we have applied novel analytical approaches to several MRI projects, and we have performed collaborative projects involving transdisciplinary work across clinical, cognitive, functional genomics as well as biostatistics work units.

The discovery of novel gene variants associated with severe mental illness (Nature Genetics, Molecular Psychiatry) also was a result of collaboration across groups. Together, we have utilized our large analytical team, leading to projects of psychiatric phenotypes, including pleiotropy. Further, we have developed Bayesian statistical tools in collaboration with several research groups at the Centre.

A number of collaborative projects build on our pipeline for functional characterization of new gene loci identified for psychiatric diseases. We have linked genotypes, clinical phenotypes, RNA expression data and stem cell technology in experimental models. Several papers focusing on this approach have been published, many in high impact journals.

Several findings related to clinical characteristics have been published, all building on tight collaboration between groups, involving biomarkers and polygenic risk models

Translational Psychiatry Group

Ole A. Andreassen

Professor

University of Oslo and
Oslo University Hospital,
director of NORMENT and
head of the Translational
Psychiatry Group

Core Researcher:
Ole A. Andreassen,
Professor, University of Oslo, Oslo University Hospital

Group members:
Dieset, Ingrid, group leader
Jönsson, Erik G., group leader

Bakken, Eivind
Bettella, Francesco
Bjella, Thomas D.
Eriksen, Jon A.
Frei, Oleksandr
Gundersen, Line
Hope, Sigrun
Hoseth, Eva Z.
Iversen, Trude J.
Khalili, Seyran
Krull, Florian
Mäki-Marttunen, Tuomo M.
Mørch, Ragni
Nærland, Terje
Li, Wen
Reponen, Elina
Shadrin, Alexey
Smeland, Olav
Srinivasan, Saurabh
Steen, Nils Eiel
Tesli, Martin
Wang, Yunpeng
Witoelar, Aree

Multimodal MRI Group
Westlye, Lars T., group leader
Alnæs, Dag
Bolstad, Ingeborg
Brandt, Christine Lycke
Doan, Nhat Trung
Dunvoll, Guro
Dørum, Erlend Solberg
Elvsåshagen, Torbjørn
Engvig, Andreas
Kaufmann, Tobias
Kolskår, Knut
Moberget, Torgeir
Norbom, Linn
Palomera, Aldo C.
Richard, Geneviève
Rokicki, Jarek
Sanders, Anne Marthe
Skåtun, Kristina C.
Tønnesen, Siren
Ulrichsen, Kristine
van der Meer, Dennis
Quintana, Daniel
Zak, Nathalia

Achievements in 2016

- Discovered common risk genes for personality traits, and their overlap with schizophrenia and bipolar disorders. Identified rare structural gene variants associated with schizophrenia.
- Discovered subcortical brain structure abnormalities in schizophrenia and bipolar disorders, through active involvement in the ENIGMA consortium.
- Identified immune factors associated with bipolar disorder and schizophrenia, and how they relate to cardiovascular risk factors.
- Developed new tools for statistical modelling of the genetic architecture of polygenic complex disorders, and discovered overlapping gene variants between mental illness and associated traits.
- Applied novel statistical tools to show that markers of human evolution are enriched in schizophrenia.

Ambitions for 2017

- Increase the number of participants at baseline, implement cross-diagnostic imaging, genotype more Norwegian samples, collaborate with the MoBa cohort, and apply novel ICT technology.
- Apply sequencing to identify rare genetic variants associated with schizophrenia, bipolar disorders, and other severe mental illness with long range phasing approach, and relate to clinical and imaging phenotypes.
- Develop novel biostatistical tools for polygenic disorders, and apply to clinically relevant settings by extending polygenic prediction tools to include clinical and imaging phenotypes including multivariate approaches.
- Start project integrating body imaging with measures of cardiovascular risk phenotypes in psychotic disorders, integrated with novel brain imaging approaches.
- Integrate “biophysical psychiatry” approach with stem cell phenotyping, EEG measures and imaging.

Synergy and Cross-Disciplinary Achievements

The scientific achievements of the group in 2016 depend to a large extent on activity across the research groups at the NORMENT Centre. After a couple of years building the Centre infrastructure and integration of the research activities, we were in 2016 able to harvest from these investments to obtain novel findings.

In collaboration with CR Ingrid Melle and her team, we have studied biomarkers and polygenic risk models in relation to clinical characteristics. Our groups have been co-supervising PhD students, which has led to more cross-disciplinary research projects. We further share post docs and support personnel involved in the Clinical Assessment Work Unit, and integration of these efforts are important for clinical translation.

In a series of studies applying MRI technology, highlighted by a Molecular Psychiatry paper describing subcortical abnormalities in bipolar disorder, we have identified key elements of brain structure and function underlying schizophrenia and bipolar disorders. This was done in close collaboration with CR Ingrid Agartz and her team. In addition, Group leader Lars T. Westlye has been essential for adding a novel analytical approach to several MRI projects, and he has co-mentored post docs and co-supervised PhD students. In collaboration with CR Kenneth Hugdahl, we have coordinated the MRI protocol across our two MRI imaging sites, and we have been involved in some of his novel application of new neuroimaging tools, constantly improving the MRI Work Unit.

A number of findings were obtained building on the collaboration with CR Srdjan Djurovic, mainly involving discovery of novel gene variants associated with severe mental illness (Nature Genetics, Molecular Psychiatry). Together we have built a team of biostatistical experts (10 post docs), enabling us to take a leading analytical role, also in large international consortia, such as the Psychiatric Genomics Consortium and ENIGMA. Further, we have a collaboration with CR Stephanie Le Hellard on analytical projects of psychiatric phenotypes, including pleiotropy. The genotype data QC pipeline and secure database have been developed and is maintained as part of two Work Units. Further, we have developed Bayesian statistical tools in collaboration with Anders M. Dale and coworkers at UCSD, as part of the exchange programme.

In collaboration with CR Srdjan Djurovic and CR Vidar M. Steen and others, we have developed a pipeline for functional characterization of new gene loci identified for psychiatric diseases. Due to the polygenic nature of the genetic architecture, a new approach is needed.
We have started linking genotypes, clinical phenotypes, RNA expression data and stem cell technology in experimental models. Several papers focusing on this approach were published in 2016, and the Work Unit for Functional genomics has been very helpful in this regard.

Cognitive traits are an important factor in severe mental illness, and in collaboration with CR Kjetil Sundet and Group leader Torill Ueland, we have published several translational studies focusing on genetic risk and immune factors related to cognitive function. This line of studies has recently been extended to include imaging phenotypes, further increasing the impact.

The Cognitive Work Unit has been supported by shared support personnel from our group and has been involved in development of novel ICT project plans for large scale phenotyping.

Clinical Psychosis Research Group

Ingrid Melle

Professor

University of Oslo and
Oslo University Hospital,
Head of the Clinical
Psychosis Research Group

Core Researcher:
Ingrid Melle,
Professor, University of Oslo,
Oslo University Hospital.

Group members:
Lagerberg, Trine Vik, group leader
Aas, Monica
Aminoff, Sofie
Anderssen, Jannicke Fjæra
Barrett, Elisabeth
Berg, Akiah Ottesen
Büchmann, Camilla Bakkalia
Demmo, Christine
Færden, Ann
Gardsjord, Erlend
Haram, Marit
Hellvin, Tone
Huflåtten, Idun Bernadotte
Høegh, Margrethe Collier
Khalili, Seyran
Kvam, Mari
Kvitland, Levi
Nerhus, Mari
Lyngstad, Siv Hege
Moldestad, Tale
Onyeka, Ifeoma
Ringen, Petter Andreas
Romm, Kristin Lie
Simonsen, Carmen
Svendsen, Ingrid Hartveit
Østefjells, Tiril

Achievements in 2016

The focus of the Clinical research group (Melle CR node) is the study on how gene x environment interactions influence the early- and long term course of schizophrenia and bipolar disorders. The main achievements in 2016 were:

- Expanded the long-term (10 year) follow-up of the first part of the "TOP" first episode cohort.
- Piloted iPhone version of sleep cycle and affect experience App (TSD App project/eNORMENT).
- Translated and approved key parts of interviews in new protocol.
- Appointed two MSCA Scientia Fellows to work with register data in relation to long-term follow-up.
- Several PhD fellows handed in their theses.
- Key papers on course and outcome in schizophrenia and bipolar disorder.

Ambitions for 2017

- Further broaden and expand the long-term follow-up study, including register data.
- Fund 20-year follow-up of TIPS study.
- Finalize new protocol that includes use of tablet based self-report.
- Complete first phase of current App project, start Android App and activity monitoring (Actigraphy).
- Contribute to establishment of research based Bipolar clinic at Oslo University Hospital.
- Restructure group to give room for new group leaders.
- Continue within-centre collaboration concerning risk factor effects (methylation, stem cells).

Synergy and Cross-Disciplinary Achievements

The Clinical group has the main responsibility for the clinical assessment team and thus serves as the gateway to the Centre's studies and lays the foundation for all research involving clinical phenotypes. There is extensive practical collaboration with all groups in the Centre.

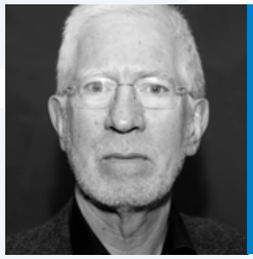
The group has a particular close collaboration with the Cognitive group - CR Sundet/Group leader Ueland - that includes common projects and co-supervising. We have a joint effort in conducting a long-term follow-up of the Centre's first episode cohort. In 2016 we have analyzed our first finding concerning the course of symptoms and cognition in early treated phase of bipolar disorder, with publications in leading journals in this research area (Bipolar Disorder) showing no effects of previous illness history on cognitive dysfunction.

We also have a close collaboration with CR Agartz' group - including practical collaborations with the clinical assessment team in the Adolescent onset study.
The collaboration includes several scientific projects concerning the relationship between clinical- and imaging phenotypes (CR Agartz / Group leader Westlye) with first/last authors from both groups and publications in high ranked journals (Psychological Medicine, Schizophrenia Bulletin). We have previously shown that early trauma influences subcortical structures in particular specific hippocampal subfields, and now show that early trauma influences the response to emotional stimuli.

There is also an overlap in practical assessment team work and co-supervisions with CR Andreassen's group, comprising work concerning environmental risk factors, biomarkers and clinical phenotypes. This particularly includes two recently finished PhD projects focusing on the role of Vitamin D in psychotic disorders that have received international interest (among the most accessed publications in Schizophrenia Research) and on the role of oxytocin genes - the latter also in collaboration with CR Djurovic's group.

The collaboration with CRs Le Hellard/Steen/Hugdahl is newer and has this far not given rise to many common publications. There is active collaboration with CR Steen and his group concerning the role of lipids for the course of clinical and cognitive symptoms in first-episode psychosis, with a common PhD candidate/co-supervision, and where the first paper is ready for submission in February-March 2017. There are also several large collaborative projects with CR Le Hellard on issues related to environmental risk factors and epigenetics, and finally practical collaboration with CR Hugdahl concerning the "eNORMENT" strategy and app-development.

Neurocognition Group



Kjetil Sundet

Professor

University of Oslo,
Head of the Neurocognition Group

Core Researcher:
Kjetil Sundet,
Professor, University of Oslo

Group members:
Ueland, Torill, group leader

Almenning, Beathe Haatveit
Aminihajibashi, Samira
Bidtnes, Vilja
Demmo, Christine
Egeland, Maj
Engen, Magnus
Espeseth, Thomas
Expósito, Verónica
Grimstad, Kristoffer
Halvorsen, Jens Marius
Lanneskog, Anna Maria
Lystad, June Ullevoldsæter
Moldestad, Tale
Sørensen, Håkon
Vaskinn, Anja

Achievements in 2016

- Documented positive effects of cognitive remediation on vocational functioning, successfully defended in PhD-thesis (JUMP-study and FEP-study, PI: Ueland)
- Secured researcher grant for studying ecological validity of social and emotional processing in psychosis (ECOVAL-study, PI: Vaskinn)
- Implemented and secured logistics for reassessing participants in 10 year follow-up study on neurocognitive predictors of functioning (PI: Ueland)
- Completed protocol and pilot experiment for schizophrenia-control fMRI study on effort network (PI: Espeseth)

Ambitions for 2017

- Continue data collection of ongoing projects and assist PhD students (n=6) to publish according to plan (PIs: Ueland, Vaskinn, Espeseth)
- Engage in research collaboration and apply for research grant on neurocognitive correlates of immune system pathology in a longitudinal perspective (PI: Ueland)
- Complete social cognitive training project by assessing outcome (PI: Vaskinn)
- Initiate study on web-based neurocognitive screening as valid supplement to standard neurocognitive assessment (PI: Espeseth)
- Establish new group leader structure

Synergy and Cross-Disciplinary Achievements

The neurocognitive group is in charge of neuropsychological assessment of all subjects recruited to the study, both at baseline and at follow-up. The group collaborates closely with the clinical group (CR Melle) in scheduling neurocognitive assessment of individuals successive to inclusion, and with the genetic (CRs Andreassen/Djurovic) and brain imaging (CR Agartz) groups for blood samples and MR-scans. The group provides essential data for several clinical studies and offers valuable data to validate findings from gene and/or brain imaging studies.

Members of the neurocognitive group contributed on ≈ 30 international publications during 2016. All papers give evidence to the partnership with other groups.
The added value of providing broad-scaled neurocognitive characteristics of all research subjects makes the NORMENT sample highly attractive for large scale cohort studies, in particular within gene-oriented research addressing how cognitive functioning is influenced.

The 10 year follow-up study demands joint efforts from several groups within the Centre (PI: Melle, Ueland, Agartz et al.). We expect within the coming year to have re-assessed a sufficient number of individuals to identify trajectories and subgroups with good and poorer outcome. The next step is to look for individual characteristics and social contingencies predicting outcome, and how to plan adequate treatment. Only a centre such as ours with close and daily contact between partners, safeguards the necessary logistics to secure such a project.

The ECOVAL-study (PI: Vaskinn) will assess function at various levels in order to specify relevant predictors for real-world functioning, including ERP-signals to cognitive and emotional stimuli in addition to standard neuropsychological and social cognitive measures.
A collaboration is established with EEG-experts within NORMENT (PI: Jönsson) and at the Department of Psychology, UiO (Prof. Andersson).

The across-group collaboration is evident in projects focusing on the impact that synaptic plasticity genes have on attention, based on analyses in the NCNG sample where we seek replication of associations between neurocognitive measures and genes upregulated by BDNF (PI: Espeseth, CRs Le Hellard and Steen). We also explore associations across groups between schizophrenia-susceptible and effort-related alleles in combination with pupil dilation data in healthy controls with (PI: Espeseth, CRs Le Hellard/Andreassen/Djurovic).

We are currently expanding our investigation of neurocognitive function (PIs: Ueland, Sundet) and immune system pathology together with other groups both within NORMENT (CR Andreassen, Group leader Dieset) and at the Institute of Clinical Medicine, UiO (Researcher Ueland) to include a broader range of immune markers, reflecting different inflammatory pathways. In addition, we wish to assess the temporal pattern of these inflammatory markers in relation to disease progression by including longitudinal sampling (CR: Melle) which will allow a more causal interpretation of the data.
This is important since the increase in many inflammatory markers in this population may be due to different demographics or comorbidities (e.g. BMI, diabetes), and not strongly related to cognitive function.

Neurocognitive assessment is time and effort consuming, although not high-tech dependent. The group is looking for ways to supplement traditional paper-and-pencil assessments with computer-based as well as web-based methodologies in targeted research projects. We have started planning the use of electronic monitoring or intervention devices (Apps) and other computerized procedures with CR Hugdahl / CR Melle / Group leader Westlye, and intend to carry out pilot-studies in 2017 for use in future studies (PIs: Espeseth, Sundet).

Psychopharmacology and Animal Studies Group

Vidar Martin Steen

Professor

University of Bergen,
Head of the
Psychopharmacology and
Animal Studies Group

Core Researcher:
Vidar M. Steen,
Professor, University of Bergen

Group members:
Brattbakk, Hans-Richard
Bringsli, Jorunn S
Duus, Inger H
Ersland, Kari M
Gjerde, Priyanthi B
Holdhus, Rita
Navdal, Marianne
Skrede, Silje
Stokowy, Tomasz

Achievements in 2016

- Completed transcriptome profiling of schizophrenia, bipolar disorder and healthy controls, with identification of psychosis-related markers of innate immunity
- Discovered positive correlations between clinical outcome and lipid levels in first episode psychosis
- Completed experimental long-term (1 year) antipsychotic exposure in rat
- Participated in international consortia, to define the polygenic background of human brain structures and cognitive functions
- Established new infrastructure for next generation sequencing

Ambitions for 2017

- Further characterize the genetic and biological mechanisms underlying activation of innate immunity markers in psychosis patients
- Study the cognitive, brain imaging and psychop-harmacological relationships between therapeutic response and lipid effects in antipsychotic-treated psychosis patients
- Examine the biological effects in the brain and peripheral tissues of long-term exposure of antipsychotic depot drugs in rat
- Perform transcriptome profiling in peripheral blood of another 1,000 subjects (schizophrenia, bipolar disorder and health controls), including both cross sectional and longitudinal samples

Synergy and Cross-Disciplinary Achievements

The main focus of the research group is to explore and characterize how psychopharmacological drugs work in the treatment of psychotic disorders, using a combination of clinical data, biomarker screening and functional studies in experimental models. The establishment of the NORMENT Centre has given us new opportunities for cross-sectional collaboration around common infrastructures, resources and competence, thereby enabling new directions for our translational psychopharmacology projects.

Of major importance, the CRs Andreassen, Melle, Sundet and Djurovic with many co-workers have collected large clinical samples and biobanks of well-characterized patients with schizophrenia, bipolar disorder and healthy controls (TOP sample). During 2016, our group completed the first phase of transcriptome profiling in peripheral blood of about 1,200 TOP subjects, and the global expression data are available as a common resource. The primary analysis of the transcriptome data has led to discovery of innate immunity markers that seem to be activated in both schizophrenia and bipolar disorder. The functional follow-up studies will be performed in close collaboration with CR Djurovic and his co-workers. We have also contributed global expression data to CR Le Hellard for her project on cannabis and psychosis. We are in progress of planning the next phase of transcriptome profiling, involving about 1,500 samples from the TOP and Bergen Psychosis Project 2 cohorts.

We have for many years been interested in the metabolic- and lipid-stimulating effects of anti-psychotic drugs. Experimental data in our lab suggest that the antipsychotics that are most potent activators of cellular lipid production are also ranked among the most efficacious drugs in the treatment of schizophrenia. Through collaboration with CRs and co-supervisors Melle and Andreassen, a new PhD candidate has so far been able to discover positive correlations between clinical outcome and serum lipid levels in antipsychotic-treated patients with first episode psychosis, using a subgroup of the TOP cohort. This study will be extended to include cognition and brain imaging phenotypes, in collaboration with CRs Sundet and Agartz and current Group leader/ upcoming CR Westlye, to focus on cognitive performance and myelination-relevant data.

Our expertise in experimental research on psychophar-macology has also contributed to several other cross-disciplinary NORMENT projects. As an example, we have recently explored the effects of mood-stabilizing and antipsychotic drugs on the expression of the psychosis risk gene ANK3 in peripheral blood, in a project headed by CR Djurovic. We will perform complementary rat studies to examine ANK3 expression in the brain.

Through our partnership in the new National Consortium for Sequencing and Personalized Medicine (NCS-PM), we have contributed in 2016 to renew the infrastructure for next generation sequencing. We have set up an Illumina HiSeq 4000 and implemented whole genome, exome and RNA sequencing. These applications are used in our projects and will be provided as service

Structural MRI Group

Ingrid Agartz

Professor

University of Oslo,
Head of the Structural
MRI Group

Core Researcher:
Ingrid Agartz,
Professor, University of Oslo

Group members:
Asp, Martine
Engen, Kristine
Gurholt, Tiril Pedersen
Hartberg, Cecilie Bhandari
Haukvik, Unn Kristin H.
Jönsson, Erik
Jørgensen, Kjetil Nordbø
Lange, Elisabeth
Lonning, Vera
Mørch-Johnsen, Lynn
Nerland, Stener
Nesvåg, Ragnar
Raballo, Andrea
Smelror, Runar

Achievements in 2016

- Identified brain structure correlates from use of prescription drugs (antipsychotics and Lithium), alcohol use and tobacco.
- We demonstrate that both second- and first generation antipsychotics affect the subcortical brain in a similar way but clozapine does not induce brain change.
- The hippocampus demonstrates subfield specific changes in severe psychosis.
- The first longitudinal neuroimaging study of first-episode psychosis shows stability of brain change over the first year after psychosis onset.
- Confirmed subcortical brain structure abnormalities in schizophrenia and bipolar disorders, through active involvement in the ENIGMA consortium

Ambitions for 2017

- Use newly developed algorithms and software to find new imaging phenotypes (cortical folding, automated WMHI characterization, free-water DTI and myelin mapping, longitudinal trajectories).
- Investigate pre- and perinatal risk factors and new biomarkers for effects on brain variability and function in schizophrenia and bipolar disorder.
- Use national registry data for detailed evaluation of pharmacological effects on the brain in adolescents and adult samples. What are the long-term effects?
- Start or expand participation of patients with early onset adolescent psychosis, “violent schizophrenia”, late-onset psychosis in the elderly population, and symptoms collaboration with BUPGEN and MoBa cohort.
- Develop and coordinate an ENIGMA for early onset adolescent psychosis, meta- and mega-analyses across international sites.

Synergy and Cross-Disciplinary Achievements

During 2016, the Structural MRI group has continued with the main focus on neuroimaging of brain neuroanatomy in schizophrenia and bipolar disorder. This venture largely depends on the integration between the different NORMENT Centre activities and CRs.

The group is together with CR Ole Andreassen and Group leader Lars Westlye active partners in international neuroimaging and imaging genetics consortia such as the IMAGEMEND and ENIGMA in schizophrenia and bipolar disorder. These collaborations have resulted in several high impact publications confirming key brain structure features in schizophrenia and bipolar disorders and discovering brain effects from commonly prescribed antipsychotic drugs for disease. We coordinate the adolescent ENIGMA Early Onset Psychosis (ENIGMA-EOP) international working group and the adolescent data collection across the NORMENT neuroimaging groups and Stockholm Early-Onset Psychosis Study (SCAPS) at Karolinska Institutet.

With CR Hugdahl, we demonstrated that auditory verbal hallucinations (AVH) in adult patients are related with thinner cortex in left Heschl’s gyrus. CR Kenneth Hugdahl and his research group have developed a smart-phone app for on-line AVH monitoring. This electronic devise is now tested in our adolescent psychosis patients which will allow the pursuit of detailed data on AVH that are frequent symptoms in adolescent psychosis. In collaboration with CR Kjetil Sundet we develop adolescent norms for the MATRICS Consensus Cognitive Battery. Complementary to the adolescent psychosis project, we have initiated collaborations with clinical cohorts (BUPGENE; CR Ole Andreassen and SCAPS) in young patients.

With the hypothesis that the contrast between grey- and white-matter MR intensities in an image reflects myelination along the cortical surface, we have shown increased contrast in highly myelinated low-level sensory and motor regions in psychosis suggestive of reduced intracortical myelin. This could cause disinhibition of sensory input, resulting in distorted perceptual processing leading to the characteristic positive symptoms of schizophrenia and will be pursued in a postdoctoral project. Group leader Lars T. Westlye was essential for adding novel technical aspects to this study.

Given the prevalence of weight gain as well as abnormal lipid profiles in psychosis, and the unique profile of clozapine, we collaborate with CR Vidar Steen for brain effects of aberrant lipid metabolism and putatively convergent effect of antipsychotics on brain white matter. Group leader Erik Jönsson uses national drug registry data to ascertain drug history at a high level of historical detail for these studies.

We collaborate with the clinical group and CR Ingrid Melle on several studies; apathy as core symptom with brain structural correlates, vitamin D as risk factor for abnormal brain development, and core negative symptoms and their relation to the striatum. Together, we are part of a negative symptoms network; EURONES. We will further the longitudinal MRI studies and have this year shown stability of brain structure change the first years after psychosis onset.

Unn Haukvik leads the “Violent Schizophrenia” project with several security wards in Norway in collaboration with CR Ingrid Melle and others. In the coming year, we expect to be successful with more direct collaboration with the genetics groups (CR Le Hellard and CR Srdjan Djurovic) although we are long term part of the imaging genetics consortia.

Psychiatric Molecular Genetics Group

Srdjan Djurovic

Professor

Oslo University Hospital
and University of Bergen,
Head of the Psychiatric
Molecular Genetics Group

Core Researcher:
Srdjan Djurovic,
Professor, Oslo University Hospital,
University of Bergen.

Group members:
Akkouh, Ibrahim
Andresen, Lavinia Athanasiu
Hansson, Lars
Hassani, Sahar
Hughes, Timothy
Impellizzeri, Agata
Inderhaug, Elin
Kjeldal, Kristine
Melbø-Jørgensen, Christian
Szabo, Attila
Sønderby, Ida E
Vandenberghe, Matthieu

Achievements in 2016

- Established pipeline for functional characterization of new gene loci identified for psychiatric diseases.
- The polygenic basis of the human brain and neurodevelopmental disorders identified, and several papers focusing on links between genotypes, clinical phenotypes, and RNA expression data have been published.
- Inclusion of samples for stem cells project and building up stem cells infrastructure; production and further characterization of induced pluripotent stem cells and induced neurons.
- Infrastructure/platform activities : biobanking, database, sample prep, QC.
- New national/international collaborations established.

Ambitions for 2017

- 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 cell
- Continuation of translational projects
- Explore how cortical network dynamics are related to genetics of psychotic disorders
- Development and improvement of genetic prediction tools for disease course and outcome
- Imaging genetics - connectomics
- Biobanking, database, sample prep, quality control
- Continuation of international collaboration (eg. EURICND, CNV ENIGMA, PGC COGENT)

Synergy and Cross-Disciplinary Achievements

The goal of the Psychiatric Molecular Genetics Group is to develop a strong research environment in molecular genetics of psychiatric disorders. Being a part of the CoE NORMENT, we have been able to dynamize major collaborative efforts studying clinical characteristics (CR Melle), neurocognitive functioning (CR Sundet), biostatistics (CR Andreassen) and brain imaging biology (CR Agartz) of psychotic disorders together with molecular genetics. The group's current research aims are to perform molecular genetic analysis of the hidden heritability of severe mental disorders, identification of genetic loci associated with neurocognitive and MR phenotypes and implications for disease mechanisms in severe mental disorders, as well as prediction of longitudinal outcome and brain phenotype by polygenic risk scores. We also want to continue and develop support for the infrastructure of the Centre, providing psychiatric genetic studies with design and planning, incl. biobanking, database, sample prep, QC (CR Andreassen).

Moreover, we have established the required competence and facilities for human induced pluripotent stem cell (hiPSC) technology unit in our Centre allowing investigation of neuronal cells from participants. As of December 2016, fibroblasts have been collected from 68 participants. Currently 21 iPSC are undergoing differentiation to neuronal pluripotent cells. 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 have experience with hiPSC differentiation, and have an in house collection of mature neurons. The derived cells are subjected to rigorous validation utilizing already established in-house protocols.

Due to synergy within NORMENT, we will use our large, existing in-house data of well characterized patients to identify clinical profiles associated with the polygenic risk, related to symptom levels (CR Melle), neurocognitive function (CR Sundet, Group leader Ueland), brain imaging features (CR Agartz, Group leader Westlye) and outcome parameters. We will have a special focus on two areas, immune-related mechanisms and neuronal excitability, which yet again depend upon synergistic approaches. These areas are also accessible for collaboration with psychopharmacology and animal studies group (CR Steen), as well as epigenetics (CR Le Hellard).

Several lines of collaborative synergy projects have been started in 2016 and they are set to continue in 2017. These include: CR Agartz – Imaging genetics, CR Andreassen – Biophys psychiatry, Biostat evolution, CR Le Hellard – Polygenic pleiotropy, Epigenetics, CR Melle – Polygenic risk scores, Vitamine D, Oxytocin, CR Steen – Transcriptomics, as well as CR Sundet, Ueland – Cognitive genetics, and Group leader Westlye – Imaging genetics, Connectomics.

Brain Imaging Group

Kenneth Hugdahl

Professor

University of Bergen,
Head of the Brain
Imaging Group

Core Researcher:
Kenneth Hugdahl,
Professor, University of Bergen.

Group members:
Bless, Josef
Craven, Alex
Dwyer, Gerard E.
Falkenberg, Liv
Hirnstein, Marco
Hjelmervik, Helene
Kovalchuk, Galyna
Marqueardt, Lyn
Sinkevicute, Igne
Stabell, Lena

Other personnel
Beresniewicz, Justyna
Ersland, Lars
Grüner, Renate
Johnsen, Erik
Kazimierczak, Katarzyna
Kompus, Kristiina
Kroken, Erik
Larøi, Frank
Løberg, Else-Marie

Achievements in 2016

- Followed-up on last year's findings of increased glutamate levels in hallucinating patients, now comparing state versus trait aspects auditory hallucinations, and on non-medicated patients
- Followed-up on the discovery in 2015 of a new generalized cognitive network in the brain (EMN), have found aberrant network regulation in schizophrenia patients compared to healthy controls.
- Followed-up on the development of a new smart-phone app for symptom registration on-line. Initiated testing the app in collaborative projects within the NORMENT

Ambitions for 2017

- Aim to study the interaction of excitatory and inhibitory neurotransmitters and how the glutamate/GABA balance relates to the spontaneous onset and offset of auditory hallucinations.
- Initiate a new series of analyses with new cognitive paradigms targeting interaction of large-scale cortical networks in auditory hallucinations
- Roll-out collaborative studies on the use of smart-phone app for hallucinatory symptom sampling in real-time
- Continue search for genetic markers of auditory hallucinations, looking at relationship between auditory hallucinations and polygenic risk scores, and epigenetic influences, respectively

Synergy and Cross-Disciplinary Achievements

The contribution by the group to the NORMENT goals and achievements has been focused on understanding the neurobiological and cognitive markers of auditory hallucinations, as a key symptom in schizophrenia. Thus, our group has a more restricted focus, in which we try to elucidate a single symptom through different levels of explanation, using the NORMENT vertical synergy approach. In order to move from the clinical to the molecular levels of explanation, we are dependent on the collaboration with other NORMENT researchers.

In collaboration with CR Agartz and her group we have developed a new smartphone app for on-line sampling of data on several key parameters related to the onset and offset of auditory hallucinations. This work is coordinated by postdoc Josef Bless, and also includes collaboration with Iris Sommer in Utrecht and Irina Holma in Helsinki. The app-project is part of a larger NORMENT initiative in phase II of the Centre, where eNORMENT, and electronic data handling on a large scale will be in focus. Our group is collaborating also with CRs Melle and Andreassen when it comes to the eNORMENT initiative, which they are coordinating. Our contribution to centre synergy will therefore be bringing in knowledge of app-technology into the clinical research domain, and we will benefit from the expertise and experience of CRs Melle and Andreassen when it comes to putting the app in a broader eHealth context.

In collaboration with CR Andreassen we have begun studying the neurochemistry of auditory hallucinations, using MR spectroscopy measures, with a focus on glutamate/GABA interactions. This collaboration will also include Group leader/new CR Lars T. Westlye, and our group is contributing with details of measurement and analysis methods since we pioneered this kind of MR spectroscopy in Norway, and also published the first study on the relationship between glutamate and auditory hallucinations (Hugdahl et al., Schizophrenia Research, 2015).

Our contribution to synergy in the Centre is that we bring in top-notch knowledge and infrastructure of MR spectroscopy, while we get access to the large NORMENT samples.

In ongoing discussions with CR Sundet and the neurocognition group we are considering new cognitive paradigms for fMRI studies, also suggested by the SAB. We are currently setting up a new cognitive paradigm for the study of how large-scale cortical networks, like the default mode network (DMN) and the extrinsic mode network (EMN), discovered by our group (Hugdahl et al., 2015, Frontiers
in Human Neuroscience), and how the up- and down-regulation of these networks is affected by auditory hallucinations. We bring the discovery of the EMN to the NORMENT and get in return expert knowledge on cognition and cognitive paradigms.

In collaboration with CRs Le Hellard and Steen, we are trying to go down to the molecular level of explanation, and reach a true vertical synergy across the clinical, cognitive, imaging ad genetic levels of explanation. Group leader Kristiina Kompus is coordinating these efforts from our side, thus having junior researchers joining senior researchers on equal terms, with the ambition to achieve true synergy and collaboration. One project is to look for polygenic risk scores in schizophrenia and MR spectroscopy data for glutamate, with auditory hallucinations as a covariate. CR Le Hellard brings her expertise knowledge of genetics and the infrastructure for such analyses, and we bring our knowledge of glutamate measurements and MR infrastructure.

Epigenetics and Functional Genomics Group

Stephanie le Hellard

Professor

University of Bergen,
Head of the Epigenetics
and Functional Genomics Group

Core Researcher:
Stéphanie le Hellard,
Professor, University of Bergen

Group members:
Abdelrazik, Heba
Banerjee, Niladri
Giddaluru, Sudheer
Polushina, Tatiana
Stavrum, Anne-Kristin

Achievements in 2016

- Updated our R package, LDsnpR to perform more gene based analyses.
- Analysed genetic overlaps between psychiatric disorders and relevant phenotypes at the gene level.
- Performed transcriptomic analysis of the effect of cannabis in the blood of patients.
- Initiated the methylation typing of 1000 TOP samples.
- Participated in consortia for the identification of genetic variants implicated in cognition and brain imaging traits (ENIGMA; CHARGE, COGENT).

Ambitions for 2017

- Establish a pipeline to analyse the effect of different environmental factors on methylation modifications in a subset of 1000 TOP samples.
- Implement tools to perform integrated analysis of genetic, epigenetic and transcriptomic datasets.
- Initialize the characterization of the effect of cannabis on stem cells from patients.
- Establish European collaborations with other groups working on methylation, and environment datasets.

Synergy and Cross-Disciplinary Achievements

The main focus of the group is to bridge discoveries from molecular genetic studies towards functional genomics and application to clinical studies. We have also developed epigenetic studies in order to explore the interaction between environmental factors and genetics. For molecular genetic studies we are still participating in the large effort of the Centre to collect large samples of genotyped samples, where our participation consists in performing quality control of the samples and imputation. We also maintain our work in cognition and imaging genetics, notably with several projects that involve the samples we have genotyped (NCNG and Betula) and the samples genotyped by the other NORMENT groups (TOP). We have several collaborative projects with Group leader Lars Westlye, where we have contributed with providing genotyping from samples with brain imaging phenotypes that are complementary to the samples studied in the TOP project. At the brain imaging level, we have also established collaborative projects with the Brain Imaging group (CR Hugdahl) and we have several ongoing projects which are looking at different genetic factors in their samples.

We have good collaboration with the biostatistics and biobanks group (CR Andreassen and CR Djurovic) and we have implemented tools that are complementary to the tools the group has and which explore other aspects of the genetic factors associated with mental disorders. Since 2015, we have started developing studies that look at the effect of environmental factors on gene expression via epigenetic mechanisms. These studies have been made possible only through the establishment of the NORMENT. These studies require expertise in molecular genetics, which we have and they require a very well-characterized and large sample which our co-CRs have collected (CR Andreassen and CR Melle). On the same sample we will be soon in a unique position to explore different levels of genomic data and their interaction: genetics, epigenetics, and transcriptomics, thanks to the characterization of the same sample at different levels, which has been done by the different groups in the NORMENT Centre (e.g. CRs Andreassen, Djurovic and Steen).

In the coming years, we will also work together with the stem cell platform to investigate the effect of known environmental factors on neurons derived from patients. This project was developed within the infrastructure that the Centre has established where it is now possible to combine functional and environmental studies.

Through regular meetings and working visits with the other groups we regularly exchange knowledge and support each other's with complementary expertise. We have provided support for different projects in NORMENT with our expertise in bioinformatics or statistical genetics, and soon with our developing expertise in epigenetics.

TOP Day 2016
Photo: Øystein Horgmo, UiO

Researcher Training

NORMENT offers a range of training and development opportunities for our PhD students, postgraduate researchers and other research staff. 41 PhD students and 43 post docs are currently working at the Centre. There are various gatherings and meetings at NORMENT with the aim of contributing to a best possible researcher training. Scientific sharing and synergy across domains is important at these events, and an underlying principle for all research activites at the Centre.

PhD Education and Training Programme
The PhD students at NORMENT are enrolled at the mandatory PhD education program at the University of Oslo and University of Bergen. In addition, the PhD students are encouraged to sign up for relevant courses and training at the Norwegian Research School in Neuroscience (NRSN) that works to coordinate and improve educational activities for PhD candidates in neuroscience.

NORMENT organizes weekly meetings where PhD students and post docs present their current research. The Centre also organizes structured workshops in the fields of statistics, academic writing, and clinical supervision, as well as genetic methods and imaging methodology. The Centre has arranged regular one-week workshops of the Structured Clinical Interview Axis 1 Diagnosis (SCID-I) DSM-IV and Positive and Negative Syndrome Scale (PANSS) with Joseph Ventura from the University of California Los Angeles, USA.

The TOP Day is an annual event at NORMENT. TOP stands for Thematically Organized Psychosis Research. This meeting allows PhD students to present their research, share ideas and give each other feedback. The meeting gathers PhD students and researchers from different research fields and backgrounds, which makes it a vertical synergy meeting across the Centre.

We have received two grants for research education and training, one focusing on international partnership, with UCSD in the USA (INTPART) and one focusing on training of PhD students (Olav Thon Foundation). We are also involved in the NORBIS programme (national research school in bioinformatics, biostatistics and systems biology), where we organize a PhD Course in GWAS and biostatistics.

NORMENT Annual Retreat 2016 took place at Quality Hotel Leangkollen outside Oslo, Sept. 28-29. A total of 115 people participated.

Norment Annual Retreat

NORMENT Annual Retreat takes place every year in September as a two day conference in an interactive and enthusiastic atmosphere. The programme consists of plenary lectures given by researchers and post docs with updated, new findings and ongoing projects, synergy workshops with project planning, as well as poster sessions by mainly master and PhD students. Our Scientific Advisory Committee contributes with comments and feedback during the Annual Retreat.

NORMENT Young Researchers Meeting

NORMENT has a special focus on young investigators' careers, both internally in the Centre, to guide and mentor our post docs, and externally, to facilitate promotion to faculty positions for the most talented researchers. The NORMENT Young Researchers Meeting started in 2015 as an annual one-day meeting for the young researchers and PhD students. This meeting is in fully planned by the young researchers themselves and is an arena for them to discuss topics that they consider important to their scientific development and career.

Weekly Research Meetings and Workshops

NORMENT strives to share with one another and during our weekly research meetings we keep our group members updated on what everyone in the Centre is working on. Each week an employee is given the opportunity to present his/her work. At these workshops anyone at the Centre can make informal presentations of their work; the core researchers, senior scientists, associate professors, postdocs, PhD students and technical research personnel. The meetings are also a possibility for senior PhD students to get feedback on their ongoing projects and scientific articles.

There are also workshops led by external fellow-researchers and individual group trainings led by the respective group leader at the Centre. To facilitate multi-site meetings, seminar and courses, we use a low-threshold communication system (www.vidyo.com).

Eva Z. Hoseth was awarded
The Einar Martens Legat Poster Prize.

Synergy Meetings

NORMENT has a focus on vertical synergy and will in each of our four main research areas aim to obtain different levels of understanding, bringing together transdisciplinary expertise and methods. To achieve this goal, we have developed a meeting place, the monthly Vertical Synergy Meeting, where we can present ideas and preliminary data to facilitate interactions and discussions. First, there is a presentation of state of the art in a given topic, then an overview of new ideas and ongoing projects. There have been 10 synergy meetings in the course of 2016, each with 20-40 participants on each meeting. They have covered topics such as stem cells, hallucinations, MR protocols, lipids and myelination, antipsychotics, imaging and genetics.

International Research Training

The Centre attracts international research talents. We actively focus on recruitment of talented post docs and young investigators through international advertise-ments and networking. We also strengthen the mobility of PhD, post doc and senior scientists recruited or exchanged with a diversity of European countries (Italy, Sweden, Denmark, France, Germany, UK, Montenegro, Iceland) in addition to the USA/Canada and Asia (India, China). All in all, the Centre staff represents more than 25 nationalities.The international research education and training with the University of California San Diego (UCSD) in the USA is funded in part by the Research Council of Norway - RCN (INTPART).

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

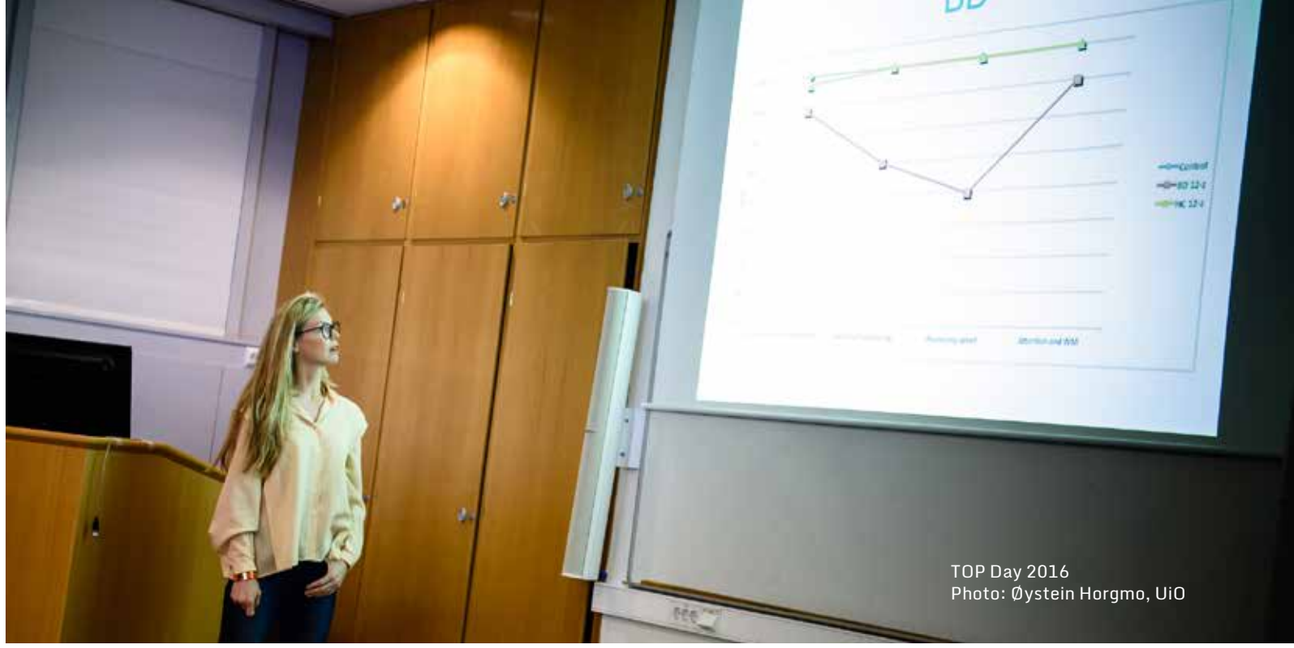
2014

- **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 Glenne 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
- **Holmén, 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

17 PhD candidates have so far completed their PhDs at the Centre.



TOP Day 2016
Photo: Øystein Horgmo, UiO

2016

- **Bolstad, Ingeborg:** Effects of aripipralzole 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



International Collaboration

The research at NORMENT requires close cooperation with leading research environments, both nationally and internationally. The researchers are participating in a series of international networks, and have several bilateral research programmes with international institutions, both in the European Union and in the USA. In addition to this, the Centre works actively to recruit excellent researchers internationally.

The Centre facilitates the exchange of staff between the participants and international collaborators. In 2016, two post docs were abroad (Kauppi, Kaufmann), and four international guest researchers were associated with the Centre.

The international collaboration includes the following institutions and research groups:

Nordic countries:

- Department of Psychiatry, Umeå Center for Functional Brain Imaging, Umeå University, Sweden, Lars Nyberg
- Department of Clinical Neuroscience, Karolinska Institutet, Sweden, Patrick F. Sullivan and Lars Farde
- University of Copenhagen, Denmark, Thomas Werge and Wes Thompson
- deCODE Genetics, Iceland, Hreinn Stefansson and Kari Stefansson

Europe:

- University of Bari, Italy, Alessandro Bertolino.
- University of Oxford, UK, Guy Goodwin.
- King's College London, UK, Gerome Breen.
- Cardiff University, UK, Mick O'donovan.
- University of Edinburgh, UK, Ian Deary.
- University of Liege, Belgium, Frank Laroi.
- INSERM, Creteil, France, Chantal Henry, Frank Bellivier
- Department of Molecular and Translational Medicine, Universita Degli, Studi di Brescia, Brescia, Italy, Annamaria Cataneo .
- Department of Pharmacological Sciences, University of Milan, Milan, Italy, Marco Andrea Riva.
- University of Mannheim, Department of Genetic Epidemiology in Psychiatry, Germany, Andreas Meyer-Lindenberg.
- University of Bonn, Germany, Markus Nöthen, Per Hoffman.
- Department of Medical genetics, Basel University Hospital and University of Basel, Switzerland, Sven Cichon.
- University of Basel, Switzerland, Stefan Bogwardt
- Department of Physiology, University of Santiago de Compostella, Spain, Miguel Lopez.

USA:

- Yale University School of Medicine, New Haven, Connecticut, USA, David Glahn, Tom McGlashan.
- Broad Institute (Harvard/MIT/MGH), Boston, USA, Jordan Smoller, Mark Daly.
- Multi-Modal Imaging Laboratory, University of California San Diego, USA, Anders M Dale, Chi-Hua Chen.
- University of Southern California, USA, Paul Thompson.
- University of California, Los Angeles, USA, Joe Ventura, Michael F. Green.
- Universithy of California, San Francisco, USA, Rahul Desikan.
- University of North Carolina, Chapel Hill, USA, Patrick F. Sullivan.

Participation in EU Projects and other International Consortia

- COGENT (Cognitive Genomics Consortium), http://www.feinsteininstitute.org/2017/01/feinstein-institute-genetic-discovery-provides-new-insight-cognitive-disorders/
- ECNP Bipolar Disorders Network, https://www.ecnp.eu/research-innovation/ECNP-networks/List-ECNP-Networks/Bipolar-Disorders.aspx
- ECNP Schizophrenia Network, https://www.ecnp.eu/research-innovation/ECNP-networks/List-ECNP-Networks/Schizophrenia.aspx
- ENIGMA (Enhancing Neuro Imaging Genetics Through Meta Analysis), http://enigma.ini.usc.edu, NIH funded
- IMAGEMEND (Imaging Genetics for Mental Disorders), http://www.imagemend.eu, EU project
- International Consortium on Hallucination Research,https://hallucinationconsortium.org/
- PGC (Psychiatric Genomics Consortium), https://www.med.unc.edu/pgc, NIH and RCN funded
- PsychDPC (Psychiatric Diagnostic and Prevention Consortium), http://www.psych-dpc.eu/, EU project

International Guest Researchers

- Cichon, Sven (University of Basel, Switzerland).
- Dale, Anders M. (UCSD, USA).
- Devor, Anna (UCSD, USA).
- Larøi, Frank (University of Liège, Belgium).
- McGlashan, Tom (Yale University, USA).
- Stefansson, Hreinn (deCODE Genetics, Iceland).
- Thompson, Wes (University of Copenhagen/UCSD, USA).

Selected Visits Abroad 2016

- Andreassen, Ole A: University of California San Diego, five 1-2 weeks periods, San Diego, USA.
- Doan, Nhat Trung: deCODE genetics, 2 months Reykjavik, Iceland.
- Frei, Oleksandr: Multimodal Imaging and Genetics Laboratory,University of California San Diego.
- Hugdahl, Kenneth: Iris Sommer and her group, Utrecht University Medical Center, The Netherlands.
- Hugdahl, Kenneth: Syastolov Medvedev/Alexander Korotkov, Human Brain Institute, St Petersburg, Russia.
- Hugdahl, Kenneth: Andrea Anta, Georg-August University, Göttingen, Germany.
- Kaufmann, Tobias: Child and Youth Psychiatry, Tübingen, Germany.
- Westlye, Lars T.: Max Planck Institute of Human Development, Berlin, Germany.
- Westlye, Lars T.: University of Copenhagen, Denmark.

Selected Visits from Abroad 2016

- Devor, Anna, associate professor from the University of California San Diego, USA.
- Fan, Chun-Chieh, MD from University of California San Diego, USA.
- Hill , William David, postdoctoral researcher from the Universtiy of Edinburgh, Scotland, and the CHARGE consortium, to study genetic data on cognitive function.
- Meyer, Nicholas, PhD research fellow from Kings College, London, UK, visit to the eNorment group, presenting his project: Detecting early signs of relapse in psychosis using remote monitoring technology: acceptability and feasibility of a passive sensing approach.
- Postuma, Daniella, professor from the Vrije Universiteit, Amsterdam, Netherlands, participated at genetics symposium at Hafjell.
- Reinbold , Céline, PhD student from the University of Basel, Switzerland, worked in the biostats group for three months.
- Thompson, Wes, professor at the University of Copenhagen, Denmark.
- Werge, Thomas, professor at University of Copenhagen, Denmark, participated in genetics symposium at Hafjell.

Illustration photo: Colourbox.no

Dissemination and Communication

NORMENT members gave 47 talks as invited speakers at international scientific meetings in 2016. In addition, 61 oral presentations were presented by NORMENT scientists. The Centre was presented in the media 35 times during the year.

Selected Presentations 2016

Aas, Monica: Putative causes, moderators, and consequences of stress and HPA axis dysfunction in psychosis, International Society of Psychoneuroendocrinology (SPNE), Miami, USA, September 8-11, 2016.

Aas, Monica: Understanding the trauma-psychosis link: can translational research bring us a step further? Early Intervention in Mental health (IEPA), Milan, Italy, October 19-22, 2016.

Andreassen, Ole A.: Inflammatory evidence for the psychosis continuum model, European College of Neuropsychopharmacology (ECNP), Vienna, Austria, September 18, 2016.

Andreassen, Ole A.: Biobank and Other Registry Resources in Nordic Countries, National Institute of Mental Health (NIMH) Workshop, Washington DC, USA, September 15, 2016.

Andreassen, Ole A.: Biophysical Psychiatry - translating large-scale data to disease mechanisms, The Future of Psychiatry, Sct Hans 200 years Anniversary Symposium, September 23, 2016.

Andreassen, Ole A.: Distinct Patterns of Cortical Thickness Reductions in Bipolar Disorders Emerge From Large-scale Brain Imaging Approach, Society of Biological Psychiatry (SOBP), Atlanta, USA, May 14, 2016.

Andreassen, Ole A.: Genetic revolution in Psychiatry - Recent discoveries and future potential, deCODE 20 years Symposium, Reykjavik, Iceland, September 2016.

Andreassen, Ole A.: Oxytocin delivered with nasal device - effects on social behavior and brain activity, Scandinavian College of Neuropsychopharmacology (SCNP), Copenhagen, Denmark, April 28, 2016.

Berg, Akiah Ottesen: Psychotic symptom profiles in immigrants and ethnic minorities, International Association for Early Intervention in Mental Health (IEPA), Milan, Italy, October 20, 2016.

Djurovic, Srdjan: Human induced pluripotent stem cell (hiPSC) enabling technologies in psychiatric molecular genetics, World Psychiatry Association International Congress, Cape Town, South Africa, November 18-22, 2016.

Doan, Nhat Trung: Distinct modes of brain variability across the Alzheimer's disease continuum, Organization for Human Brain Mapping (OHBM) Conference, Geneva, Switzerland, June 26-30, 2016.

Gardsjord, Erlend S.: Subjective quality of life among patients in symptomatic remission compared to non-remission,Early Intervention in Mental health (IEPA), Milan, Italy, October 19-22, 2016.

Haram, Marit: Contribution of oxytocin receptor polymorphisms to amygdala activation in psychotic disorders, International Association for Early Intervention in Mental Health (IEPA), Milan, Italy, Oct. 20-22, 2016.

Hugdahl, Kenneth: Genetics and auditory verbal hallucinations: more questions than answers, Simon McCarthy-Jones, Trinity College, Dublin, Ireland, June 2016.

Hugdahl, Kenneth: In Vivo Measurement of Neurotransmitters using Magnetic Resonance Spectroscopy - What, How and Why? Paul Mullins, Bangor University, UK, June 2016.

Hugdahl, Kenneth: Auditory hallucinations: A single-symptom approach to clinical psychology, Second National Congress of Clinical Psychology, Sofia, Bulgaria, October 06-09, 2016.

Johnsen, Erik: Update on metabolic side effects of antipsychotics, and evidence-based management, Scandinavian College of Neuropsychopharmacology, Århus, Denmark, April 27-29, 2016.

Kaufmann, Tobias: Disintegration of sensorimotor brain networks in schizophrenia, European Psychiatry (EPA) Congress , Madrid, Spain, March 12-15, 2016.

Kompus, Kristiina: Glutamatergic processing in the auditory cortex and beyond: Relationships with auditory verbal hallucinations, Workshop on Hallucinations and Predictive Processing, Durham University, UK, July 07-08, 2016.

Le Hellard, Stephanie: Keynote lecture on Psychiatric Genetics, NORBIS summer school (national research school in bioinformatics, biostatistics and systems biology), Bergen, June 14, 2016.

Mäki-Marttunen, Tuomo: A stepwise neuron model fitting procedure designed for recordings with high spatial resolution: Application to layer 5 pyramidal cells, University of Hertfordshire, UK, November 23, 2016.

Melle, Ingrid: Hallucinations without delusions in patients with first-episode psychosis, clinical correlates and implications for pathophysiological models, European Psychiatric Association Annual Conference, Madrid, Spain, April 2016.

Melle, Ingrid: The polygenic background for schizophrenia and neurodevelopment, Robert Sommer Reward Symposium, Giessen, Germany, November 2016.

Melle, Ingrid: Untreated Bipolar Illness and its Association to Outcome in First Episode Mania, International Early Psychosis Association Bi-Annual Conference, Milan, Italy, October 2016.

Moberget, Torgeir: Cerebellar grey matter volume in schizophrenia - a multi-site study of 543 patients and 760 controls, Organization for Human Brain Mapping (OHBM) Conference, Geneva, Switzerland, June 26-30, 2016.

Raballo, Andrea: Psychopathology of mood disorders, Faculty of Medicine, Lisbon University, Lisbon, Portugal, January 15-16, 2016.

Smeland, Olav B.: Genetic overlap between Schizophrenia, Bipolar Disorder and the Big Five personality traits, Schizophrenia International Research Society, Florence, Italy, April 2016.

Sundet, Kjetil: A social path to functioning in schizophrenia, CINS II ISAB Meeting, Copenhagen, October 28-29, 2016.

Ueland, Torill: Integrating cognitive remediation with work rehabilitation, Cognitive Remediation in Psychiatry, New York, USA, June 10, 2016.

Vaskinn, Anja: Autistic traits in schizophrenia and their relationship to theory of mind and social functioning, Schizophrenia International Research Society Conference, Florence, Italy, April 02-06, 2016.

Media Coverage 2016

Aas, Monica: Barndomstrauma og psykiske lidelser, blog post at Forskning.no, January 2016 (http://forskning.no/blogg/akademiet-yngre-forskere/barn-domstrauma-og-psykiske-lidelser)

Aas, Monica: Nokpunktet - intervju med Per Fugelli, blog post at Forskning.no, June 2016 (http://forskning.no/blogg/akademiet-yngre-forskere/nok-punktet-det-kommer-pluss-det-kommer-minus-intervju-med-prof)

Andreassen, Ole A.: Gen og psykisk sjukdom: Komplekse samanhengar, interview in GENialt, February 2016 (http://www.bioteknologiradet.no/2016/02/gen-og-psy-kisk-sjukdom-komplekse-samanhengar/)

Andreassen, Ole A.: Medisinfrie tiltak for psykoselidelser er fortsatt et sjansespill, article written together with Ulrik Malt and Jan Ivar Røssberg in Aftenposten, July 2016 (http://www.aftenposten.no/meninger/debatt/Medisinfrie-til-tak-for-psykoselidelser-er-fortsatt-et-sjansespill-600211b.html)

Berg, Akiah Ottesen: Hvordan påvirker kultur og gener vår psykiske helse?, blog post at Forskning.no, May 2016 (http://forskning.no/blogg/forskningssykehuset/er-du-fodt-pa-feil-klode)

Berg , Akiah Ottesen: Hvordan du ønsker flyktninger velkommen til ditt nabolag, kan påvirke helsa til flere generasjoner, interview in Dagbladet Magasinet, June 2016 (http://www.dagbladet.no/magasinet/hvordan-du-onsker-flyktninger-velkommen-til-ditt-nabolag-kan-pavirke-helsa-til-flere-generasjoner/60386961)

Elvsåshagen, Torbjørn: Fant ledetråd i søvn-mysterium, publicity in Dagens Medisin, June 2016 (https://www.dagensmedisin.no/artikler/2015/06/15/fant-ledetrad-i-sovn-mysterium/), as well as VG, Dagbladet, Forskning.no, and interview at «God morgen Norge» at TV2.

Engvig, Andreas: Kroppen din, interview in episode 5 about memory and memory training at TV2, 28 April 2016 (http://sumo.tv2.no/programmer/fakta/kroppen-din/)

Hugdahl, Kenneth: Å høre stemmer som ikke finnes, chronicle in Bergens Tidende, December 2016 (http://www.bt.no/btmeninger/kronikk/A-hore-stemmer-som-ikke-finnes-326914b.html)

Hugdahl, Kenneth: Er hjerneforskningen i ferd med å avskaffe vår frie vilje?, interview in Dagen, May 2016

Hugdahl, Kenneth: Fikk prestisjestipend for andre gang, article in Bergens Tidende, March 2016 (http://www.bt.no/nyheter/lokalt/Fikk-prestisjestipend---for-andre-gang-307112b.html)

Hugdahl, Kenneth: Hjerneforskning er blitt norsk eksportsuksess, publicity at NRK Dagsrevyen and at NRK.no, January 2016 (https://www.nrk.no/hordaland/hjernefors-kning-er-blitt-norsk-eksportsuksess-1.12772320)

Hugdahl, Kenneth: The Master Mind, interview in the UiB Magazine, spring 2016

Hugdahl, Kenneth: Kenneth Hugdahl får toppstipend for andre gang, UiB Aktuelt, March 2016 (http://www.uib.no/aktuelt/96723/kenneth-hug-dahl-f%C3%A5r-toppstipend-andre-gang#)

Kaufmann, Tobias: Én søvnløs natt endrer forbindelser i hjernen, publicity in Dagens Medisin, January 2016 (http://www.dagensmedisin.no/artikler/2016/01/15/sovn-los-natt-endrer-forbindelser-i-hjernen)

Kaufmann, Tobias: Sleep Deprivation Alters Brain Connectivity, publicity in Discover Magazine, January 2016 (http://blogs.discovermagazine.com/neuroskep-tic/2016/01/01/sleep-deprivation-brain/#.WE-2F30cO0c)

Lagerberg, Trine Vik: Hvordan påvirker kultur og gener vår psykiske helse?, blog post at Forskning.no, May 2016 (http://forskning.no/blogg/forskningssykehuset/er-du-fodt-pa-feil-klode)

Mäki-Marttunen, Tuomo: Neuronimallinnuksen käyttö skitsofrenian tutkimuksessa, chronicle in Best Practice (in Finnish), December 2016 (https://bestprac.fi/2016/12/18/neuronimallinnuksen-kaytto-skitsofrenian-tutkimuksessa/)

Mäki-Marttunen, Tuomo: Simulating Schizophrenia at the Neuronal Level, publicity in BioTechniques, Feb. 2016 (http://www.biotechniques.com/news/Simulating-Schizophrenia-at-the-Neuronal-Level/biotechniques-363225.html#.WJJLS_krK70)

Nerhus, Mari: Low vitamin D levels linked to depression and cognitive deficits in psychotic disorders, publicity in the Pharmaceutical Journal, October 2016 (http://www.pharmaceutical-journal.com/news-and-analysis/research-briefing/low-vitamin-d-levels-linked-to-depression-and-cognitive-deficits-in-psychotic-disorders/20201899.article

Nerhus, Mari: Study shows low vitamin D levels are associated with increased negative and depressive symptoms in psychotic disorders, publicity in Medical News Today, Oct. 2016 (http://www.medicalnewstoday.com/releases/313614.php)

Nerhus, Mari: Supervitaminen mange glemmer å tenke på: Derfor er D-vitamin så viktig for deg, interview in Dagbladet, October 2016 (http://www.dagbladet.no/tema/supervitaminen-mange-glemmer-a-tenke-pa-derfor-er-d-vitamin-sa-viktig-for-deg/63973271)

Nerhus, Mari: Vitamin D hos pasienter med psykoselidelser - betydningen av etnisk bakgrunn, article in Best Practice, April 2016 (https://bestprac.no/vitamin-d-hos-pasienter-med-psykose-lidelser-betydningen-av-etnisk-bakgrunn/)

Røssberg, Jan Ivar: Er medisinfrie soner et nødvendig skille eller konstruert polarisering?, article in Aftenposten, July 2016 (http://www.aftenposten.no/meninger/debatt/Er-medisin-frie-soner-et-nodvendig-skille-eller-konstruert-polarise-ring--Jan-Ivar-Rossberg-585834b.html)

Illustration photo: Oslo University Hospital

Societal Impact and Innovation

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.

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.

Research Training and Recruitment

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.

User Representatives

NORMENT has established a User Council which provides input to research strategy, gives advice on practical research protocols and helps with recruitment of participants and assists in dissemination activities. We have also employed a part time User Representative to assist us in our work and who acts as a link to the users' organizations. The User Representative participates in daily activities of the Centre, and is involved in meetings, helps with dissemination activities, and provides input to practical operation procedures. Further, the representative helps with education of non-clinical researchers at the Centre, and otherwise helps the Centre in daily administrative matters. In our experience, after working with the mandate of the User Council and goal of the User Group position we are convinced that user representation in the Centre is improving the quality of the research.

Society and Health Innovations

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 dyfunction and biostatistical tools.

NORMENT Staff

Core Researchers

- Agartz, Ingrid
- Andreassen, Ole A.
- Djurovic, Srdjan
- Hugdahl, Kenneth
- Le Hellard, Stephanie
- Melle, Ingrid
- Steen, Vidar M.
- Sundet, Kjetil S.

Group Leaders/ Senior Scientists

- Dieset, Ingrid
- Espeseth, Thomas
- Haukvik, Unn Kristin
- Hirnstein, Marco
- Johnsen, Erik
- Jönsson, Erik
- Kompus, Kristiina
- Lagerberg, Trine Vik
- Romm, Kristin Lie
- Røssberg, Jan Ivar
- Ueland, Torill
- Westlye, Lars T.

Visting Scientists

- Dale, Anders
- Devor, Anna
- Larøi, Frank
- Thompson, Wesley K.

Researchers

- Engvig,Andreas
- Hughes, Timothy
- Nærland, Terje
- Pedersen, Geir
- Skrede, Silje
- Stavrum, Anne-Kristin
- Steen, Nils Eiel
- Tesli, Martin
- Valstad, Mathias

Post Docs

- Aas, Monica
- Abdelrazik, Heba
- Alnæs, Dag
- Aminoff, Sofie Ragnhild
- Andresen, Lavinia Athanasiu
- Berg, Akiah Ottesen
- Bettella, Francesco
- Bless, Josef
- Doan, Nhat Trung
- Elvsåshagen, Torbjørn
- Eriksen, Jon Alm
- Ersland, Kari M.
- Falkenberg, Liv
- Frei, Oleksandr
- Gurholt, Tiril Pedersen
- Hartberg, Cecilie B.
- Hassani, Sahar
- Hellvin, Tone
- Hjelmervik, Helene
- Hope, Sigrun
- Impellizzeri, Agata
- Kaufmann, Tobias
- Krull, Florian
- Laloyaux, Julien
- Li, Wen
- Moberget, Torgeir
- Mäki-Marttunen, Tuomo Mikael
- Onyeka, Ifeoma Nkeiruka
- Palomera, Aldo Cordova
- Polushina, Tatiana
- Quintana, Daniel
- Raballo, Andrea
- Rokicki, Jarek
- Shadrin, Alexey
- Simonsen, Carmen
- Smeland, Olav Bjerkehagen
- Szabo, Attila
- Sønderby, Ida Elken
- van der Meer, Dennis
- Vandenberghe, Matthieu
- Vaskinn, Anja
- Wang, Yunpeng
- Witoelar, Aree

PhD Students

- Almenning, Beathe Haatveit
- Anderssen, Jannicke Fjæra
- Banerjee, Niladri
- Bolstad, Ingeborg
- Brandt, Christine Lycke
- Büchmann, Camilla Bakkalia
- Demmo, Christine
- Dunvoll, Guro Granerud
- Dwyer, Gerard Eric
- Dørum, Erlend Solberg
- Egeland, Maj Kristoffersen
- Engen, Magnus Johan
- Gardsjord, Erlend Strand
- Gjerde, Priyanthi Borgen
- Haram, Marit
- Hoseth, Eva Zsuzsanna
- Iversen, Trude Sesilie Jahr
- Jørgensen, Kjetil Nordbø
- Kolskår, Knut
- Kvitland, Levi
- Lange Elisabeth
- Lonning, Vera
- Lyngstad, Siv Hege
- Lystad, June Ullevoldsæter
- Mørch, Ragni
- Mørch-Johnsen, Lynn
- Nerhus, Mari
- Norbom, Linn-Christin
- Reponen, Elina
- Richard, Geneviève
- Sanders, Anne Marthe
- Sinkevicute, Igne
- Skåtun, Kristina
- Srinivasan, Saurabh
- Smelror, Runar
- Svendsen, Ingrid Hartveit
- Tønnesen, Siren
- Ulrichsen, Kristine
- Wedervang-Resell, Kirsten
- Zak, Nathalia
- Østefjells, Tiril

Other Research Personnel

- Bakken, Eivind
- Bidtnes, Vilja
- Grimstad, Kristoffer
- Gundersen, Line
- Huflåtten, Idun Bernadotte
- Huitfeldt, Caroline
- Høegh, Margrethe Collier
- Kvam, Mari
- Lanneskog, Anna Maria
- Lund, Martina Jonette
- Melbø-Jørgensen, Christian
- Moldestad, Tale
- Nævdal, Marianne
- Rustan, Øyvind
- Stabell, Lene
- Sørensen, Håkon
- Wedervang-Resell, Kirsten

Technicians

- Akkouh, Ibrahim
- Beresniewics, Justyna
- Bjella, Thomas Doug
- Brattbakk, Hans-Richard
- Bringsli, Jorunn Skeie
- Buer, Liliana
- Craven, Alex
- Giddaluru, Sudheer
- Hansson, Lars Johan
- Holdhus, Rita
- Kazimierczak, Katarzyna
- Khalili, Seyran
- Kovalchuk, Galyna
- Nerland Stener
- Nævdal, Marianne
- Stokowy, Tomasz

User Representatives

- Johansen, Karoline
- Kristensen, Elisabeth

Administrative Personnel

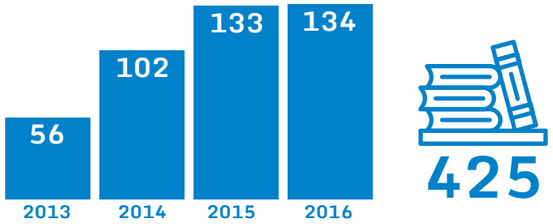
Eftevåg, Åshild Maria
Administrative Manager/ Coordinator

Asghar, Asma
Executive Officer, NORMENT Part Oslo University Hospital

Frøland, Kate Eli
Senior Executive Officer, NORMENT Part University of Bergen

Storli, Ragnhild Bettina
Higher Executive Officer, NORMENT Part Oslo University Hospital and University of Oslo

Publications



During the first 3.5 years, the Centre has published a total of 425 scientific papers. Here we present a selection of the papers with most impact during the first period of the Centre. In addition, we list the 134 journal publications in 2016, of which 18 were published in scientific journals with an impact factor of above 10, including Nature, Nature Genetics, Nature Neuroscience, JAMA Psychiatry, Molecular Psychiatry, and Biological Psychiatry.

2013

Andreassen OA, Djurovic S, Thompson WK, Schork AJ, Kendler KS, et al. Improved detection of common variants associated with schizophrenia by leveraging pleiotropy with cardiovascular-disease risk factors. Am J Hum Genet. 2013;92(2):197-209.

Andreassen OA, Thompson WK, Schork AJ, Ripke S, Mattingsdal M, et al. Improved detection of common variants associated with schizophrenia and bipolar disorder using pleiotropy-informed conditional false discovery rate. PLoS Genet. 2013;9(4):e1003455.

Schork AJ, Thompson WK, Pham P, Torkamani A, Roddey JC, et al. All SNPs are not created equal: genome-wide association studies reveal a consistent pattern of enrichment among functionally annotated SNPs. PLoS Genet. 2013;9(4):e1003449.

2014

Aas M, Etain B, Bellivier F, Henry C, Lagerberg T, et al. Additive effects of childhood abuse and cannabis abuse on clinical expressions of bipolar disorders. Psychol Med. 2014;44(8):1653-62.

Brandt CL, Eichele T, Melle I, Sundet K, Server A, et al. Working memory networks and activation patterns in schizophrenia and bipolar disorder: comparison with healthy controls. Br J Psychiatry. 2014;204:290-8.

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NORMENT
Norwegian Centre for
Mental Disorders Research

Visiting adress in Oslo:
Oslo University Hospital HF
Psychosis Research Unit/TOP
Ullevål Hosipital, building 49
Kirkeveien 166
N-0450 Oslo

Visiting adress in Bergen:
University of Bergen
Haukland University Hospital Campus
Lab. Building (6th floor) and
Basic Biology Building (BBB; 9th floor)
Jonas Liesvei 87
NO-5021 Bergen

Postal adress:
Oslo University Hospital HF
Division of Mental Health and Addiction
Psychosis Research Unit/TOP
Ullevål Hospital, building 49
P.O. Box 4956 Nydalen
N-0424 Oslo

UiO : NORMENT – Norwegian Centre for Mental Disorders Research
University of Oslo

Phone: +47 23 02 73 50

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