Abstract book

for

Psychiatry Research Day 2024

12 November at 12-16

Auditorium G206 145, Aarhus University Hospital,
Entrance G, Palle Juul-Jensens Boulevard 99, 8200 Aarhus

Program

12.00-12.40	**Poster session — and sandwiches**
12:40-12:45	**Welcome to Psychiatry Research Day** Opening speech by Jakob Paludan, Chief Medical Officer
12:45-13:15	**Presentations – Part 1:** Moderator Charlotte Rask
12:45-13:15	**"Epilepsy and psychiatric co-morbidity"** **Keynote:** Jakob Christensen, Clinical Professor, Department of Clinical Medicine - The Department of Neurology
13:15-13:30	**"Aberrant brain connectivity in preadolescent children at familial high-risk for schizophrenia or bipolar disorder"** Martin Dietz, Assistant Professor, CFIN - Department of Clinical Medicine, Aarhus University
13:30-13:45	**"Infancy predictors of Functional Somatic Symptoms in pre- and late adolescence - a longitudinal cohort study"** Lina Münker, PhD student, psychologist, Department of Child and Adolescent Psychiatry
13:45-14:25	**Poster session –** and break with coffee/tea and cake
14:25-15:40	**Presentations - Part 2:** Morten Deleuran Terkildsen
14:25-14:55	**"Treatment of Substance Use Disorder (SUD) among youth age 15 and 25: Specific attention to youth with dual diagnosis"** **Keynote:** Mads Uffe Pedersen, Professor, Department of Psychology and Behavioural Sciences, Centre for Alcohol and Drug Research
14:55-15:10	**"Receiving information on machine learning-based clinical decision support systems in psychiatric services increases staff trust in these systems: A randomized survey experiment"** Erik Perfalk, PhD student, medical doctor, Department of Affective Disorders
15:10-15:25	**"The efficacy of ball blankets on insomnia in depression in outpatient clinics: a randomised crossover multicentre trial"** Sanne Toft Kristiansen, Clinical Nurse Specialist, MCN, PhD, Psykiatriens Hus, Aarhus University Hospital
15:25-15:40	**"Well-being in schoolchildren with neurodevelopmental disorders: A nationwide study"** Josefine Klakk, PhD student, Cand.Scient.San.Publ, The National Centre for Register-based Research, NCRR, Aarhus BSS, Aarhus University
15:40-16:00	**Closing session and award of prize for best presentation and best poster** Moderator Per Hove Thomsen

Abstracts for oral presentations

Abstract #01

Psychiatry Research Day 2024

Aberrant brain connectivity in preadolescent children at familial high-risk for schizophrenia or bipolar disorder

Martin Dietz, Assistant professor, CFIN - Department of Clinical Medicine, Aarhus University

Background
Schizophrenia and bipolar disorder are characterized by impairments of social cognition and recent research has identified alterations of the social brain. However, it is unknown whether familial high-risk (FHR) of these disorders is associated with neurobiological alterations already present in childhood.

Objectives
To answer this question, we used functional magnetic resonance imaging (fMRI) and analysis of brain connectivity to identify differences within the mentalizing network of preadolescent children at FHR-SZ or FHR-BP compared with population-based controls (PBC). We hypothesized that children at FHR-SZ or FHR-BP would exhibit deviant brain activation and aberrant brain connectivity in the mentalizing network compared with PBC.

Methods
As part of The Danish High Risk and Resilience Study - VIA 11, we examined children at familial high-risk of schizophrenia (FHR-SZ, n = 121, 50% females) or bipolar disorder (FHR-BP, n = 75, 47% females) and population-based controls (PBC, n = 128, 48% females). Using functional magnetic resonance imaging and dynamic causal modeling, we investigated brain activation and effective connectivity during the social cognition paradigm from the Human Connectome Project.

Results
We found similar activation of the mentalizing network across groups, including visual area V5, dorsomedial prefrontal cortex (dmPFC), and posterior superior temporal sulcus (pSTS). Nonetheless, both familial high-risk groups showed aberrant brain connectivity in the form of increased feedforward connectivity from left V5 to pSTS compared with PBC. Children at FHR-SZ had reduced intrinsic connectivity in bilateral V5 relative to PBC, whereas children at FHR-BP showed increased reciprocal connectivity between left dmPFC and pSTS, increased intrinsic connectivity in right pSTS, and reduced feedforward connectivity from right pSTS to dmPFC compared with PBC.

Conclusion
Our results provide first-time evidence of aberrant brain connectivity in the mentalizing network of children at FHR-SZ or FHR-BP. Longitudinal research is warranted to clarify whether aberrant brain connectivity during mentalizing constitutes an endophenotype associated with the development of a mental disorder later in life.

Abstract #02

Psychiatry Research Day 2024

'Infancy predictors of Functional Somatic Symptoms in pre- and late adolescence - a longitudinal cohort study'

Lina Münker, PhD student, Department of Child and Adolescent Psychiatry

Purpose
Physiological regulatory problems in infancy (i.e., problems with sleeping, feeding, and tactile reactivity) have been associated with impairing Functional Somatic Symptoms (FSS) at ages 5-7. We aimed to extend this finding by examining not only the association of physiological regulatory problems, but also other infancy factors (i.e. emotion dysregulation and contact problems) with FSS in pre- and late adolescence.

Methods
Standardized behavioral assessments and self-report questionnaire data from assessment waves at 0-1, 11-12 and 16-17 years of the population-based Copenhagen Child Cohort (CCC2000) were linked with Danish register data on maternal postpartum psychiatric illness and family adversity as covariates. Multiple linear regression analyses were performed to examine the association between infancy factors and FSS in pre- and late adolescence.

Results
Only infancy physiological regulatory problems significantly predicted preadolescent FSS (b = 0.38, 95% CI [0.14, 0.62]) also when accounting for maternal postpartum psychiatric illness and family adversity. The association was attenuated for late adolescent FSS.

Conclusion
Infancy physiological regulatory problems may represent early signs of a dysregulated stress system and were found to significantly predict FSS in pre- but not late adolescence. Implications for early FSS prevention could include testing interventions promoting infants' regulation of sleep, feeding and tactile reactivity.

Keywords: Functional Somatic Symptoms; Risk factors; Adolescent; Infancy physiological regulatory problems; Infancy emotion dysregulation; Infancy contact problems; Maternal postpartum psychiatric illness; Family adversity.

Abstract #03

Psychiatry Research Day 2024

Receiving information on machine learning-based clinical decision support systems in psychiatric services increases staff trust in these systems: A randomized survey experiment

Erik Perfalk, PhD student, Medical doctor, Department of Affective Disorders

Background
Clinical decision support systems based on machine learning (ML) models are emerging within psychiatry. To ensure their successful implementation, healthcare staff needs to trust these systems. Here, we investigated if providing staff with basic information about ML-based clinical decision support systems enhances their trust in them.

Methods
We conducted a randomised survey experiment among staff in the Psychiatric Services of the Central Denmark Region. The participants were allocated to one of three arms, receiving different types of information: An intervention arm (receiving information on clinical decision-making supported by an ML model); an active control arm (receiving information on standard clinical decision process without ML support); and a blank control arm (no information). Subsequently, participants responded to various questions regarding their trust/distrust in ML-based clinical decision support systems. The effect of the intervention was assessed by pairwise comparisons between all randomization arms on sum scores of trust and distrust.

Findings
Among 2,838 invitees, 780 (response rate: 27%) completed the survey experiment. The intervention enhanced trust and diminished distrust in ML-based clinical decision support systems compared with the active control arm (Trust: mean difference= 5% [95% confidence interval (CI): 2%; 9%], p-value < 0.001; Distrust: mean difference=-4% [-7%; -1%], p-value = 0.042)) and the blank control arm (Trust: mean difference= 5% [2%; 11%], p-value = 0.003; Distrust: mean difference= -3% [-6%; -1%], p-value = 0.021).

Interpretation
Providing information on ML-based clinical decision support systems in hospital psychiatry may increase healthcare staff trust in such systems.

Abstract #04

Psychiatry Research Day 2024

The efficacy of ball blankets on insomnia in depression in outpatient clinics: a randomised crossover multicentre trial

Sanne Toft Kristiansen, Clinical Nurse Specialist, MCN, PhD, Psykiatriens Hus, Aarhus University Hospital

Background
Many patients with depression experience insomnia that profoundly affect
their health and well-being. Pharmacological treatments for insomnia may have side effects an entail a risk of drug addiction. For some, non-pharmacological treatments for insomnia may therefore be preferable.

Objective
In this randomised crossover trial, we investigated the efficacy of the Protac Ball Blanket® on insomnia among patients with depression.

Methods
We included 45 patients diagnosed with unipolar depression, who also reported subjective insomnia and poor sleep quality (Pittsburgh Sleep Quality Index Score > 5). Each patient slept 2 weeks with a Protac Ball Blanket® and 2 weeks with a control duvet. Randomisation defined the order of the 2-week sleep periods. Patients acted as their own controls in this design. The primary outcome measured was changes in total night-time sleep. Secondary outcomes included sleep-onset latency, number of awakenings, wake after sleep onset, daily use of pro necessitate sedatives and hypnotics, subjective sleep quality (Pittsburgh Sleep Quality Index), insomnia severity (Insomnia Severity Index), symptoms of depression (Hamilton Depression Rating Scale, Major Depression Inventory), symptoms of anxiety (Beck Anxiety Index), and patient-reported outcomes concerning interpersonal sensitivity, neurasthenia, anxiety and depression (Self-Reported Symptom State Scale).
Paired two-sided t-tests were used to compare the means of the differences in outcomes.

Results
The Protac Ball Blanket® increased total night-time sleep by 12.9 min (95% confidence interval: 1.21-24.63, p = 0.031). Among the secondary outcomes, it reduced the Hamilton Depression Rating Scale by 2.78 (95% confidence interval: -5.44; -0.11, p = 0.042) and Insomnia Severity Index by 2.98 (95% confidence interval: -5.45; -0.50, p = 0.020). No significant changes were observed in sleep-onset latency, number of awakenings, wake after sleep onset, Pittsburgh Sleep Quality Index, Major Depression Inventory, Beck Anxiety Index, Self-Reported Symptom State Scale, and medication use.

Conclusion
These results suggest that the Protac Ball Blanket® may benefit some patients as an adjunct non-pharmacological treatment to improve sleep in depression.

Abstract #05

Psychiatry Research Day 2024

"Well-being in schoolchildren with neurodevelopmental disorders: insights from a nationwide study"

Josefine Klakk, PhD student, MSc PH, The National Centre for Register-based Research, NCRR, Aarhus University

Background
Neurodevelopmental disorders (NDDs) are leading causes of disability among school-aged children, often affecting behavior, memory, or learning abilities. One in ten are diagnosed with a NDD by age 16. Studies comparing well-being across the spectrum of NDDs are limited.

Objective
To investigate the well-being in children with NDDs in Danish public primary and lower-secondary schools using the Danish National Well-being Surveys from 2015 to 2022.

Methods
We conducted a register-based cohort study with matched populations to examine children's well-being from grades 0-9. We included all children born in Denmark between 2000 and 2014. From this population, we identified all children with specific NDDs (e.g. autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD)) and randomly sampled 10 reference children without the specific NDD per child, matched on age and sex, using exposure density sampling. Only children who had filled in ≤1 well-being survey were included. We used logistic regression models to estimate odds ratios (ORs) for reporting poor well-being, adjusting for relevant confounders.

Selected results
From a population of 918,320 children, 771,340 (85%) responded to ≤1survey, including 16,520 (2.1%) children with ASD matched to 165,200 reference children, and 22,180 (2.9%) children with ADHD matched to 221,800 reference children. A total of 141,580 children (24% girls) with ASD and their unaffected peers completed 570,560 well-being surveys in grades 4-9 from 2015 and 2022, alongside 187,350 children (27% girls) with ADHD and their unaffected peers completing 804,370 surveys. The results indicated that children with ASD and ADHD had increased odds of reporting poor overall well-being (ASD: adjusted OR (aOR) 2.32 [95%CI 2.26-2.39], ADHD: aOR 2.25 [95%CI 2.20-2.30]) compared to matched reference children without ASD and ADHD. Children with ASD and ADHD also had increased odds of specific measures for well-being compared to children without ASD and ADHD, including poor social (ASD: aOR 2.49 [95%CI 2.42-2.57], ADHD: aOR 2.24 [95%CI 2.18-2.62]) and poor academic (ASD: aOR 2.12 [95%CI 2.07-2.18], ADHD: aOR 2.22 [95%CI 2.18-2.27]) well-being.
Conclusion: Children with ASD and ADHD experience significantly poorer overall and specific well-being compared to peers, highlighting the need for targeted support in educational settings.

Funding
The Independent Research Fund Denmark (3166-00134B)

Abstracts for Posters

Abstract #06

Psychiatry Research Day 2024

A nationwide register-based study of healthcare usage and psychiatric comorbidity in borderline personality disorder in Denmark

Alisha Hall, PhD student, Department of Clinical Medicine

The author has declined publication of this abstract

Abstract #07

Psychiatry Research Day 2024

Machine learning-based prediction of acute somatic illness in individuals with mental illness

Andreas Aalkjær Danielsen, MD, Part-time Lecturer, Department of Affective Disorders, Aarhus University Hospital – Psychiatry

Background and aim:
Mental illness requiring treatment with psychiatric hospital services is associated with reduced life expectancy. A significant proportion of this reduction is attributed to somatic illness. Studies have shown that diagnosis of somatic illness in individuals with mental illness is often delayed when compared to the general population. Accordingly, treatment of somatic illness often begins at more advanced stages, worsening the prognosis. Therefore, it is crucial to diagnose somatic illness in individuals with mental illness more promptly than is currently the case. The aim of this study is to investigate if severe acute somatic illness in patients with mental illness can be predicted using machine learning trained on electronic health record data.

Method
The study is based on data from the PSYCOP cohort, which includes all individuals with at least one contact with the Psychiatric Services of the Central Denmark Region in the period from January 1, 2011 to November 22, 2021. Data from the cohort includes every contact with public hospitals (both psychiatric and somatic) across the Central Denmark Region and contains detailed information gathered from practice, such as laboratory results, medication, diagnoses, and clinical notes. An acute somatic hospital admission will serve as the operational definition of severe acute somatic illness. Two machine learning models, elastic net logistic regression and XGBoost, will be trained on 85% of the cohort to predict an acute somatic admission within the next two months. Predictions will be issued for every visit to an outpatient psychiatric clinic in Central Denmark Region where the patient has not been admitted to a somatic department in the past two years. The best performing model will be validated on the remaining 15% of the patients.

Preliminary results
Will be presented at the meeting.

Conclusion
If a machine learning model can accurately predict severe acute somatic illness in individuals with mental illness, a decision support system based on this model could assist clinicians in identifying high-risk patients at an earlier stage. This may lead to more timely interventions and potentially increase the lifespan for individuals with mental illness.

Abstract #08

Psychiatry Research Day 2024

Course of neurocognitive development in children at familial high risk of schizophrenia or bipolar disorder: A prospective cohort study from 7 to 11 to 15 years of age

Andreas Færgemand Laursen, PhD Student, psychologist, Psychosis Research Unit, AUH; Department of clinical medicine, AU

Background
Schizophrenia (SZ) and bipolar disorder (BP) are severe mental disorders with shared and distinct clinical, cognitive, and genetic risk factors. These risk markers are also present in the offspring, who have an increased risk of developing severe mental illness.
SZ is a neurodevelopmental disorder and neurocognitive impairments are presenting years before the manifestation of overt clinical symptoms. Findings regarding premorbid neurocognitive impairments in BP are less conclusive. Investigating the course of neurocognitive development before illness offers insights into both shared and illness-specific vulnerability markers.
The neurocognitive results from previous assessments of the presented cohort showed stable neurocognitive deficits in children at familial high risk (FHR) of SZ and stable neurocognitive functioning in children at FHR-BP that were comparable to population-based controls (PBC).

Objective
The aim is to study the neurocognitive development in adolescents at FHR-SZ and FHR-BP compared with PBC from age 7 to 11 to 15.

Methods
The Danish High Risk and Resilience Study (VIA) is a population-based cohort of 522 children (202 FHR-SZ, 120 FHR-BP, and 200 PBC). The VIA 15 study is the third wave of assessments at 15 years of age with a retention rate of 81,8% of the original cohort. Neurocognitive functioning was assessed with a comprehensive neurocognitive test battery of validated tasks covering a wide range of cognitive functions known to be impaired in SZ and BP. These include tests of intelligence, processing speed, attention, verbal and visuospatial memory, verbal fluency, working memory, and executive functions.

Results
Data analysis is currently ongoing. Available preliminary results will be presented.

Perspectives
Examining the development of neurocognitive deficits in children at FHR-SZ and FHR-BP will elucidate shared and distinct endophenotypes and help differentiate the pathophysiology of these severe mental illnesses. The long-term perspective is to use the knowledge on the developmental trajectories to guide intervention studies and inform preventive interventions to improve functioning, quality of life, and potentially even prevent transition to mental illness.

Abstract #09

Psychiatry Research Day 2024

A longitudinal study comparing both biological parents and offspring cognition in families with parental schizophrenia or bipolar disorder

Anette Faurskov Bundgaard, PhD student, Psychosis Research Unit, Aarhus University Hospital, Psychiatry

Background
Neurocognitive deficits are core features of schizophrenia (SZ) and bipolar disorder (BP), and research has found that cognitive impairments are early vulnerability markers for these disorders. Children at familial high risk (FHR) for SZ show widespread cognitive impairments already in infancy, and children at FHR for BP also displays cognitive impairments, although results being more divergent. Studies comparing patients and their first-degree relatives show that first-degree relatives generally displays cognitive impairments that lie in between the respective patient group and controls. In these studies, first-degree relatives are treated with no regard to type of kinship even though studies suggest that especially offspring are more disadvantaged compared to other relatives. To our knowledge, no study has investigated the association between cognition in parents and offspring simultaneously with the same methodology in a longitudinal manner in families with parental SZ and BP.
Therefore, this study aims to investigate the association between parent and offspring intelligence, processing speed and verbal working memory in a developmental perspective from the offspring was 7 to 15 years old, and to assess whether this association is influenced by parental SZ or BP.

Methods
The study is part of the Danish High Risk and Resilience Study – VIA 15, a longitudinal nationwide cohort of families with either 0, 1 or 2 parents diagnosed with SZ or BP. At first assessment (VIA 7), 522 Danish children age 7 and their parents participated. At first follow-up (VIA 11) 465 families participated again and at second follow-up (VIA 15) 427. In VIA 7 both biological parents and their offspring were assessed with the same comprehensive neuropsychological test battery. This study we will focus on intelligence measured with Reynolds Intellectual Screening Test and processing speed and verbal working memory both measured with Wechsler Adult Intelligence Scale – 4th edition and Wechsler Intelligence Scale for Children – 4th edition.

Results
Data analysis is ongoing. Preliminary results will be presented at the Psychiatry Research Day.

Conclusion
Assessing the association between parent and offspring cognition in a developmental perspective can add to our understanding of the mechanisms underlying SZ and BP, which can help develop more effective interventions.

Abstract #10

Psychiatry Research Day 2024

Pharmacoepigenomics for mental disorders

Anna Starnawska, Postdoc, Department of Biomedicine, Aarhus University, Denmark

Background
Genomic and epidemiological research of mental disorders (MDx) has successfully identified genetic and environmental factors that modulate their risk, but until now these findings have had limited applicability in development of improved or novel treatments for these conditions. A limiting factor is lack of knowledge on the impact of pharmacological compounds on human brain. Firstly, it needs to be acknowledged that an effect of exposure to a compound, including administered medication, extends beyond the commonly studied drug and drug-target interactions. Secondly, studies on the impact of compounds on gene regulation are often conducted in peripheral tissues, which are less relevant to MDx, or in postmortem brain samples, which are confounded by lifelong disease exposure, environmental factors, and medications for comorbid conditions.

Aim
This project aimed: i) to fill the knowledge gap on what is the impact of pharmacological compounds on gene regulation in human neurons and ii) to highlight how this knowledge can be harvested to study MDx, their possible new treatments, treatment outcomes, and possible side effects.

Methods
Human glutamatergic neurons were exposed in quintuplicates to two different doses of compounds (CPx) of high interest for MDx (valproic acid, fluoxetine, ketamine, cannabidiol) or cortisol. Genome-wide DNA methylation levels from all of the exposed and unexposed neurons were quantified with the use of the Infinium MethylationEPIC BeadChip. We subsequently performed epigenome-wide association studies (EWASes) to determine where in the genome each CPx changes DNA methylation in human neurons. We further investigated if genes that undergo epigenetic changes due to CPx are associated with MDx and their intermediate phenotypes.

Results
We have successfully established a protocol for a pharmacoepigenomic study of human glutamatergic neurons and provide recommendations for a successful study design that: i) minimizes confounding technical effects and ii) allows for comparison of epigenetic changes between multiple CPx in one experimental setup. High quality whole-genome DNAm data is now available for 114 samples and all CPx and cortisol treatment groups are well represented in the data.

Conclusions
To provide better and novel treatments for mental illness it is crucial to first understand how compounds used or considered for treatment of MDx impact gene regulation of a tissue relevant for these conditions. We believe that this novel neuronal pharmacoepigenomic resource can be combined with other omics approaches to study treatment approaches for MDx.

Abstract #11

Psychiatry Research Day 2024

Health Anxiety in the Danish Population: Is health anxiety associated with reduced heart rate variability?

Anneline Rauch, Medical Student, The Research Clinic for Functional Disorders and Psychosomatics

Background and objectives
Health anxiety (HA) is characterized by preoccupation with and an intensive fear of having a serious illness, despite showing no objective medical signs of illness. Heart rate variability (HRV) is a reflection of balance in the autonomous nervous system, and is found to be decreased in persons with different forms of anxiety (Cheng 2022). Having a reduced HRV is associated with an increased risk of cardiovascular disease (Hillebrand 2013). We aim to explore possible associations between functions of the autonomic nervous system (measured as HRV) and HA. We aimed to compare persons with high illness worry, understood as HA, to individuals with low illness worry, used as controls, and hypothesize that individuals with HA have overall reduced HRV compared to those without HA.

Method
In this cross sectional study, data from the DanFunD study with 6857 participants from the general adult population in Denmark will be used. Participants had been randomly selected from the nationwide Danish registries and invited to participate (Dantoft 2017).
HA cases will be identified using Whiteley-6-R, and relevant variables of HRV will be analyzed to measure the function of the autonomic nervous system. Linear regression will be conducted to explore possible associations between functions of the nervous system (HRV) and HA, adjusting for relevant variables identified through a Directed Acyclic Graph.
The DanFunD study has been approved by the ethical Committee of Copenhagen County and the Danish Data Protections Agency. All participants signed a written informed consent form.

Results
Results differed between males and females. Analyses showed that males with HA score lower on all HRV metrics, with some results being statistically significant. In females the results were more varied with some HRV indices suggesting a difference between the groups, and others showing no difference.

Conclusion
In this large population study aiming to investigate the association between HA and balance of the ANS, quantified as HRV, we found a pattern of ANS imbalance in males but not one in females. This finding somewhat supports our hypothesis and calls for further investigation. Knowledge of HRV in HA patients will allow for a more nuanced understanding of the physiological mechanisms of HA, which may eventually contribute to better treatment.

Abstract #12

Psychiatry Research Day 2024

Prevention of Eating Disorders among Young Women with Psychiatric Illness: Testing the Efficacy of the Body Project

Caroline Bruun Abild, PhD student, Steno/ICM AU

Objective
Eating disorders are associated with substantial costs, both personal and economic. Additionally, current treatments have limited efficacy. This calls for effective evidence-based prevention programs. The Body Project is a dissonance-based intervention that has effectively reduced future onset of eating disorders in numerous countries among young women. Previous studies have primarily included young women with body dissatisfaction. To the best of our knowledge, no studies have specifically tested the effect of the Body Project in women with psychiatric illnesses (e.g., mood disorders, anxiety disorders, and personality disorders). As these women have more than four-fold risk of developing a subsequent eating disorder, they represent an ultra-high-risk group for whom the Body Project would be relevant.

Method
We are planning a randomized controlled trial to test the efficacy of an online peer-led version of the Body Project in women with psychiatric illnesses. The Body Project consists of four one-hour group sessions and women with psychiatric illnesses other than eating disorders will be invited to participate. The effect of the Body Project will be compared with the effect of expressive writing, and a two-year follow-up period will be applied to assess the risk of subsequent eating disorders in the two intervention groups.

Results
The poster will include a presentation of the project, including the design and methods. Discussion: With low cost and promising results from prior studies this could have an impact on prevention of eating disorders in a broader sense including specific vulnerable groups in the future.

Abstract #13

Psychiatry Research Day 2023

Investigations of synaptic plasticity after chronic mild stress

Celine Knudsen, Research Assistant, Translational Neuropsychiatry Unit, Aarhus University

Background
Major depressive disorder (MDD) is a debilitating disease characterized by depressed mood and anhedonia, affecting millions of people worldwide. Despite significant research, the molecular mechanisms underlying MDD remain elusive. Historically, the monoamine hypothesis has dominated the field, but recent studies indicate that synaptic plasticity is involved in the pathophysiology and the antidepressant (AD) response. Especially synaptic density and glutamatergic neurotransmission have been in the spotlight since it was shown that subanesthetic doses of the anesthetic ketamine exhibits rapid-acting AD effects. Another drug of interest is agomelatine (AGO), which antagonizes serotonin receptors and agonizes melatonin receptors.

Objective
This study aims to explore the role of synaptic plasticity in MDD using a chronic mild stress (CMS) model in rats, focusing on the metabotropic glutamate receptor subtype 5 (mGluR5) and the synaptic vesicle glycoprotein 2A (SV2A).

Method
Key brain regions implicated in MDD, including the medial prefrontal cortex (mPFC) and hippocampus (HP), were investigated after AGO treatment. The CMS model ran for 10 weeks, with AGO treatment administered during the final 5 weeks. Animals were divided into four groups based on their sucrose consumption test results: Control, anhedonic-like, AGO responders and AGO non-responders. mGluR5 and SV2A levels were measured using autoradiography, and Western blotting was conducted to analyze proteins involved in synaptic plasticity.

Results
Results showed elevated mGluR5 levels in the prelimbic cortex (PreL) following CMS, while AGO treatment reduced mGluR5 levels in both the PreL and infralimbic cortex (IL) in responders. This was corroborated by a decrease in mGluR5 protein levels in the mPFC after treatment. Additionally, indications of reactive astrogliosis were observed in depressive-like rats based on elevated GFAP protein levels. The mGluR5 level in the HP was not affected by CMS or AGO, and neither were the synaptic density in the mPFC or the HP.

Conclusions
In conclusion, this study demonstrates a region-specific increase in mGluR5 levels in the mPFC associated with depressive-like behavior. AGO responders showed normalized levels of mGluR5 in the mPFC, suggesting the mGluR5 modulation may be a key factor in the AD response.

Abstract #14

Psychiatry Research Day 2023

Psychotic Risk in Pediatric Obsessive-Compulsive Disorder: Correlations with Clinical Traits and Treatment Results

Davíð R. M. A. Højgaard, Psychologist, PhD, Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry, Denmark

Background
Children and adolescents with obsessive-compulsive disorder (OCD) face a heightened risk of developing psychotic disorders, however, the characteristics of psychotic vulnerability in children and adolescents with OCD remain largely unexplored.

Method
This study used the 15 item Thought Problems subscale from the Child Behavior Checklist (CBCL) to investigate the prevalence of psychotic vulnerability in children and adolescents with OCD from Scandinavia (n = 215) and the United States (n = 125). Participants with and without psychotic vulnerability were compared on various clinical characteristics, including psychosocial functioning, anxiety and depression, both before and after cognitive-behavioral therapy (CBT). We also explored whether psychotic vulnerability could predict CBT outcomes, measures with The Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS).

Results
Psychotic vulnerability was observed in 41.6% of the Scandinavian sample and 34.4% of the North American sample. In both groups, children and adolescents with psychotic vulnerability exhibited more depressive symptoms and lower psychosocial functioning at baseline. Post-CBT, those with psychotic vulnerability in the Scandinavian group continued to show poorer psychosocial functioning and had more symptoms from the symmetry/hoarding dimension, whereas in the North American sample, it was associated with the contamination-cleaning dimension. Psychotic vulnerability did not influence CBT outcomes in either group.

Conclusions
Consistent with prior research, our findings indicate that a comprehensive, second-tier evaluation of psychosis risk is warranted in numerous cases of youth with obsessive-compulsive disorder (OCD), especially in children and adolescents exhibiting impaired global functioning. Additionally, our results suggest that immediate CBT outcome is not affected by psychotic vulnerability in pediatric OCD.

Abstract #15

Psychiatry Research Day 2024

Supporting Personal Recovery: Testing a Narrative Identity Intervention

Dinne S. Christensen, Postdoc, Department of Psychology and Behavioural Sciences, Aarhus University

Background
Severe mental illness often leads to profound negative consequences, including unemployment, social isolation, and stigma. These consequences are not sufficiently addressed by treatments focusing on symptom remission and functional level, but require explicit attention because they stand in the way of personal recovery. Personal recovery refers to living a satisfying and meaningful life within the limitations caused by mental illness and is increasingly emphasized in mental health care and by service-users. A key aspect of personal recovery is (re)constructing a positive identity through narrating one's life with meaning, purpose and value. However, evidence-based narrative identity interventions targeting personal recovery are lacking.

Objectives
This study aims to examine the feasibility and effectiveness of the recently developed Guide to Narrative Repair (GNaR), a narrative identity intervention designed to promote personal recovery in individuals with severe mental illness.

Methods
We will employ a multiple single-case intervention design with an A-B-A structure. Twenty stable outpatient participants with severe mental illness will be recruited in collaboration with mental health service providers. The intervention consists of 11 individual sessions focusing on life story (re)construction. It contains sessions to aid participants in addressing negative narrative identity stemming from mental illness and functional impairments and sessions to scaffold memory and interpretations to support the growth of positive narrative identity. Final sessions focus on the construction of a realistic and hopeful future story. Feasibility will be assessed through participant retention and satisfaction. Intervention effects will be evaluated by administering standardized measures of personal recovery before, during, and after the intervention.

Hypotheses
We hypothesize that participants will show improvements in personal recovery during and after the intervention, with sustained effects at a 3-month follow-up.

Conclusion
This study will provide critical preliminary data on the feasibility and efficacy of a narrative identity intervention for personal recovery in severe mental illness. The findings will lay the groundwork for larger-scale studies and potential implementation in clinical practice.

Abstract #16

Psychiatry Research Day 2024

Rationale for a positivity-focus in pain-alleviating interventions: Insights from a systematic review and meta-analysis

Ditte Hjortnæs, Stud.cand.psyk. + student assistant, Department of Psychology and Behavioural Sciences, Aarhus University

Background
Pain conditions and psychiatric disorders are often comorbid. Emotions have been proposed to modulate pain, and psychological interventions often aim to reduce pain by decreasing negative emotions and distress. Although numerous studies have investigated the effects of emotions on pain, a systematic, quantitative synthesis of this literature has been lacking. This systematic review and meta-analysis presents the first quantitative synthesis of experimental studies testing the effects of induced emotions on induced pain.

Methods
The databases of PsycInfo and PubMed were searched up until April 10, 2023, for studies with non-clinical samples, testing the effects of different emotion induction conditions and control conditions on between-group or within-group differences in self-reported pain. The primary studies were assessed for risk of bias, and the effects were pooled with a random effects model. The traditional frequentist analysis was supplemented with a Bayesian meta-analysis to evaluate the strength of evidence.

Results
78 relevant records of 71 independent studies were identified. Pooled results showed a statistically significant pain-attenuating effect of positive emotion induction compared to control conditions (between-group: Hedges g = −0.48, 95% CI: −0.72; −0.25, K = 9; within-group: g = −0.24, 95% CI: −0.32; −0.15, K = 40), while within-group, but not between-group analyses, showed a statistically significant pain-exacerbating effect of negative emotion induction (between-group: g = −0.29, 95% CI: −0.66; 0.07, K = 10; within-group: g = 0.14, 95% CI: 0.06; 0.23, K = 39). Supplementary Bayesian analyses supported the effect of positive emotion induction, but not the effect of negative emotion induction.

Conclusion
Taken together, the results indicate a pain-attenuating effect of positive emotion induction, while the results for negative emotion induction are less clear. These findings suggest that pain-alleviating interventions may benefit from promoting positive emotions in addition to reducing negative emotions and distress. If the results generalise to clinical populations, examining how to implement such focus in interventions might prove a promising research area with the prospect of enhancing treatment effect and improving well-being of psychiatric patients who experience pain.

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Abstract #17

Psychiatry Research Day 2024

Macrobiotics treatment against psychiatric and cognitive side effects of chemotherapy

Edel Kristina Krøger Silseth, Medical student/research year, and **Agnete Kvorning,** TNU, Department of Clinical Medicine, Aarhus University

Background
Chemotherapy causes severe sickness and cognitive disturbances (chemo-brain) in up to 75% of the patients receiving this treatment. These adverse effects are believed to be caused in part by an imbalance of pro- and anti-inflammatory cytokines and it has also been shown that the microbiota modulate the efficacy and toxicity of chemotherapy. Parasitic worms (helminths) can reduce inflammation, restore the gut barrier, and beneficially modulate the host microbiota. Molecules derived from the helminth Trichuris spp (TSP) are a novel source of biologic therapies, which directly modulate the immune response and microbiota. We hypothesize that helminths ESPs can be beneficial and have protective effects against cognitive impairment and psychiatric side effects from chemotherapy.

The objective of this project is two-fold
1) to examine the protective effects of helminth ESPs on chemotherapy-induced sickness and chemo-brain, and 2) to explore which underlying biological mechanisms that are altered by helminth ESPs.

Methods
Male Sprague-Dawley rats will be injected with ESPs prior to chemotherapy-treatment (DOX) during 4 weeks, whereafter they will undergo behavioral testing. During the treatment they will be housed in Noldus Phenotyper Cages, which allows consistent recording of behavior. The experiment consists of 4 experimental groups: 1) sal + PBS, 2) sal + ESPs, 3) DOX + PBS, 4) DOX + ESPs.
The behavioral tests will include Porsolt's swim test and sucrose preference test for depression, elevated plus-maze for anxiety, open field test for thigmotaxis and novel object recognition test for cognitive measurements.
After testing, the animals will be sacrificed and tissue, blood, feces, intestines and spleen will be harvested for further analysis.

Results
The pilot project showed a significant difference between the weight of ESP- treated and saline-treated rats: ESP-treated kept a higher %body weight throughout the whole treatment. This was not because of a difference in food intake.
The ESP-treated showed a tendency of increased locomotion in the open field test, indicating a higher degree of well-being. They showed reduced memory loss by performing significantly better in the y-maze test compared to the control group.

Conclusion
The pilot project provides promising results which could indicate that helminth ESP has protective effects against chemo-brain.

Abstract #18

Psychiatry Research Day 2024

Neuroepigenomics of THC and CBD Exposure during Pregnancy in the Developing Brain

Eleni Sia, PhD student, Translational Neuropsychiatry Unit (TNU)

The landscape around cannabis use is dramatically changing, shifting the clinical interest towards substance abuse during pregnancy and the long term effects on the offspring. Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) can cross the placental barrier and influence the long-term molecular and behavioral outcome of the offspring, in a sex-dependent manner. Only a limited number of studies utilizing animal models have evaluated prenatal Δ9-THC exposure and offspring adverse outcomes, with most of them focusing on males. Most importantly, the vast majority of data available is over 30 years old. Despite notable activity in recent years attempting to address the mechanisms underlying the effects that reach adolescence, the gap in our knowledge is still evident.

Here, we aim to understand the cellular, molecular and phenotypic outcomes of THC and CBD exposure during pregnancy employing a translational science approach using mice and brain organoids models. Tissue collection will be performed in different developmental stages, followed by behavioral assessments of cognition and social behavior at adolescence. We will perform whole-genome analysis from fluorescence-activated cell sorting (FACS) isolated neurons of the prefrontal cortex (PFC) and hippocampus. This will target neural progenitors, as well as excitatory and inhibitory neurons. Epigenetic markers, specifically 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC) at CpG sites, will be identified using long-read Nanopore sequencing.

The results of this study will shed light on the epigenetic pathways implicated in cannabis consumption during pregnancy and the protracted offspring neurodevelopmental outcomes, revealing new targets for the development of personalized therapies.

Abstract #19

Psychiatry Research Day 2024

Do children and adolescents with functional abdominal pain disorders show cognitive biases towards gastrointestinal related material?

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The author has declined publication of this abstract

Abstract #20

Psychiatry Research Day 2024

Temporal stability of an electronic health record-driven prediction model for type 2 diabetes among individuals with mental illness

Frida Hæstrup, PhD Student, Department of Affective Disorders, Aarhus University Hospital – Psychiatry, Aarhus, Denmark

Background
Clinical prediction models are emerging across a wide range of medical fields, including psychiatry, often with the goal of diagnostic classification or predicting patient outcomes (prognosis). Despite their initial promise, there is an increasing body of literature raising concern about real-world applicability of clinical prediction models and calls for validation of generalizability before such models are implemented in clinical practice. In modern medicine, standards of care, baseline risks for medical conditions, data registration procedures, and available treatment options change over time. Such changes affect population characteristics, possibly causing performance drifts in clinical prediction models. As such, investigation of temporal stability – i.e., maintained performance of a prediction model on new patients - is vital prior to potential clinical implementation. Accordingly, we set out to investigate the temporal stability of a previously trained model for prediction of incident type 2 diabetes (T2D) in individuals with mental illness.

Methods
The original model was trained on routine clinical electronic health record data from patients receiving treatment in the Psychiatric Services of the Central Denmark Region in the period from 2013 to 2021. It is a simple hyperparameter-tuned XGBoost model that - based on information on sex, age and mean HbA1c within the past 2 years - predicts whether a patient will meet criteria for T2D in the 2 years following each physical contact to the Psychiatric Services. In the present study, we reused said model, fitted exclusively on patient data from January 1, 2013 to December 31, 2017, and examined how well it generalized (with regard to prediction of T2D) to patient data from 2018, 2019, 2020, 2021, and 2022, respectively.

Results
Based on AUROC estimates from the above-mentioned years (2018=0.84, 2019=0.83, 2020=0.87, 2021=0.80, 2022=0.82), we observed only slight variations in the model's ability to predict T2D (a linear model estimated a performance decrease of 0.006 (SE 0.0005) per year).

Conclusion
The high temporal stability of the T2D prediction model bodes well for clinical implementation, where it may support tailored interventions to reduce the risk of T2D and early detection.

Abstract #21

Psychiatry Research Day 2024

Visual-aided Detection of Undiagnosed Bipolar Patients with Unipolar Depression

Jakob Grøhn Damgaard, Msc, Research assistant, Afdeling for Depression og Angst, AUH Psykiatrien

Misdiagnosis of bipolar disorder as unipolar depression is a significant clinical challenge, with studies indicating that up to 20% of patients initially diagnosed with unipolar depression may have an underlying bipolar disorder. This misdiagnosis can lead to inappropriate treatment strategies, worsening patient outcomes.
This project aims to enhance the early detection of bipolar disorder among patients initially diagnosed with unipolar depression using big data analysis. It involves developing and implementing a combined machine learning (ML) and data visualization framework to better identify patients who may have been misdiagnosed. Conventional supervised ML models are limited in this context, as they learn from existing diagnoses and thus fail to recognize patients who wrongfully remain undiagnosed with bipolar disorder. To overcome this, the project proposes a series of innovative dynamic visual tools to help clinicians better understand the behavior of clinical prediction models and identify patients likely to have an underlying bipolar disorder despite their unipolar depression diagnosis.
The core concept involves compressing clinically relevant EHR data (retrospective data) into a dense mathematical representation that encodes each patient's profile. These data variables will be resampled every 30 days to generate updated patient feature vectors over time. An ML algorithm will be trained on these representations to predict patients at risk of being diagnosed with bipolar disorder. To address the model's limitations in identifying misdiagnosed cases, the patient representations will be projected into a two-dimensional space, allowing for temporal visualization of patient trajectories, i.e., how patient profiles change over time. These visualizations may highlight patients whose data patterns resemble those of confirmed bipolar disorder cases or show a trajectory indicating a shift towards bipolar disorder. Such patients could be flagged for further clinical evaluation, potentially leading to earlier diagnoses and improving treatment outcomes and resource utilization.
This project not only aims to improve the diagnostic process for bipolar disorder but also seeks to establish a general methodological framework for detecting misdiagnosed cases in clinical datasets, contributing to more effective use of machine learning in healthcare.

Abstract #22

Psychiatry Research Day 2024

Validating the Transdiagnostic Self-injury Interview across mental disorders

Jesper Nørgaard Kjær, MD, Psychosis Research Unit, Aarhus University Hospital, Psychiatry, Aarhus, Denmark

Background
Non-suicidal self-injury is the deliberate and self-inflicted damage of body tissue without suicidal intent that causes psychological and physical harm. It is a major health concern especially in psychiatric settings, where around 50 % of all inpatients engage in NSSI. Documentation in medical files are not systematized and misclassifications are frequent, e.g. when self-injury is classified as a suicide attempt.
The Transdiagnostic Self-injury Interview (TSI) is a measure for NSSI in clinical settings. It assesses onset, frequency, methods, and somatic treatment.

Objectives
The aims are to demonstrate the validity of TSI by investigating criterion validity, clinical correlates, and interrater reliability.

Methods
Recruiting sites are in- and outpatient units at the Department of Psychosis and Department of Affective Disorders, Aarhus University Hospital, Psychiatry.
The inclusion criteria are currently undergoing in- or outpatient psychiatric treatment; being 18 years of age or older; diagnosed with a mental disorder. The exclusion criteria are: Mental states that severely interfere with interviewing the patient (e.g. ongoing abuse of psychoactive substances, severe psychosis, severe neurodevelopmental disorders, IQ < 70, dementia).
TSI will be compared the Deliberate Self-Harm Inventory, that is a validated 15-item self-report inventory. Validated measures for suicidality, emotional reactivity, depression, anxiety, psychotic symptoms, functional impairment, and history of trauma are included to examine clinical correlates of TSI.
During training the three raters will rate six videos of TSI interviews. ICC has to be >0.60 before the raters can include participants to the study by themselves.

Results
Data collection is ongoing and will end in August, 2025. Preliminary results will be presented.

Conclusion
If validated, we expect that TSI can be implemented nationally and used for early screening in psychiatric settings. Improved registration of NSSI will advance register data making it possible to conduct detailed studies on risk factors for life-threatening NSSI behavior, suicide and coercion. This will advance our understanding of clinical trajectories, which is a precursor for personalized treatment and development of specialized interventions.

Abstract #23

Psychiatry Research Day 2024

Perspectives of Healthcare Professionals on Mental Health Issues in Children and Adolescents with Congenital Heart Defects: A Qualitative Study

Julie L Hejl, MD, Department of child and adolescent psychiatry, Research unit

Introduction
By age 18, 35.1% of children with congenital heart defects (CHD) are diagnosed with or treated for a mental health disorder such as autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and severe stress reactions. Early detection and treatment of such disorders are crucial, as untreated mental health disorders in childhood can have long-lasting effects, including lower education attainment and weaker labor market attachment. While guidelines for neurodevelopmental screening in children with CHD have existed since 2012, these programs are not widely implemented and often focus only on early developmental assessments, overlooking broader mental health issues. Studies indicate under-recognition of mental health disorders in pediatric cardiology clinics, and while specific mental health screening tools are suggested, they impose additional demands on cardiology providers, whose role in managing mental health remains unexplored.

Objective
This qualitative study aims to explore how those working in the field of pediatric cardiology perceive their role in the management of mental health issues of children and adolescents with CHD.

Methods
Twelve healthcare professionals were recruited through an e-mail sent out to all nurses and medical doctors working in the field of pediatric cardiology in the Danish hospital setting using purposive sampling, aiming for variation in participant sex, age, profession (nurse or medical doctor), years of experience in pediatric cardiology and workplace. Participants were interviewed online using a semi-structured guide with open-ended questions. The focus was on how they perceived their roles and responsibilities when working with children with CHD, particularly regarding their role in managing mental health issues in these children and adolescents. The interviews will be analysed using interpretative phenomenological analysis (IPA).

Results and conclusion
The results will be ready during fall of 2024. We anticipate that this study will provide valuable insights on how to effectively enhance knowledge and clinical awareness of mental health issues in children with CHD among healthcare professionals.

Abstract #24

Psychiatry Research Day 2024

Internet-delivered psychological treatment of health anxiety by proxy: Results from a single-case experimental design

Katrine Ingeman, Psychologist, PhD, Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry, Denmark

Background
Health anxiety by proxy is described as parents' excessive worries about their child's health and fear that a serious illness is being overlooked in their child. Health anxiety by proxy is a novel research area. Therefore, prevalence is unknown and no specialized treatment for this condition exist.
PROXY is a newly developed eight-week psychological internet-delivered treatment for parents with health anxiety by proxy. It is based on Acceptance and Commitment Therapy with written material, videos, audio and written therapist contact. The single-case experimental approach enables a trial with very few participants that still investigates effect. This study aims to test the feasibility and potential effect of PROXY on parents' worries about their children's health.

Methods
A single-case experimental design with replicated randomized AB-phases was conducted. Each participant was randomized to a baseline period between 7-26 days before entering treatment. Throughout the study, participants reported their anxiety level, impact of anxiety and value-based action on a daily basis through a text-message system. Data was submitted to visual analysis and supplemented with statistical tests of effect.

Results
Four participants suffering from health anxiety by proxy received treatment in PROXY. Overall, results were ambigous. Visual analysis showed that PROXY was an effective treatment for two of the participants with effect sizes of -0.71 and -0.61 for daily anxiety level, respectively and visual improvements of daily impact and value-based action. One participant only improved on impact of anxiety and one participant did not improve on any of the daily outcome measures. All participants stated that they were happy with the treatment but two participants experienced that their health anxiety for their own health deteriorated during the eight-week treatment, and two participants thought that the treatment was too short.

Conclusion
PROXY may hold potential as a specialized treatment for health anxiety by proxy. However, more work is needed in relation to when and how PROXY should be presented to parents with health anxiety by proxy, and further tests of effect is nessecary with more participants.

Abstract #25

Psychiatry Research Day 2024

Depression treatment trajectories and associated social determinants: A three-year follow-up study in 66,540 older adults undergoing first-time depression treatment in Denmark

Kazi Ishtiak-Ahmed, Research Statistics, Affective Disorders, AUHP

The author has declined publication of this abstract

Abstract #26

Psychiatry Research Day 2024

Exploring microRNAs and inflammatory cytokines in plasma from female adolescents with major depressive disorder

Kristine Johannessen, Research Assistant, Department of Clinical Medicine, Aarhus University

Major depressive disorder (MDD) in adolescents is a prevalent psychiatric condition worldwide with severe consequences. Diagnosing adolescent MDD is challenging due to its heterogeneity, highlighting the need for reliable biomarkers to aid in diagnosis or monitoring of a treatment response. Circulating microRNAs (miRNAs) have emerged as promising biomarkers for various diseases. Moreover, growing evidence shows that miRNAs regulate many processes involved in the pathogenesis of MDD, suggesting their suitability as biomarkers of MDD. Numerous hypotheses have been proposed to explain the pathophysiology of MDD, including a bidirectional relationship between MDD and inflammatory processes. Still, more research regarding the inflammatory role in adolescent MDD is needed. Therefore, we aimed to identify dysregulated miRNAs in plasma from female adolescents with depression before and after a short period of antidepressant treatment. This was followed by investigations of potential target genes and pathways of the dysregulated miRNAs. Additionally, the plasma protein levels of 27 inflammatory markers were investigated to explore the role inflammation plays in adolescent MDD.

This study applied the NanoString nCounter technology to identify dysregulated miRNAs in plasma from female adolescents with MDD before and after antidepressant treatment (n=27), compared to healthy controls (n=8). A multiplexed immunoassay using the Bio-Plex 200 System was also performed to assess the plasma levels of 27 inflammatory cytokines from female adolescents with MDD before and after antidepressant treatment (n=32) compared to healthy controls (n=14).

Several dysregulated miRNAs were identified in female adolescents with MDD, suggesting their potential as diagnostic biomarkers. Others were regulated with treatment, indicating their potential as biomarkers of an antidepressant response. Some of the dysregulated miRNAs were found to be involved in regulating inflammatory responses. Additionally, the levels of PDGF-BB and IL-7 were increased in female adolescents with MDD compared to healthy controls, while IL-9 and MIP-1β levels decreased with antidepressant treatment.

In conclusion, the findings of this study confirm the potential of specific miRNAs as biomarkers in female adolescents with MDD and indicate a possible relationship between specific miRNAs and inflammation.

Abstract #27

Psychiatry Research Day 2024

Managing Functional Gastrointestinal Disorders in Children: A Qualitative Study of Parental Experiences with Internet-Based Cognitive Behavioural Therapy

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The author has declined publication of this abstract

Abstract #28

Psychiatry Research Day 2024

Treatment Resistant Depression (TRD) and treatment response of repetitive Transcranial Magnetic Stimulation (rTMS)

Lea Holst, Research year student, Department of Affective Disorders, Aarhus University Hospital—Psychiatry, Aarhus, Denmark

Background
Treatment-Resistant Depression (TRD) is commonly defined as an inadequate response to two or more antidepressant trials. The severity of TRD can be evaluated by means of the Maudsley Staging Method (MSM). The MSM consists of five domains including duration of the depression, symptom severity, number of treatment failures, augmentation therapy, and electroconvulsive therapy use. The Danish Medicines Council has suggested that the MSM could guide treatment decisions. However, the use of MSM in clinical practice is lagging and the evaluation of TRD in clinical practice has remained subjective and unstandardized.

Objective
To evaluate the use of MSM in clinical practice, we investigate the association between MSM scores and response to repetitive transcranial magnetic stimulation (rTMS) treatment, as measured by the 17-item Hamilton Depression Rating Scale (HAM-D17).

Methods
Patients with unipolar depression referred to six weeks of treatment with rTMS were consecutively invited to participate in the study. The study was a multi-center study with inclusion sites in Randers, Viborg, and Skejby, Denmark. Demographic information and clinical data were retrieved from the patient's Electronic Health Record (EHR). The patients were assessed on the MSM within the first two weeks of the treatment. Ratings on the HAM-D17 and self-administered questionnaires including the depressive symptoms, side effects, and quality of life were completed on a weekly basis. Additionally, three side-effect interview assessments were conducted during the six weeks rTMS treatment. A power calculation estimated the inclusion of 65 patients.
Response is to be evaluated by means of the Spearman's rank correlation coefficient (rho) between MSM score and HAM-D17. An adequate response is defined as a 50% decrease in the Hamilton score or below the threshold for remission.

Results
Data collection is ongoing. As of September 2024, a total of 59 out of 65 participants have been recruited.

Future perspectives: A systematic assessment of TRD according to the MSM in clinical practice, holds promise for predicting treatment outcomes and guiding treatment decisions. Integrating MSM, for instance, during the recording of patient medical history, could enhance its practical utility in everyday clinical settings.

Abstract #29

Psychiatry Research Day 2024

Brain activation and aberrant effective connectivity in the mentalizing network of preadolescent children at familial high-risk of schizophrenia or bipolar disorder

Lotte Veddum, Psychologist, Postdoc, Psychosis Research Unit, Aarhus University Hospital

Introduction
Schizophrenia and bipolar disorder are characterized by social cognitive impairments and recent research has identified alterations of the social brain. However, it is unknown whether familial high-risk of these disorders is associated with neurobiological alterations already present in childhood.

Methods
As part of The Danish High Risk and Resilience Study – VIA 11, we examined children at familial high-risk of schizophrenia (FHR-SZ, n = 121, 50% females) or bipolar disorder (FHR-BP, n = 75, 47% females) and population-based controls (PBC, n = 128, 48% females). Using functional magnetic resonance imaging and dynamic causal modeling, we investigated brain activation and effective connectivity during the social cognition paradigm from the Human Connectome Project.

Results
We found similar activation of the mentalizing network across groups, including visual area V5, dorsomedial prefrontal cortex (dmPFC), and posterior superior temporal sulcus (pSTS). Nonetheless, both familial high-risk groups showed aberrant brain connectivity in the form of increased feedforward connectivity from left V5 to pSTS compared with PBC. Children at FHR-SZ had reduced intrinsic connectivity in bilateral V5 relative to PBC, whereas children at FHR-BP showed increased reciprocal connectivity between left dmPFC and pSTS, increased intrinsic connectivity in right pSTS, and reduced feedforward connectivity from right pSTS to dmPFC compared with PBC.

Conclusions
Our results provide first-time evidence of aberrant brain connectivity within the mentalizing network of children at FHR-SZ or FHR-BP. Longitudinal research is warranted to clarify whether aberrant brain connectivity during mentalizing constitutes an endophenotype associated with the development of a mental disorder later in life.

Abstract #30

Psychiatry Research Day 2024

A Systematic Review of Pharmacogenomic Markers Associated with Drug-Induced QT Prolongation

Marlene Schouby Bentestuen, PhD Student, Psychosis Research Unit, Aarhus University Hospital Psychiatry

Background
QT prolongation is a significant risk factor for malignant arrhythmias and sudden cardiac death. Commonly used drugs, e.g. antibiotics, antidepressants, and antipsychotics, can cause prolongation of cardiac repolarization resulting in drug-induced QT prolongation (diQTP). Although several pharmacogenetic markers have been identified, a comprehensive and systematic review of all pharmacogenetic associations across drug classes for diQTP is currently lacking.

Objectives
To identify and provide an overview of all published pharmacogenetic markers and the associated drug classes for diQTP.

Methods
This systematic review with a pre-registered protocol followed PRISMA-P recommendations. We systematically identified, reviewed, and assessed the quality of peer-reviewed published reports on pharmacogenomic markers of diQTP using standardized data extraction and risk of bias tools. The reports were categorized by their study design and individual gene associations were classified as either pharmacokinetic or -dynamic. The identified diQTP-associated genes were further subjected to pathway enrichment analyses. Descriptive statistics for the variants by study category and by associated drug classes were computed.

Results
Of 4,493 records identified, this review included 84 studies. Despite identifying 210 unique variations across 42 drug classes, only a small proportion of these findings were consistently replicated across studies (replication rate 9 %) with KCNE1-Asp85Asn as the most consistent finding. 82 % of the diQTP-associated genes originated from studies examining candidate genes, indicating a potential bias toward known genetic markers. The diQTP-associated genes were most associated with "cardiac conduction" (false discovery rate, FDR = 4.71e-14) and "muscle contraction" (FDR = 4.71e-14) pathways. Further, we found a significant overlap between diQTP-associated genes and congenital long QT syndrome genes.

Conclusion
We identified key diQTP-associated genes, drugs, and pathways. However, no robust pharmacogenomic markers were identified due to low replication rates. The overrepresentation of candidate genes introduced bias and limited discovery of new genetic factors underlying diQTP. More research is warranted applying less biased study designs, e.g. genome wide associations studies considering both coding and non-coding, common and rare variants.

Abstract #31

Psychiatry Research Day 2024

Changes in polygenic burden for psychiatric disorders across two decades of birth cohorts

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Background
During the recent decades, the incidence of several psychiatric disorders has increased, but no previous study has investigated whether the polygenic burden based on common variants for psychiatric disorders in diagnosed individuals has changed over time.

Objectives
To explore changes in polygenic scores for schizophrenia, depression, autism, and ADHD in the general population and in case populations according to birth cohorts.

Methods
Based on iPSYCH2015, a Danish population-based case-cohort study, we included 41,132 individuals from a random subcohort and 60,293 individuals diagnosed with schizophrenia spectrum disorders, depression, autism, or ADHD. Individuals were born between May 1, 1981 and December 31, 2008 and followed up for a psychiatric diagnosis between January 1, 1994 and December 31, 2015. We estimated 10-year changes in polygenic scores based on linear regressions of average score across birth year. Moreover, we estimated hazard ratios for being diagnosed or the number of additional cases per 100,000 person-years given a one standard deviation increase in polygenic score according to three broader periods of birth year.

Results
The average polygenic score in the random subcohort showed no or only minor changes across birth year. In case populations, the average polygenic score decreased across birth year, most predominantly for schizophrenia (per 10 years: -0.13 standard deviations (SDs), 95% confidence interval (CI): -0.18; -0.07) but also for depression (-0.06 SDs, 95%CI: -0.10, -0.03) and autism (-0.08 SDs, 95%CI: -0.13, -0.04), and to a limited degree for ADHD (-0.03 SDs, 95%CI: -0.08, 0.02). The hazard ratio for being diagnosed decreased across the three broad birth cohort periods for schizophrenia but remained stable for the other disorders. The number of additional cases per 100,000 person-years decreased for both schizophrenia and depression, whereas autism and ADHD showed increases.

Conclusion
In iPSYCH2015, polygenic burden for psychiatric disorders changed across two decades among diagnosed individuals. For schizophrenia, the polygenic score itself and its ability to predict diagnosis decreased over time, whereas depression, autism, and ADHD showed diverse changes over time.

Abstract #32

Psychiatry Research Day 2024

Somatic health perception among forensic psychiatric patients: A comparison of self-reported and clinically assessed health

Nikoline Busk, stud. Med., Department of Forensic Psychiatry

Background
Self-reported health is recognized to be a reliable predictor of both mortality, morbidity and hospitalization. However, for forensic psychiatric patients, the accuracy of self-assessment is only sparsely examined, therefore there is uncertainty about the reliability of self-reported health among these patients as psychiatric conditions may affect forensic psychiatric patients' perception of the physical health. This lack of clarity brings into question whether self-reported measures can be considered accurate when compared to more objective clinical assessments in this case Clinical Frailty Score.

Aim
The aim of this study is to compare forensic psychiatric patients' self-perceived health measured by single-item question with their general practitioners' assessments based on the Clinical Frailty Score. The study will further analyze discrepancies between these assessments to identify possible risk factors in cases with patient-doctor disagreement.

Methods
This is a cross-sectional study conducted on data extracted in 2021 as part of a cohort study on integrating primary care services into specialized forensic hospital wards in Denmark. The population consists of 75 forensic psychiatric inpatients in two medium secure forensic hospitals in Central Denmark Region.
In this study self-reported health is measured by single-item questions from SF-12 answered though questionnaires and this is compared to Clinical Frailty Score assessed by general physician. Descriptive statistics is used to explore self-reported health in forensic psychiatric patients and illuminate inconsistencies between patient and physician evaluations.

Results
The results will be published in a peer-reviewed journal and presented at national and international conferences.

Conclusion
This study provides valuable insights into the largely unexplored area of forensic psychiatric patients' understanding of their own somatic health, the reliability of self-reported health data, and how these correspond with objective clinical measures. These findings may be used in optimizing care by predicting, preventing, and treating somatic illnesses.

Abstract #33

Psychiatry Research Day 2024

eLi12: An early health economic assessment on optimizing lithium treatment via estimating 12-hour lithium levels

Ole Köhler-Forsberg, MD, Associate Professor, Psychosis Research Unit

Background
Lithium blood tests should be taken 12 hours after the last lithium dose, but the majority are taken with wrong timing. We have developed a new method to estimate the 12-hour lithium level independent of when the blood test is taken, termed eLi12. As economic evaluations can provide useful input for the prioritization of scarce healthcare resources supporting decision makers, we performed an early health economic assessment on implementing eLi12 into the Danish healthcare system.

Methods
We identified studies on the effect and safety of lithium treatment and costs of bipolar disorder. To estimate the expected annual consequences and cost savings of eLi12, we identified 28,000 patients with bipolar disorder in Denmark in 2023, whereof 34% are treated with lithium. We applied a societal perspective including both direct and indirect costs using a mixed-costing approach considering Danish DRG tariffs, primary care fee schedules, pharmacy purchase prices, and expert knowledge. We assumed implementation costs of DKK500.000 per Danish Region and used different estimates on the potential improvement of lithium treatment with eLi12 (i.e., 1%-15% improvement on mood episodes, suicide, intoxications and hospitalizations) to model the annual Net Monetary Benefit (NMB) and expected reduction in productivity costs.

Results
Implementation of eLi12 resulted in a positive NMB between DKK14-64 million/year and a reduction of DKK19-194 million/year in productivity costs due to bipolar disorders based on an improvement between 1-10%. In the scenario with 15% improvement, this increased to DKK98 and DKK291 million/year, respectively. Implementation of eLi12 resulted in a Quality Adjusted Life Years (QALY) gain for patients in all scenarios.

Conclusions
A new method to estimate 12-hour lithium levels, termed eLi12, is reliable and national implementation may result in substantial savings in the healthcare sector and reduced productivity costs.

Abstract #34

Psychiatry Research Day 2024

Beyond diagnostics: A dimensional approach to mental health profiling

Per Qvist, Associate Professor, Department of Biomedicine, Aarhus University

Background
Mental health is a multifaceted trait extending beyond the absence of mental illness (MDx). It arises from a complex interplay between hereditary factors and exposures, encompassing emotional, psychological, and social dimensions. Declining mental health may progress into MDx. However, ambiguity between pathological and non-pathological states challenges traditional diagnostic classifications, necessitating a dimensional approach for precision psychiatry.

Methods
Comprehensive phenotypic data from a sex-balanced segment of young Europeans (mean age ~23 years, n ~300) was included in the study. Reflecting general population prevalence, >13% of participants had been diagnosed with one or more MDx. Data includes psychometric assessments (e.g., personality, awareness, mindfulness, perception, cognition, emotional control, sleep, impulsiveness, and stress), brain imaging, and circulatory OMICs markers. Polygenic scores (PGSs) were constructed for hundreds of brain and mental health-related traits. Archetypal (soft-clustering) analyses were conducted on psychometric data and PGSs to identify extreme observations and display participants on the phenotype spectrum as convex combinations of these findings. Associations between archetype scores and OMICs and imaging variables were assessed using standard statistical tests.

Results
Deep psychometric archetypal profiling effectively stratified participants into risk clusters defined by personal and family history of MDx. Highlighting their biological basis, clusters were characterized by distinct biological features, and individual PGSs (e.g., well-being, MDx, and brain MRI measures) significantly predicted liability to psychometry-based archetypes. Intriguingly, overlaps between psychometric and PGS-based archetypes were significant, identifying subsets of samples with multiple MDx diagnoses and particularly elevated genetic MDx risk burden.

Discussion
This study demonstrates the feasibility of data-driven stratification of the general population into distinct risk groups and highlights the relevance of multimodal archetypal analyses for detection of latent structures underlying psychopathology. By integrating psychometric and biological data, our study advances the understanding of mental health by embracing a dimensional perspective, laying the foundation for personalized mental health care strategies.

Abstract #35

Psychiatry Research Day 2024

Helpful and Hindering Factors in Group-based Cognitive-Behavioral Therapy for Obsessive-Compulsive Disorder: A Qualitative Study

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The author has declined publication of this abstract

Abstract #36

Psychiatry Research Day 2024

Prediction of Manual, Mechanical, and Chemical Restraint among Psychiatric Inpatients via Machine Learning Applied to Electronic Health Record Data

Sara Kolding, PhD student, Department of Clinical Medicine, Aarhus University

Objective
To determine whether integrating related forms of restraint into the training process of machine learning models may improve prediction of mechanical restraint based on electronic health record data.

Methods
The dataset comprised electronic health records from the PSYchiatric Clinical Outcome Prediction cohort, focusing on adults (≥18 years) with at least one psychiatric admission in the Central Denmark Region between 2015 and 2021, and no history of restraint in the preceding year. The cohort contained 15,570 patients covering 36,147 admissions. The risk of either restraint or mechanical restraint in the 48 hours following admission was predicted for each admission day. Predictors included data from demographics, diagnoses, and medications. Hyperparameters of two machine learning algorithms (logistic regression and XGBoost) were determined using five-fold cross validation on an 86% training split. The proficiency of the best-performing models in predicting mechanical restraint was validated using a 14% held-out, geographically distinct sample.

Results
The analyses are being finalised and the results will be presented at Psychiatry Research Day 2024.

Conclusions
The preliminary results suggest that restraint can be predicted from electronic health records, using machine learning models. While grouping outcomes during training did not notably improve the validation performance of individual outcomes, predicting grouped outcomes did increase positive predictive value and, thus, clinical utility. A decision support tool based on routine clinical data could potentially inform prevention of physical coercion.

Abstract #37

Psychiatry Research Day 2024

Sexual assault is a risk factor for developing Functional Somatic Disorders: results from a longitudinal cohort study

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An increasing number of Sexual Assaults (SA) are being reported. This study investigated associations between SA and incident functional somatic disorder (FSD), including three functional somatic syndromes (FSS): chronic widespread pain (CWP), Irritable Bowel (IB) and chronic fatigue (CF), in a 5-year follow-up period.

A total of 4229 participants from the DanFunD 5-year follow-up investigations were included. SA was measured at baseline, while incident FSD cases were established based on measures at baseline and follow-up, with symptom questionnaires as well as diagnostic interviews for sensitivity analysis. Risk ratios (RRs) for each FSD were calculated in nine models with SA as the primary exposure by generalized linear models with binomial family and log link and were adjusted for other potential risk factors.

Results showed that SA was significantly associated with FSD (RR=1.69; 95% CI=1.17-2.44) single-organ FSD (RR=1.65; 95% CI=1.14-2.38), multi-organ FSD (RR=6.47; 95% CI=1.93-21.75), FSS (RR=1.54; 95%CI=1.14-2.07), CWP (RR=1.89; 95% CI=1.11-3.23), while associations with IB (RR=1.60; 95% CI=0.81-3.16), and CF (RR=1.47; 95% CI=0.89-2.42) fell below statistical significance. Overall, SA victims experienced a significantly higher frequency of incident somatic symptoms than individuals not exposed to SA, with symptoms emerging from the musculoskeletal, gastrointestinal, cardiopulmonary, and fatigue-related organ systems among SA victims. This study found no evidence that emotional distress (e.g., anxiety or depression) modified the relationship between SA and FSD. The results were validated with sensitivity analysis using diagnostic-interview cases.

In conclusion, this study demonstrates that SA is a powerful risk factor for the development of FSD in a 5-year period, with widespread effects across multiple bodily systems. Despite limitations posed by small samples of cases in some delimitations, the pooled analysis underscores the high risk for FSD, emphasizing the critical need for further research and targeted interventions to address the long-term biopsychosocial consequences of SA.

Abstract #38

Psychiatry Research Day 2024

Experiences of receiving internet-based treatment ("One step at a time") for multi-system functional somatic disorder: Preliminary findings from qualitative interviews

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Nikoline Busk,

Background
Multi-system Functional somatic disorders (FSDs) are prevalent and may impair patients' quality of life. Effective treatments are available, but access to treatment is limited. Internet-based therapy is becoming increasingly popular and is a cost-effective and accessible alternative. We sought to test the effectiveness of an internet-based, therapist-assisted cognitive behavioral treatment (""One step at a time"") in a randomized controlled trial, using both quantitative and qualitative approaches to evaluate the outcome. Here we present preliminary results from a series of qualitative interviews with users after end of treatment.

Methods
Semi-structured qualitative interviews with 9 patients were conducted after a follow-up consultation with a medical doctor approximately 4 months after treatment. Interviews of 30-60 min based on an a priori developed interview guide were recorded and transcribed. Results were analyzed by two researchers using thematic analysis.

Results
All interviews were conducted by the same interviewer (TTL). 8 out of 9 participants were female, mean age of 38 (SD=14) years. The thematic analysis resulted in 6 main themes: 1) Varied experiences of outcome, 2) The therapeutic process, 3) Cause of outcome, 4) Discipline and effort, 5) The essential therapist, 6) Internet-therapy.

Discussion
Findings from the current study indicated that internet-based treatment for multi-system FSD was a feasible, effective acceptable. They furthermore provided insights into the significant differences in how patients with severe FSD use internet-based treatment and what they take away from it. It also underlined several of the barriers which constrained the therapeutic process, of which some were inherent to the treatment and others stemmed from the personal characteristics and situation of the patients. Findings from the current interviews provide rich insights into the complexity of internet-based psychological treatment and highlights the importance of using a non-reductive and encompassing approach to the evaluation of efficacy.

Conclusion
Preliminary findings from 9 interviews showed that most patients experienced the treatment as meaningful and helpful. Nevertheless, there were several barriers for engaging fully with the treatment, which limited patients in achieving their treatment goals.

Abstract #39

Psychiatry Research Day 2024

Inflammation Resolution to Enhance Depression Treatment and Diagnostics

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Major Depression Disorder is one of the most disabling diseases worldwide, affecting 322 million people and about 30-50% of patients fail to show a substantial clinical response to conventional antidepressant therapy. Individuals who are non-responders or partial responders to antidepressants are defined as suffering from treatment-resistant depression (TRD). Among the various etiological hypotheses of depression, there are the theory of neuroinflammation and the dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis. HPA axis overactivity is often normalized after effective antidepressant treatment and some studies have suggested that failure of antidepressants to normalize the HPA axis may be a predictor of treatment resistance. Plus, data suggests that adrenocortical activation mediates the relationship between IL-1 and stress-induced depression. Specialized lipid pro-resolving mediators (SPM), derived from omega-3 and omega-6 polyunsaturated fatty acids (PUFAs), such as arachidonic acid (AA), docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) seem to have a very important active profile for ending inflammation and, consequently, improving emotional behaviors related to mood disorders. The SPMs were identified and classified into four categories: lipoxins, resolvins, maresins and protectins. These lipids are agonists of G protein-coupled receptors. However, the underlying mechanisms of these remarkable effects concerning depression remain unclear. It is our hypothesis that a dysregulation of SPMs may represent a viable approach to overcoming pharmacoresistance to monoaminergic antidepressants, and this system could be an effective way to improve this condition. To test this hypothesis, we will investigate the SPMs relation on neuron-microglia and neuron-astrocytes co-culture cells under different insults, using human-derived iPSC cells. First, we will analyze different types of insults (cortisol, IL1-beta and ATP) with or without antidepressant to quantify the SPMs in the medium and the expression of proteins related to SPMs action (their receptors, FKBP5, BDNF, TrkB, PSD95 and Synapto). Then, we will treat the cells with SPMs and analyze the possible recovery from the insults models.